

PSYCHO-PHYSIOLOGICAL MARKERS OF OVERREACHING AND OVERTRAINING IN ENDURANCE SPORTS: A REVIEW OF THE EVIDENCE

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Abstract

We review the latest evidence from studies that have examined psycho-physiological markers of overreaching (OR) and overtraining (OT) in endurance-based sports. MEDLINE (PubMed), SportDiscus®, AdisOnline and Ingentaconnect® were searched without time or language restrictions using free text words. Hand searching was conducted, with searches supplemented by a review of the bibliography of each retrieved article. There were 152 studies identified and associated with OR/OT in the context of endurance-based exercise. Collectively, a multitude of psycho-physiological markers have been implicated in their relationship with OR/OT in swimming, cycling and running activities. There is no single marker that can be used to identify OR/OT, and we discuss problems associated with the identification of OT. We also discuss prevalence, symptoms, diagnosis of OR/OT, and provide recommendations to coaches and athletes.

Key Words: *overreaching, overtraining, endurance*

Introduction

To invoke physiological adaptation during exercise training, training load should be gradually progressed over time, allowing for improvements in athletic performance [1,2]. Subsequently physiological adaptations and progression of training state increase only if the magnitude of change is above the habitual level [3], and training principles of specificity and overload are adhered to [4,5].

The apparent limitation of exercise performance in endurance sports is the ability of the athlete to endure strenuous training without breakdown or maladaptation of the physiological system [6]. As training loads increase, physical exhaustion can occur, particularly in the presence of inadequate regeneration periods [7]. When such disturbances occur, accepted terminology used to describe the attenuation in subsequent athletic performance includes overreaching and overtraining. A number of other interchangeable terms are also used including overtraining syndrome, staleness, chronic fatigue in athletes, sports fatigue syndrome, and the unexplained underperformance syndrome (UUS) [8,9]. For reasons of simplicity, we will only refer to the terms overreaching (OR) and overtraining (OT).

Prevalence

At higher levels of competition, the training load required for endurance-based sports can be as high as 20 hours per week [10-12]. Chronic exposure to high volumes of exercise training/competition can result in high levels of energy expenditure on a regular basis re-

sulting in athletes displaying specific symptoms across a broad spectrum of sports [13-15]. Koutedakis and Sharp [16] showed that 15% of 257 elite athletes from a variety of sports were found to exhibit symptoms of OT, and it has been reported that between 7-20% of elite athletes may show signs of OT at any given time [17]. The prevalence of OT is thought to be highest in endurance-based sports requiring high volume, intense training, such as swimming, cycling, triathlon and to a lesser extent marathon running [8,18]. For example, it has been suggested that over 65% of long-distance runners will exhibit OT symptoms at some time in their competitive career [19,20]. The majority of OT cases occur with endurance athletes most likely due to the nature of the training cycles for each sport and the amount of recovery allowed between each training session [8]. Whilst it is appreciated that OT may well occur in athletes across all levels of competition, it is more likely for a high level competitor to be exposed to such training cycles.

Definitions

Both OR and OT involve quantitative issues of training load balanced against qualitative issues of physiological and psychological stress, with the duration of recovery time and the persistence of symptoms being the main difference between the two classifications. This has led to the following definitions:

Overreaching can be defined as: *“the accumulation of training and/or non-training stress resulting in short-term decrement in performance capacity with or*

without related physiological and psychological signs and symptoms in which restoration of performance capacity may take several days or weeks" [21].

Overtraining can be defined as: *"the accumulation of training and/or non-training stress resulting in long-term decrement in performance capacity with or without related physiological and psychological signs and symptoms in which restoration of performance capacity may take several weeks or months"* [21].

When athletes and coaches do not sufficiently respect the balance between training and recovery, OR and possibly OT are more likely to occur [22]. Whilst OR has qualitatively similar symptoms to OT it is more transitory and can be resolved with periods of rest and/or recovery. Subsequently, OT has been described as a 'long term' form of overloading, whereas OR is simply short term OT [23]. Additionally, it has been suggested that OT is, in certain terms, the result of disparity between load and load tolerance [15]. Unsurprisingly the majority of research has focused on OR due to the substantial ethical considerations associated with deliberate inducement of symptoms of OT [24]. Therefore, the majority of evidence is based on our understanding of the acute inducement of OR and not the chronic effects resulting in OT.

Symptoms

The symptoms associated with OR and OT are diverse and dependent upon the athlete's psychological and physiological character [25]. Consistently reported symptoms include reduced sporting performance [8,26-29] increased feelings of physical fatigue [26-28,30] and decreased maximum heart rate [7,30-32]. Other reported symptoms include mental fatigue without associated physical fatigue, elevated basal metabolic rate, loss of body weight, and both acute and chronic alterations in a host of systems including neural and endocrine function [17]. However, whilst the universal criterion associated with OT in particular is a decrease in sporting performance, not all aspects of performance are affected simultaneously, nor are they impacted to the same degree which increases the difficulty of identifying a true positive case [29].

OT can be partitioned into sympathetic (beta-dowoid) or parasympathetic (addisonoid) based on the prominence of either aspect of the autonomic nervous system (ANS). However a combination of both can exist with an increased prevalence of the sympathetic-type during early stages with a shift towards parasympathetic over time [33]. Whilst specific symptoms associated with sympathetic-type OT include hyperexcitability; restlessness, and performance decrements [34,35] parasympathetic symptoms include high fatigue ratings, apathy, altered mood, and suppressed immune and reproductive function [35]. During early stage OT, the sympathetic system

is continuously altered, however, during advanced OT, sympathetic activity is inhibited [36]. Sympathetic-type symptoms are largely associated with explosive, anaerobic-type sports, whilst parasympathetic type is mostly associated with endurance sports [37].

Diagnosis

Identification of OR or OT can be complex since symptoms may be similar to those reported during routine training making it difficult to disassociate them [38]. It is therefore unlikely that the diverse symptoms of chronic OT in particular, can be explained by a single mechanism [18]. Furthermore, whilst OT represents the most frequent and often feared dysfunction in athletes, there are no single objective parameters suitable for its identification [39]. Thus, coaches, sports scientists and clinicians should be aware of the plethora of potential physiological and psychological markers which could be used in its identification. It is not surprising given the non-specific nature of the condition, that a myriad of physical, biochemical, psychological, musculoskeletal, haematological, cardiorespiratory and nutritional factors have been associated with the identification of both OR and OT. However, symptoms may be grouped into four main categories: psychological; physiological, biochemical and immunological [40,41]. The purpose of this review is to critically summarise the multitude of studies surrounding OR and OT in the context of these categories, and also in relation to endurance-based sports.

Search strategy

Electronic Search Strategy

Electronic database searches including MEDLINE (PubMed), SportDiscus[®], AdisOnline and Ingentaconnect[®] were searched without time or language restrictions using the subject search terms "overreaching" and "overtraining". Different forms of the same word were also included e.g. "over trained", "over-trained", "over-trained", "over training", "over-training", "over reaching", "over-reaching", "over reached", "over-reached" and "overreached". Other relevant key words and associated derivatives were also searched including but not restricted to "overtraining syndrome", "staleness", "chronic fatigue in athletes", "sports fatigue syndrome", and the "unexplained underperformance syndrome". General examinations also took place, with searches supplemented by a review of the bibliography of each retrieved article relevant to the topic under appraisal. Studies published between 1957 and 2012 were included in our search criteria. Searches took place between November 2010 and June 2013. There were 152 studies identified and associated with overreaching or overtraining that utilised endurance-based exercise as a test basis. Research papers were included if the topic

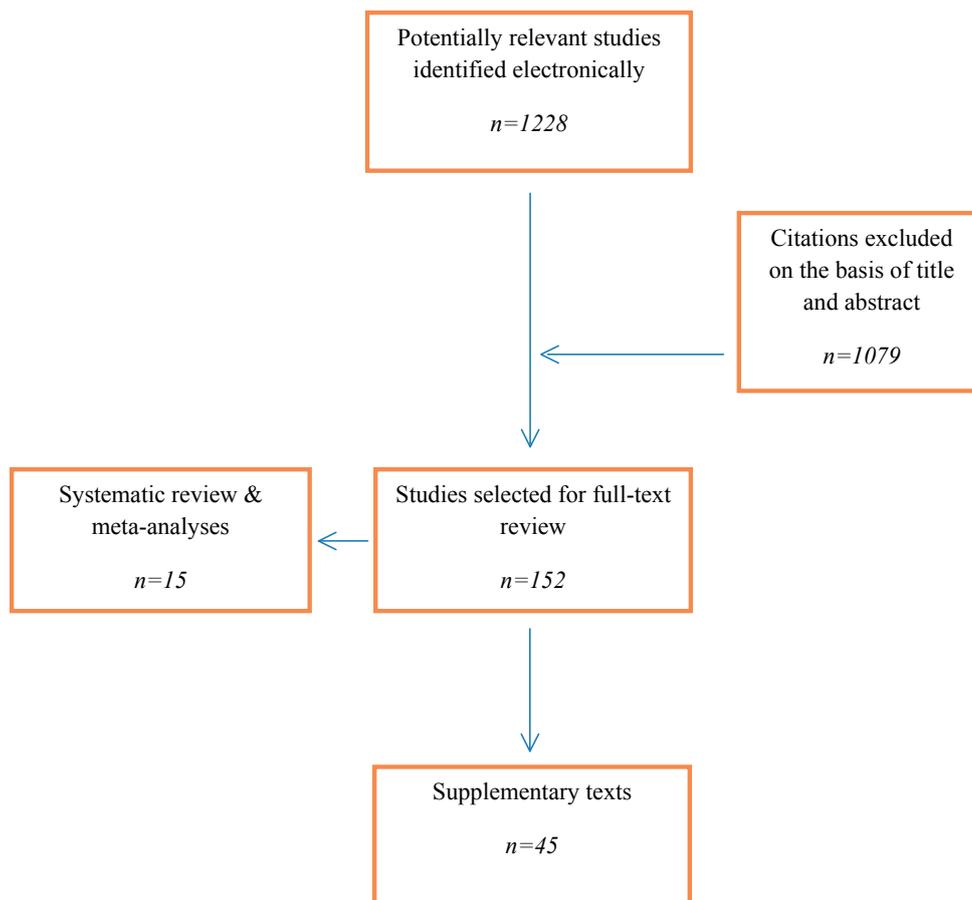


Fig. 1. Flow chart outlining search criteria and study selection

concerned overreaching and/or overtraining in the context of endurance-based sport. Title, abstract and full-text assessments were performed. The flowchart in Figure 1 outlines the search criteria and study selection which underpins the systematic review. The review summarises all relevant data as identified during full text review. The primary research goal attempts to examine the physiological and psychological markers commonly associated with OR and OT to determine, if any, the most likely underlying mechanisms.

Physiological Factors

Resting Heart Rate

Some early studies have reported increases in resting heart rate (RHR) [43-46] and sleeping heart rate [31,42,47-49] in both OR and OT. An increase in RHR of between 11-23% in 12 healthy male marathon runners after doubling their training load for 14 days was reported [49], with the authors proposing that sympathetic modulation contributed to a reversal of bradycardia, with the development of stress-related cardiac perturbation responsible for deterioration in sporting performance. It has also been suggested that sleeping HR may be a more accurate assessment of OT indices compared with morning RHR [31,50]. Jeukendrup et al [31] reported that whilst morning RHR did not change during a 2 week period of OT using 7

male competitive cyclists, the mean HR during sleep showed a significant ($P < 0.05$) increase. However it has also been suggested that as HR during sleep has intrinsic, inter-individual differences of up to 8 beats. min^{-1} , consideration needs to be given when changes in HR due to training status are interpreted [51]. An abundance of studies have found no difference between RHR and indices of OT [7,26,31,32,52-7]. A previous meta-analysis [58] reported only a non-significant, trivial increase in RHR ($P = 0.07$) suggesting that it could not be used as a valid marker and a time effect suggested that an increase in RHR may be used as a valid sign of short-term fatigue only. There is no current consensus on whether alterations in RHR can be used to predict OR/OT in endurance athletes [51].

Maximum Heart Rate

Maximal heart rate (HR_{max}) can decrease by 5-10 $\text{b}\cdot\text{min}^{-1}$ in endurance athletes dependant upon whether they exhibit symptoms of OR or OT [17]. A number of studies using endurance athletes such as runners and cyclists have reported such decreases [7,30-32,59-61]. This may be due to disturbances in the autonomic nervous system (ANS) which is responsible for altered HR response during OT [35] as well as neuroendocrine dysfunction related primarily to catecholamine depletion and/or reduced

Table 1. Summary of psycho-physiological markers implicated in the occurrence of overreaching/overtraining in endurance-based sports

Central Parameter	Hypothesis / Marker Variation	Studies	Reference	Reviews & Meta-analyses	Reference
<i>Physiological</i>	↑RHR; ↓MHR; ΔHRV; ΔECG; ↓HRr	Hedelin et al (2000); Dressendorfer et al (2000); Pichot et al (2000); Baumert et al (2006); Borrensen & Lambert (2007)	68; 49; 48; 75; 85	Bosquet et al (2001); Aubert et al (2003); Halson & Jeukendrup (2004); Urhausen & Kindermann (2002)	58; 1; 21; 175
<i>Immunological</i>	↑URTI; ↓Ig; ↓Leukocytes; ↓Lymphocytes; ↓Neutrophils; ↓Glutamine	Nieman et al (1990); Gabriel et al (1998); Gleeson et al (1995); MacKinnon & Hooper (1994); MacKinnon & Hooper (1996)	92; 94; 105; 96; 27	Walsh et al (2011); Halson & Jeukendrup (2004); Gleeson (2002)	98; 21; 104
<i>Inflammatory</i>	↑Cytokines; ↑Hs-CRP; ↑cf-DNA	Smith (2000); Farhangimalek (2009); Margeli et al (2005)	29; 130; 154	Kasapis & Thompson (2005)	81
<i>Central Fatigue</i>	↑fTryp; ↓BCAA (↑fTryp:BCAA); ↓Glycogen	Lehmann et al (1996); Tanaka et al (1997); Usitalo et al (2006); Costill et al (1988)	162; 56; 163; 59	Petibois et al (2002); Cunha et al (2006)	169; 38
<i>Neuroendocrine</i>	↓ACTH; ↓GH; ↓Cortisol; ↓LH; ↓FSH; ↓NEp; ↓IGF-BP3; ↓TST:Cortisol	MacKinnon et al (1997); Rowbottom et al (1997); Hug et al (2003); Urhausen et al (1998); Lehmann et al (1998)	28; 173; 40; 174; 35	Urhausen & Kindermann (2002); Gleeson (2002); Cunha et al (2006); Urhausen et al (1995)	175; 104; 38; 33
<i>Performance</i>	↓[La ⁻] _b ; ↓V _{O₂peak}	Bosquet et al (2001); Lehmann et al (1996); Meeusen et al (2010); Jeukendrup et al (1992); Snyder et al (60); Urhausen et al (1998); Fry et al (1992)	179; 162; 63; 31; 60; 32; 180	Halson & Jeukendrup (2004);	21
<i>Psychological</i>	↓Mood state; ↑Stress	Urhausen et al (1998); Fry et al (1994); O'Connor et al (1991); Morgan et al (1988); Jürimäe et al (2002)	32; 115; 185; 192; 200	Urhausen & Kindermann (2002); Halson & Jeukendrup (2004);	175; 21

Marker variations are denoted as increased (↑) or decreased (↓) in OR/OT; RHR = resting heart rate; MHR = maximum heart rate; HRV = heart rate variability; ECG = electrocardiogram; HRr = heart rate recovery; URTI = upper respiratory tract infection; Ig = immunoglobins; Hs-CRP = high-sensitivity C-reactive protein; cf-DNA = circulating cell-free plasma DNA; fTryp = free tryptophan; BCAA = branch chain amino acid; ACTH = adrenocorticotropin; GH = growth hormone; LH = luteinising hormone; FSH = follicle stimulating hormone; NEp = norepinephrine; IGF-BP3 = insulin growth factor-binding protein 3; TST = testosterone; [La⁻]_b = blood lactate

sympathetic drive [17]. Explanations for reduced HR_{max} after increased and prolonged training volume include increased parasympathetic activity, increased stroke volume and plasma expansion, and decreased β-adrenergic receptor number and/or density [62].

To date most studies involving HR responses have found marked decreases in HR_{max} in the presence of symptoms of both OR and OT [50]. However there have been no differences found between athletes diagnosed with OR and those athletes diagnosed with OT [63]. Furthermore, Billat et al [64] found no significant changes in HR_{max} in 8 participants that performed 4 weeks of overload training consisting of three interval training sessions at $\dot{V}O_2$ max following 4 weeks of normal training. No useful diagnostic pattern in HR_{max} has also been reported after monitoring

changes in performance, fatigue and recovery in 16 male triathletes over 4 weeks of intensified training followed by a 2 week taper [65]. However the results obtained for this study were possibly due to the relatively short training period used, which may have been insufficient to induce either a significant increase or decrease in HR_{max} in previously well-trained athletes.

Heart Rate Variability

Relative parasympathetic or sympathetic dominance can be assessed by the examination of beat-to-beat variability of the R-R interval known simply as heart rate variability (HRV) [66]. HRV can be measured routinely and non-invasively via standard heart rate monitoring and is measured in both time and frequency domain analyses.

The time domain provides information on beat-to-beat variation and can be directly derived from R-R intervals, or from the difference between R-R intervals [67]. Alternatively, frequency domain analyses measure multiple HRV waveform frequencies. High frequency (HF) HRV in particular has been associated with parasympathetic modulation [67,68] and is mediated through respiratory sinus arrhythmia (RSA) and vagal activity [69]. Alternatively, low frequency (LF) modulation has been associated with sympathetic dominance [48]. Consequently, the LF/HF ratio as an index of sympathovagal balance is considered to be a non-invasive measure of autonomic cardiovascular control [58].

Monitoring HRV in athletes may be an appropriate tool for the early identification of OT [67] however only a few studies have investigated its efficacy [48,61,68,70-76]. It has been reported that in an OT athlete, HF and total power were higher during than before OT, and also after a period of recovery had been administered [68]. As a predominance of HF reflects parasympathetic modulation, OT athletes were reported to be in a heightened parasympathetic state. Consequently it was concluded that the shift towards increased HRV suggested a cardiac imbalance with extensive parasympathetic modulation as a consequence of OT. Conversely, global and progressive increases in LF dominance throughout 3 weeks of heavy training, and decreases in HRV in the 3 weeks following intensive physical activity have also been reported [48]. This suggested that not only was HRV an effective indicator of accumulated training load, but that heavy training load shifted cardiac autonomic balance toward sympathetic dominance over parasympathetic modulation. Similarly, intensified physical training has resulted in a shift towards parasympathetic inhibition and sympathetic activation during a training camp consisting of 2 weeks of running and cycling in 10 healthy athletes (including triathletes) [75] whilst Pichot and co-workers [74] also reported shifts towards sympathetic dominance in 6 test subjects who increased training load on a cycle ergometer. Interestingly, an increased parasympathetic rebound was recorded in the week following overload training and complete return to pre-training HRV values was reported 7 weeks post-intervention.

In contrast to other studies, no change in HRV during a short-term stimulus to induce OT with no significant change in either HF or LF power has been reported in 9 elite-level canoeists [61]. This observation was also reported by Uusitalo et al [76] who found no change in cardiac autonomic modulation assessed via vagal blockade in a supine position and following head-tilt in 9 female athletes following 6-9 weeks of increased training volume. Results indicated that progressively increased training load did not induce

significant changes in intrinsic heart rate or cardiac autonomic modulation.

HRV analysis may be an appropriate screening tool for monitoring the effects of physical training load on athletic performance [67]. HRV indices magnify variations in ANS activity which makes them more useable and reliable in comparison to other autonomic methods such as RHR [48]. Equally, it has been argued that HRV and RHR should be used as markers of short-term fatigue only, whereas submaximal and maximal HR should be used as markers of OT [58]. It has been suggested that the lack of uniformity in findings relating to HRV is most likely related to different techniques and methods of presenting HRV analyses, as well as differing methods of quantifying OT and inter-individual variation in both HRV and OT [21]. The relationship between cardiac autonomic imbalance and OT varies on an individual basis [71]. Inconsistencies between studies may be explained by a lack of performance assessment data and the fact that positive or negative responses to training are not always reported, therefore determination of OT is not always clear. The observation of cardiac autonomic imbalance in OT athletes indicates that the monitoring of HRV could provide a promising measurement for future detection. However, the lack of well controlled studies would suggest that further investigation is required before more definitive conclusions can be drawn.

Electrocardiography

Documented electrocardiographic (ECG) changes include T-wave abnormalities, ST segment changes, PR and QT time interval changes, and arrhythmias in endurance athletes with symptoms of OT [25,77-80]. Kennedy & Mayhew [77] observed the effect of a 10-week season on the T-wave (ventricular repolarisation) of seven university level, cross-country runners. T-wave abnormalities were reported in one subject at rest, as well as at five and ten minutes post-exercise. It was suggested that the abnormalities were the result of chronic fatigue or OT. As the study was performed on a small sample size, and the apparent T-wave changes occurred in one subject, any conclusions based on this data must be carefully interpreted. It is possible that any abnormalities were transient and the result of an intensified training cycle [79].

Prolonged, intense endurance exercise acutely increases serum concentration of the inflammatory markers interleukin-6 (IL-6) and high-sensitivity C-reactive protein (Hs-CRP) [81]. Such inflammatory markers have been associated with the presence and future risk of developing atrial fibrillation (AF) [82,83] however, this remains speculative until further research is conducted. Confounding factors including increased vagal tone and cardiac hypertrophy may

also induce similar changes in normal ECG waveforms to symptoms of OT [84], and this requires further consideration. Currently, it is considered that any association between ECG and OT should be viewed cautiously. Future research would benefit from the assessment of ECG recordings across a complete training macrocycle.

Post-Exercise Heart Rate Recovery

Heart rate recovery (HRr) has commonly been used as a simple, non-invasive test for the determination of cardiovascular parasympathetic function and has been shown to respond to both acute and chronic changes in training load [23,25,26,85-87]. For example, 28 participants were grouped dependent upon whether they increased, decreased or kept a constant training load over a 2-week period [85]. Training load was quantified using the training impulse (TRIMP) method. The group that increased training load reported a slower mean HRr% (5.6 ± 8.7) in comparison to the group that decreased load (2.6 ± 3.9 , $P = 0.03$). Sub-maximal HR was not affected by acute changes in training load. An association between changes in HRr and cycling performance in a group of 14 well-trained cyclists participating in a 4-week high-intensity training programme has been reported [86]. Subjects were grouped dependent upon presentation of increased or decreased HRr, and the group that displayed a superior HRr showed an improved average power during a 40-km time trial, resulting in a tendency for a faster 40-km time ($P = 0.059$). Findings suggested that HRr may be a potential marker to monitor changes in endurance performance and contribute to a more accurate prescription of training load in well-trained and elite cyclists [86].

It has been suggested that HRr is an indirect marker of autonomic function and changes therein may offer a practical way of quantifying the physiological effects of training [85]. HR and HRr after submaximal exercise are markers that can be easily monitored on a regular basis using non-invasive techniques [88]. Individual HRr may be an effective monitoring/screening tool for identifying risk of both OR and OT in endurance athletes. However, it is currently not known whether impaired sporting performance, which is associated with training-induced fatigue, is accompanied by blunted HRr in endurance athletes [86]. The calculation of the TRIMP may become an interesting avenue of investigation for determining the severity of OT.

Immunological Factors

Upper Respiratory Tract Infection

Evidence appears to link OT with immunosuppression and increased vulnerability to infection, with recurrent infections evident during periods of maximum training or competition [28,89,90]. Light to

moderate exercise may increase immune responsiveness, however, high-level competitive sport, especially if it involves extensive endurance training, may lead to a degree of immunosuppression [89]. Epidemiological data suggests increased risk of upper respiratory tract infection (URTI) particularly in endurance sports such as marathon and ultra-marathon races [91] however, there have been few studies that have considered the relationship between URTIs and either OR/OT [27,92-4]. 13% of those running in the Los Angeles marathon exhibited URTI symptoms in comparison to 2% in the control group [92]. Likewise, 5 of 15 (33%) well-trained athletes (12 cyclists, 3 triathletes) also exhibited URTI symptoms [94] whilst symptoms were also evident in 56% of a sample of elite-level swimmers showing symptoms of OT in comparison to 12.5% in a non-OT group after increased training volume over a 4-week period [27,96]. The relationship between OT and immunosuppression has also been reported in a number of anecdotal reports indicating increased prevalence of URTIs in endurance-athlete populations [22,29,96,97].

It should be noted however that many people involved in strenuous exercise do not develop URTIs [98,99]. Also, whilst some studies have observed URTI incidence following single-bout exercise or periods of intensified training, there is only one study that investigated URTI incidence alongside OT symptoms [27], suggesting that incidence may well be linked just as much to intensified training as it is to reduced performance through OT. Furthermore, much of the data collected on URTI has been anecdotal and self-reported, not from clinically diagnosed sources. Caution must therefore be taken when assessing the reliability of such findings. Significant uncertainties around the specificity of URTIs for identifying OT currently exist, particularly in high performance sport [98]. Nevertheless, a dose-response relationship between increased risk of URTI and increased training volume has been reported in endurance athletes [18]. Increases in training volume and intensity may increase the duration of the 'open window' of immunosuppression [22,91,98]. The substantiation of a direct link between the development of a URTI and symptoms of OR or OT is currently inconclusive and further research is required to evaluate this relationship.

Immunoglobins

Immunoglobins (Ig) serve to bind to the surface antigens of pathogens, thereby stimulating the activation of other immune cells [99,100], and are a major first line resistor against pathogenic microorganisms [98,101]. Intensive training can result in a chronic suppression of mucosal Ig levels [99,102], with the degree of suppression being linked to training volume and load. Reduced salivary IgA levels are

associated with increased risk of URTI during heavy training [18,96,99] and measurements of salivary IgA levels over the course of a full season provide a useful predictor of URTI [103]. Immunoglobins are considered to be an important mechanism of host defence, particularly against pathogens that cause URTI [104]. Suppression of salivary IgA, serum IgA, IgG and IgM in elite swimmers undertaking long-term, intensive training over a 7 month period in comparison to controls has previously been reported [105], as well as an 18-32% decrease ($P < 0.05$) in IgA in OT (stale) elite swimmers in comparison to well-trained swimmers after 6 months of training [96]. Similarly, decreased resting IgA levels have been reported in national level swimmers after chronic high intensity training [106]. However, no significant reduction in salivary IgA were reported after intensified training in 8 cyclists, indicating that some markers of immune function do not appear to be related to the decline in performance associated with either OR or OT [107].

Leukocytes

Carried within the blood and lymph are white blood cells or leukocytes that play a central role in the immune response [108]. Low resting leukocyte levels have been reported in distance runners [53,109]. and may indicate long-term immuno-suppression in endurance athletes [110]. The role of leukocytosis in both OR and OT has been examined and data appears to be equivocal [26,28,53,111,112]. Progressive decreases in leukocytes have been reported following 4-weeks of intensive training in distance runners who exhibited clear symptoms of OR [53]. Similarly, reduced leukocyte levels have been reported during unaccustomed increases in training volume in seven distance runners [112]. However the majority of studies have found no relationship between resting leukocyte levels and OT [26,28,111].

Lymphocytes

The function of a lymphocyte (a type of leukocyte) includes mounting an augmented, cell-mediated response when a host is infiltrated by a pathogen. This can be achieved by the proliferation of T-cell and B-cell lymphocytes that identify antigens and stimulate a response [113]. It has been reported that circulating lymphocytes are also associated with immunosuppression following acute, intensive exercise, although the underlying mechanism behind this remains unclear [18,90].

Resting peripheral lymphocyte count appears to be unaltered by intensive training [28,94,105,111,114,115]. Whilst activation of lymphocyte levels increased (elevated CD25⁺ and HLA-DR⁺ and CD3⁺:CD25⁺ ratio), there was no significant change in resting peripheral lymphocyte numbers following a 10-day intense exer-

cise training protocol [115]. Furthermore, no significant changes in T-cells, B-cell subsets, or HLA-DR⁺ after 7-months of training were evident in 26 elite endurance swimmers [105]. Transient decreases in lymphocytes have been reported during the initial stages of a 4-week training programme of increasing intensity in 24 elite swimmers [28], however, lymphocytes had normalised by the end of training indicating that temporary perturbation was unlikely to be of biological significance. Finally it has been reported that OT did not lead to clinically relevant alterations in blood-borne immuno-phenotypes including circulating lymphocytes, however, it was reported that the expression of CD45RO (T-cells) was higher in 15 OT athletes compared to healthy, well-trained controls [94].

It is unclear if there is any biological significance of apparent activation of blood-borne lymphocytes during intensive exercise training [18]. With heavy training, there is a fall in the CD4⁺:CD8⁺ ratio (T-cells), however, there are no established differences between athletes with OT and healthy, well-trained athletes [18]. Further research is required to clarify this relationship.

Neutrophils

Neutrophils are responsible for internalising extracellular bacteria in order to fight infection (phagocytosis) [108], and appear to be sensitive to periods of prolonged, intensive training [18,116]. No change in neutrophil levels following prolonged, intensive training over a six-month season have been reported using a sample of 14 elite swimmers in which 3 were classified as being OT. However, an 80% increase in neutrophil activation was reported at the end of training [26]. The increase was accounted for by the inclusion of a taper before major competition, and neutrophil concentrations were consistent with subjects not exhibiting symptoms of OT prior to the taper. The available evidence, although limited, appears to indicate that neutrophil activation may be a useful monitoring tool during heavy and prolonged exercise training.

Glutamine

Plasma glutamine is an important fuel for cells of the immune system and is decreased in athletes after prolonged, strenuous endurance exercise [117]. Lymphocytes, macrophages, and natural killer cells all utilise glutamine for proliferation, therefore reduced plasma glutamine concentration due to overworked muscle may be responsible for impaired immune function [21,89,117]. Such immuno-depression and reduced bioavailability of glutamine may be considered as a marker of OT [118].

A number of studies have described associations between reduced plasma glutamine and OT in endur-

ance athletes [27,119-122]. Low glutamine levels are associated with increased risk of infection and may partially explain the increase in URTI incidence in endurance athletes [21]. It has also been reported that athletes suffering from OT may appear to maintain low plasma glutamine levels for months or even years after diagnosis [120]. A 9% difference in glutamine levels between OT athletes ($503 \mu\text{mol}\cdot\text{l}^{-1}$) and healthy controls ($550 \mu\text{mol}\cdot\text{l}^{-1}$) has been identified [119], as well as lower glutamine levels (23% reduction) in 8 of 24 elite swimmers diagnosed with OT after 2 weeks of intensified training [27]. However, of the 42% of participants with symptoms of URTI, only one was diagnosed with OT suggesting that the appearance of URTI is not fully related to changes in plasma glutamine in OT swimmers. Amongst elite athletes diagnosed as chronically fatigued, consistently low resting plasma glutamine of $330\text{--}420 \mu\text{mol}\cdot\text{l}^{-1}$ have also been reported [121].

Whilst some studies have found lowered glutamine levels in athletes with OT compared to healthy controls, other studies have reported no significant differences [123]. Since injury, infection, nutritional status, and acute exercise can all influence plasma glutamine levels, these factors must be controlled and/or taken into consideration if it is to be considered a useful marker of impending OR/OT [124,125]. To date there is no direct evidence supporting a causal link between low plasma glutamine, impaired immune function, and increased susceptibility to infection in athletes [126], and whilst the use of glutamine warrants further investigation, its mechanistic role in the development of OR and OT currently seems questionable [107].

Inflammatory Factors

Cytokines

Cytokines facilitate an influx of lymphocytes, neutrophils, monocytes and other cells, which participate in the clearing of antigens and healing of tissue [127]. It has been argued that high volume/intensity training alongside insufficient rest periods will increase systemic trauma from which circulating monocytes are activated by cytokines, in turn producing large quantities of pro-inflammatory interleukins IL- 1β , and/or IL-6, and/or tumour necrosis factor alpha (TNF α) [29]. The stimulation of cytokines into the bloodstream is mediated by the duration of exercise, blood glucose levels, and the bioavailability of muscle glycogen [128].

Plasma cytokines, in particular IL- 1β , IL-2, IL-6 TNF α , have been linked to OT largely due to the increased circulating monocytes associated with mediation of pro-inflammatory markers [29,89,97,115,129-131]. Significant increases in post-exercise plasma levels of IL- 1β , IL-6 and TNF α were evident after 8 weeks of prolonged, intense training in 24 elite male

cyclists [130]. Serum IL-2 concentration was increased in 5 endurance-trained soldiers from $0.06 \text{ U}\cdot\text{ml}^{-1}$ at day 1 of 10 days of intensive interval running (twice daily, maximal sprints), to $0.17 \text{ U}\cdot\text{ml}^{-1}$ at day 11. Further increases ($1.00 \text{ U}\cdot\text{ml}^{-1}$) occurred during a 5-day active-recovery period [115]. Post-exercise increases in circulating TNF α have been reported during acute bouts of high intensity training in 8 college level rowers [132], as well as 10 runners [127]. Acute increases in IL-6 levels have also been found in highly-trained triathletes [133]. Additional insights have been gained from other forms of short-term physical activity such as near maximal/short duration endurance exercise [131]. It has been suggested that elevated levels of circulating cytokines could account for the signs and symptoms of OT as they have a direct influence on the central nervous system (CNS). The severity and presentation of symptoms may vary but could include lethargy, weakness, malaise, and an inability to concentrate, similar to the description of under-performance related syndromes [134]. Whilst current research is limited and whilst long-term exercise programmes suggest that IL levels may chronically increase due to tissue damage associated with high volumes/intensities of exercise, little is known about their effects or contribution to OT [135]. The mechanisms underlying OT may not as yet have been clearly identified, but are indeed likely to involve increased cytokine production resulting from the physical stress of intense daily training with inadequate recovery [95].

High Sensitivity C-Reactive Protein

High-sensitivity CRP (Hs-CRP), along with IL- 1β , IL-6 TNF α , is a biomarker of systemic inflammation [136]. Whilst moderate levels of exercise have been found to reduce systemic inflammation [136], excessive musculoskeletal stress associated with insufficient periods of rest [38] and recovery can induce an acute increase in localised inflammatory markers, or tissue trauma [41,137]. Hs-CRP serum levels increase not only after trauma, tissue necrosis, infection, and surgery, but also as a consequence of chronic fatigue [138,139] and endurance exercise [140,141]. There is a close relationship between Hs-CRP and cytokine concentration, with Hs-CRP increases related to the level of circulating cytokine production [136,142] via the cholinergic anti-inflammatory pathway [143]. This could be associated with OT as increased Hs-CRP leads to systemic inflammation and reduced performance following severe bouts of exercise [144,145]. Whilst physical exercise and training induces beneficial adaptations, prolonged exhaustive exercise increases reactive oxygen species (ROS), which could cause muscular injuries with inflammatory consequences indicating jeopardised performance and possibly OT [146]. A previous review of the effects of physical activ-

ity on inflammatory markers has concluded that prolonged, intense endurance exercise acutely increases not only serum IL-6 but Hs-CRP levels as well [81]. Furthermore, significantly elevated Hs-CRP levels ($P < 0.001$) have been recorded 5-days post-race after an Ironman triathlon in 42 well-trained triathletes, with levels still higher than baseline values at 19-days [147]. This may indicate that low-grade systemic inflammation reflects incomplete muscle recovery. Similarly, a 152-fold increase in Hs-CRP after a 246km footrace in 15 well-trained athletes and 108-fold increase 48 hours later has been previously documented [141]. Interestingly elevation in Hs-CRP levels persisted after normalisation of IL-6 levels.

Whilst it has been suggested that Hs-CRP is a conventional marker of excessive training load [137], it has also been proposed that most biomarkers such as Hs-CRP, are not capable of detecting OT, but are helpful in providing information on the athletes' global health status, and therefore are useful in the context of an exclusion diagnosis [22]. Whilst research linking Hs-CRP and OT is currently limited, there is growing evidence indicating a link between systemic, acute phase inflammation, and excessive exercise [137,141,146-149].

Cell-Free DNA

Whilst only small amounts of serum levels of cell-free DNA (cf-DNA) are present in a healthy individual, specific variations in the concentration of cf-DNA correlate significantly following cellular death and tissue injury [150,151]. Increased concentrations of cf-DNA have been reported in a number of illnesses and autoimmune diseases ranging from cancer to hepatitis and arthritis [150,151], as well as during periods of exercise-induced inflammation mediated by physical exhaustion. This is most likely due to exercise-induced oxidative and cytokine stress in skeletal muscles and immune-competent cells [152]. A small number of studies have found acute but significant increases in cf-DNA using a range of endurance-based testing protocols [152-6].

For example, 25 trained half marathon runners (12 males and 13 females; age range 28-56 years) were tested for circulating cf-DNA testing before, immediately after, and 2-hours post-race. Pre-race mean (SD) cf-DNA was 18.01 (2.80) $pg/\mu L$ (maximum, 27.4 $pg/\mu L$). Immediately post-race, levels significantly increased (maximum, 702.4 $pg/\mu L$; mean (SD), 334.4 (139.41) $pg/\mu L$; $P < 0.0001$), however at the 2-hour post-race stage circulating levels had returned to baseline (maximum, 112.3 $pg/\mu L$; mean (SD), 30.44 (18.99); $P < 0.0001$) suggesting only an acute cf-DNA inflammatory response [153]. Conversely, Margeli et al. [154], reported not only acute increases in cf-DNA levels immediately after 15 healthy male subjects

participated in a 246 km race (age range 31-46 years) (pre-race 14.8 ± 13.9 genome equivalents/ ml^{-1} vs immediate post-race 146.2 ± 161.5 genome equivalents/ ml^{-1}), but also 48 hours post-race (51.5 ± 73.2 genome equivalents/ ml^{-1}). In another study using an ultra-distance foot-race [152], the cf-DNA levels of 14 trained runners (9 males and 5 females) were sampled pre-exercise, immediately post-exercise, 2 hours post-exercise, and 48 hours post-exercise; cf-DNA levels were significantly increased immediately after the race ($P < 0.001$), were still elevated 2 hours post-race ($P < 0.005$) but were significantly lower than the immediate post-race values ($P < 0.05$). Furthermore, cf-DNA levels had returned to pre-exercise levels by 24 hours post-race suggesting no chronic effect.

While these studies demonstrate acute increases in cf-DNA after single bouts of strenuous exercise, there appears to be limited investigation related to chronic overload training. Fatouros et al. [157] reported increased cf-DNA 96 hours post-exercise after testing for potential chronic exercise-induced inflammation. However the testing protocol involved a multi-joint, systemic resistance training protocol as opposed to endurance-based exercise. As resistance training involves the utilisation of different metabolic pathways and higher levels of anaerobiosis relative to endurance-training, it is suggested that these findings be currently accepted with caution. Furthermore it remains difficult to draw precise conclusions as to how different muscle actions and exercise modes may influence the release of cf-DNA [151]. The origin of cf-DNA remains widely unexplained, and the intensity and duration of the related physical exposures that are necessary to provoke such increases are a matter of current investigation [151]. High inter-individual differences between baseline and post-test levels, as well as differing test protocols and measurement methods must also be taken into account. However cf-DNA appears to be a novel marker of cellular tissue damage, therefore offering the potential to be a sensitive measure of OT. Further investigations focusing on chronic exposure for endurance-based sports with standardised measurement approaches are strongly recommended.

Central Fatigue Hypothesis

Branch Chain Amino Acids & Free Tryptophan

During prolonged exercise, branch chain amino acids (BCAAs) such as leucine, isoleucine and valine are taken up by the muscle rather than the liver in order to contribute to oxidative metabolism. At the same time fatty acids compete with tryptophan for albumin binding sites leading to increased entry of free tryptophan (fTryp) into the brain [56,158,159]. A consequence of increased fTryp concentration relative to the reduction in BCAAs in the brain is its conversion to the neurotransmitter 5-HT, or serotonin [159] which

can result in premature fatigue [158] and endocrine function inhibition, most notably of the hypothalamic hormones and post-synaptic reflex inhibition during exercise [160]. This has been referred to as the 'central fatigue hypothesis' [160,161]. An increase in fTryp in relation to BCAA (fTryp:BCAA ratio) has been observed (0.019 vs 0.014) in distance runners after an unaccustomed increase in training mileage over a 28-day period [162]. However, similar increases (0.021 vs 0.014) were also reported following a 28-day period of increased exercise intensity suggesting that the fTryp:BCAA ratio is inconsistent in its response to intensified training. Furthermore, an unchanged fTryp-BCAA ratio despite a 40% increase in training volume has been reported in 10 highly-trained endurance runners [56], and no long-term changes in 5-HT neurotransmission in athletes diagnosed with OT in comparison to well-trained athletes have been reported [163]. Studies have attempted to manipulate central serotonergic activity during exercise, but this work has yet to provide support for a significant role of serotonin in the fatigue process [164]. Consequently, as brain function is dependent upon the interaction of a number of systems, it is unlikely that a single neurotransmitter is responsible for central fatigue [165]. To date there have been too few studies undertaken to confidently assess the effect of fTryp:BCAA on OT in endurance athletes. Scope for further investigation has been proposed [162], however currently research suggests an inability to distinguish between OT and well-trained athletes using this biomarker [166].

Glycogen Utilisation

It is generally accepted that 8-10g of carbohydrate/kg/day⁻¹ (CHO) are required to maintain maximal glycogen stores, equating to 60-70% of the overall calorie intake from a normal-calorie diet [13]. However some shorter distance triathletes have been reported to derive as little as 53.8% of their overall intake from CHO [13]. These amounts may not be sufficient enough to maintain adequate glycogen repletion following multiple daily training sessions. Low glycogen repletion as a mechanism for OR and OT has centred on the notion that significant increases in training volume reduce the athlete's ability to maintain adequate muscle glycogen storage and the catabolic cost has been suggested as the contributory result of central fatigue and ultimately OT [59,60,167,168]. The effects of 10 days of intensified training on glycogen load in 12 highly trained swimmers has previously been investigated [59]. Of the 12 participants, 4 were unable to tolerate the demands of the training load and were subsequently found to have consumed 1000 kcal per day less than the other 8 participants, in conjunction with much lower mean CHO intake (5.3 vs 8.2g.kg per day). Therefore chronic muscular fatigue may occur due to failure to

ingest sufficient CHO to match the energy demands of heavy training. Further, following several intensive and prolonged endurance training sessions, glycogen depletion may become chronic if CHO ingestion is inappropriate [59]. However, 8 competition-level cyclists who increased their training load for 15 days whilst at the same time increasing CHO intake in order to maintain muscle glycogen levels (160g of CHO 2-hours post-exercise) still met at least 3 out of 5 pre-determined criteria for OR [60]. This suggests that other mechanism(s) may be a contributory indicator. Rather than being responsible for the occurrence of OR or OT in endurance-trained athletes, repeated depletion of glycogen stores may induce subtle changes within the metabolic pathways that contribute to the skeletal muscle energy supply [169]. Long-term glycogen depletion however, may lead to increased BCAA oxidation [170], which in turn may be responsible for central fatigue processes.

Neuroendocrine Factors

Trials have demonstrated that cytokines (IL-1 β , IL-6 and TNF α) stimulate the hypothalamus-pituitary-adrenal (HPA) axis [128]. Both OR/OT must be viewed on a continuum with a disturbance, an adaptation, and finally a maladaptation of the HPA axis resulting in performance decrements [63,171]. This model is well established and was labelled as the "General Adaptation Syndrome" in 1946 [172]. Several studies have provided evidence that alteration in sympatho-adrenal activity occurs during OT, such as reduced urinary output and increased/decreased catecholamine activation [28,173]. A reduction in adrenocorticotrophin (ACTH) and growth hormone [35,174,175] reduced cortisol [60], reduced luteinising hormone, reduced follicle stimulating hormone [22], reduced urinary excretion of norepinephrine [28], reduced insulin growth factor-binding protein 3 (IGF-BP3) [40] and altered testosterone:cortisol ratio [21,33,40] have also been reported as potential hormonal markers of OT. This growing body of evidence indicates that changes in sympathetic hormone release may precede, and possibly contribute to, subsequent development of OT-like symptoms.

Impact on Sporting Performance Factors

Blood Lactate

Decreases in blood lactate ($[La^-]_b$) concentrations during endurance training are the result of improvements in lactate utilisation and clearance [176-178]. In athletes with signs of OT, it is possible that autonomic dysregulation results in decreases in $[La^-]_b$ concentration caused by a decreased capacity of the muscle to produce lactate [179]. Whilst some studies have shown little change in resting $[La^-]_b$ levels [54,60], a number of studies have reported lowered $[La^-]_b$

concentrations during maximal and/or submaximal performance [31,32,54,60,61,63,112,154,179-181]. A number of studies also have attempted to disassociate optimal training from both OR and OT by combining $[La^-]_b$ with ratings of perceived exertion (RPE) [54,65,179], whilst a minority of studies have shown no change in $[La^-]_b$ levels during submaximal and/or maximal exercise [64,171]. A rightward shift of the lactate curve as well as a significant decrease in peak blood lactate ($[La^-]_{b,peak}$) (9.6 mmol·L⁻¹ vs 8.2 mmol·L⁻¹ ($P < 0.05$) respectively) after 4 weeks of intensified training has been observed in 10 experienced endurance athletes [179]. A subsequent leftward shift of the lactate curve following 2 weeks of recovery training was also reported. Likewise, a decline in submaximal $[La^-]_b$ levels (2.9 mmol·L⁻¹ vs 2.4 mmol·L⁻¹) as well as maximal $[La^-]_b$ levels (11.3 mmol·L⁻¹ vs 9.5 mmol·L⁻¹) after an unaccustomed increase in training load has also been reported in a group of well-trained runners [162]. A decline in maximal $[La^-]_b$, following a two-bout maximal cycle ergometer test, which saw values lower in a group of participants diagnosed with OT (6.8 mmol·L⁻¹ for test 1, 5.8 mmol·L⁻¹ for test 2 (mean values)) compared with those diagnosed with OR (9.9 mmol·L⁻¹ for test 1, 9.8 mmol·L⁻¹ for test 2 (mean values)) have been reported, indicating that $[La^-]_b$ values could be used to differentiate OT from OR [63]. Elevated $[La^-]_b$ concentrations have been reported 2 minutes after performing an incremental cycle ergometer test to volitional exhaustion after induced muscle damage 48 hours previously (12.0 ± 1.4 mmol·L⁻¹ vs 10.9 ± 1.3 mmol·L⁻¹) in 10 recreationally healthy subjects [182]. However increases in $[La^-]_b$ were attributed to an increased rate of glycogenolysis possibly arising from an increased recruitment of Type II muscle fibres. As endurance sport is predominantly associated with aerobiosis [183], and therefore recruitment of type I muscle fibres, this may question the validity of such findings.

A diminished maximal $[La^-]_b$ concentration in concert with unchanged or slightly reduced submaximal performance levels has been consistently reported in endurance athletes displaying symptoms of OT [22]. Furthermore decrements in maximal performance is paralleled by reduced maximal $[La^-]_b$ concentrations [175]. It has also been suggested that the ease and speed at which the $[La^-]_b$:RPE ratio can be determined may make it useful for coaches and athletes in monitoring intensive exercise training and recovery as well as indication of OR [54]. However a rightward shift in the lactate profile following training is not only associated with OR/OT but also with an improvement in aerobic fitness profile, therefore caution should be applied in order to avoid a mis-diagnosis [179]. Submaximal $[La^-]_b$ values are seemingly less effective as markers of OR/OT. It has been suggested that reduced muscle

glycogen availability may limit substrate availability for $[La^-]_b$ generating anaerobic glycolysis, as well as reduced catecholamine concentrations which also mediate glycogenolysis and anaerobic glycolysis [17].

Peak Oxygen Uptake

There is a lack of consensus regarding the value of peak oxygen uptake for identifying OT in endurance athletes. Some studies have reported decreased peak oxygen uptake ($\dot{V}O_{2peak}$) [31,32,60,70,112,180,184] including an 8% decrease in $\dot{V}O_{2peak}$ (4.8 l·min⁻¹ vs 4.4 l·min⁻¹) after 2 weeks of short-term intensified training in 7 male cyclists [31], whilst $\dot{V}O_{2peak}$ decrements (4.9 l·min⁻¹ vs 4.7 l·min⁻¹) have been reported after 15 days of intensified training in 8 male competitive cyclists [60]. A decline in time-to-fatigue performance of 27% [32] and a 29% [172] decline following periods of intensified training has been previously reported. Conversely, others have reported unchanged $\dot{V}O_{2peak}$ following unaccustomed periods of increased training load [56,59,65,185]. For example, no change was identified in aerobic capacity after 10 successive days of increased training in an attempt to determine the physical effects of training overload [59]. Similarly, no difference in $\dot{V}O_{2max}$ was reported after increasing the training volume of 10 highly-trained endurance runners by 40% for two weeks in order to induce a state of OR [56]. There is currently no consensus on the most appropriate performance test in the identification of OR or OT however time-to-fatigue based protocols appear to show greater changes in exercise capacity in athletes displaying symptoms [21].

Psychological Factors

Mood State

Mood state appears to be sensitive to periods of intensified training amongst endurance athletes [186], and can be used to successfully identify athletes predisposed to OR and subsequently OT [187-189]. The profile of mood state questionnaire (POMS) includes six specific mood states (anger, depression, tension, confusion, vigour, fatigue) in order to elicit a total mood disturbance (TMD) score [17] with an "inverted iceberg profile" evident in athletes with symptoms of OT [190]. Subsequently, studies have identified clear psychological distress and TMD in athletes with both OR and OT [7,31,32,55,115,180,186,191]. For example, increased fatigue ratings and decreased mental concentration in endurance athletes following a period of intensified training resulting in a 27% decrement in performance have been reported [32]. The authors concluded that mood state measured by POMS was amongst the most sensitive measures for diagnosing OT. Similarly, increases in the fatigue related subscale of an abbreviated POMS questionnaire, as well as a decrease in vigour and TMD have also been reported

[115]. The study also reported an increase in confusion scores during the training phase, however this change was not significant. Increased TMD and depression in female college swimmers that were significantly higher ($P < 0.05$) during OT than in those who showed no performance decrement have also been reported [191]. Additionally, associations between training volume and ratings of anger ($r = -0.58$), vigour ($r = -0.54$), and fatigue ($r = -0.53$) have been reported, however no relationship between training volume and tension, depression, confusion and global mood were found [186].

Studies have also reported increased global distress during intensified training without identified signs and symptoms of OT [185,189,192]. In each of these studies, deterioration in global mood state was reported in the absence of reduced performance in swimmers following 3 days [185] to 10 days [192] of intensified training. 2 out of 3 elite-level swimmers demonstrated symptoms of staleness provided higher scores on several POMS measurements in comparison to controls [189]. Athletes reporting signs of staleness may not necessarily report different mood state scores compared to "fresher" athletes, however, TMD scores may help to identify athletes predisposed to staleness before physiological symptoms are presented. The consensus of previous work would indicate that OT in particular can be characterised by a negative psychological state [189] and mood state may be a useful indicator in endurance athletes. However, POMS should be used with caution as it is not yet clear whether it can predict OT in all groups of endurance athletes, or whether it is an effective predictor during all phases of the training cycle [17]. Furthermore, the elevation of any specific subscale should not be used to confidently predict OT [193]. The reliability of POMS could be improved if it is considered in conjunction with performance measures [21].

Recovery-Stress

A sustained mismatch between exercise-induced stress and recovery can result in athletes being unable to continue prolonged training at a specific load/intensity which could ultimately lead to OR and subsequently OT. Additional social, educational, occupational, economical and nutritional stressors, in addition to lengthy travelling and monotonous training may also contribute to the risk of OT in the endurance athlete [194]. Kenttä & Hassmén [195] have previously proposed a total quality recovery (TQR) model, a theoretical model highlighting individual athletes' risk of OR/OT in the context of different physical and psychosocial capacities. It is proposed that in order to minimise OR/OT stress associated with training should be met with appropriate recovery practices [193]. Mood state identified by POMS may not be

sufficient to explore recovery processes. This has led to the development of a 77-item recovery-stress questionnaire known as the REST-Q Sport [194]. Introduced to accommodate the inclusion of athlete intervention, the REST-Q Sport was designed as a direct alternative to the POMS [193,194,196]. Whilst the POMS can reveal changes in mood state it cannot reveal if such changes are due to increases in stress or decreases in recovery [197]. The REST-Q Sport has been used in a small number of studies focusing on OR/OT [196,198-200]. For example, increased training loads of 100% have been found to elevate somatic stress and reduce recovery [198]. with significant associations found between training load and fatigue ($r = 0.49$), somatic complaints ($r = 0.50$), and sleep disturbances ($r = 0.58$). The study also reported that changes in specific stress and recovery subscales, as well as a decrease in performance, indicated OR. Participants provided with the REST-Q Sport on 4 separate occasions over a 6-week period of basal, increased training volume, and decreased training volume provided significant changes in recovery-stress concurrent with increased training loads, suggesting that the REST-Q Sport was effective at monitoring stress and recovery as well as detection of OR in its early stages of development [198]. Furthermore, an investigation of physiological, biochemical, and psychological markers of OR in 16 experienced male triathletes was undertaken [201]. Although no significant changes to physiological variables were observed, the study found that the REST-Q Sport showed an impaired recovery-stress state with increased training load ($P < 0.05$), indicating that it may provide a practical tool for recognising OR in its early stages of development. The REST-Q Sport is a practical tool at an individual level with the ability to predict how athletes will perform after a cycle of training and recovery [193]. As well as being used as a monitoring tool, the REST-Q Sport may also give direction to treatment and/or intervention [201]. Also, the REST-Q Sport has been developed from the REST-Q, a questionnaire aimed at the general population [194]. To date there is limited research linking the REST-Q Sport to OR or OT but provides an interesting rationale for future research into recovery-stress and psychosocial aspects of excessive training loads. Whilst the REST-Q Sport is promising, further research needs to be conducted to determine its validity/reliability for identifying or predicting OR/OT in endurance athletes.

Recommendations for Preventing OR/OT: Considerations for Athletes and Coaches

Coaches and athletes should focus on deleterious changes in performance until a more robust diagnosis of OR/OT is identified. For most coaches/athletes, simple field tests and detailed field notes of training records will provide a more realistic way of assessing

potential risk. Monitoring of training frequency, intensity and duration should be recorded alongside athlete perceptions of training load/volume using TRIMP, session RPE, or combined psycho-physiological surrogate markers including $[La^-]_b$:RPE ratio. In order to provide coaches with preventative steps towards the identification of OT, a regular programme of health screening should be introduced from a multi-disciplinary team. It is feasible for monitoring to be conducted at the end of each athletes training mesocycle (every 6-12 weeks dependent on the sport and specific training requirements), or alternately, at the end of a cycle of rest and regeneration. Further research is required to determine the optimal timing of the health screening assessment.

Athletes should be allowed to recover/rest from illness or early signs of OR and not be rushed back into training. The coach should regularly rotate training requirements so the athlete does not become stale. Coaches should carefully monitor the non-structured aspects of their athletes' lifestyle (e.g. sleep patterns, nutritional intake, travel schedules, changes in time zones) to ensure external stressors are not affecting training performance. These stressors could be monitored by regular completion of psychological questionnaires including POMS and/or REST-Q Sport. In reality, a test battery including invasive, laboratory based techniques, for example, blood-borne assays are not pragmatic on a regular basis. Further research could focus on the development and validation of less invasive salivary-based assays for identifying markers of OT. The implications of OR/OT for athletic performance and the long-term health status of athletes has recently been highlighted by the development of a joint ACSM/ECSS Position Statement on the Prevention, Diagnosis and Treatment of the Overtraining Syndrome [202] and we strongly recommend this statement (including the very useful diagnostic checklist) to coaches and endurance athletes.

Conclusions

Both OR and OT involve the accumulation of psycho-physiological stress resulting in performance decrements in athletes undertaking endurance-based sports. However, the precise definition of either OR or OT is still open to debate, and recent developments in the diagnosis and treatment of the condition(s) have been frustratingly slow. Guidance informed by research investigations has been hindered by the temporary inducement of OR and not chronic OT. The induction of longer-term damage to psychological, immunological and neuroendocrine systems will continue to provide serious ethical challenges in the future.

A multitude of variables have been implicated in the identification of OT and it is clear that no single biomarker can be used for diagnostic purposes. In

order to identify and reduce the risk of OT symptoms, careful monitoring of individual responses to training should be adopted. Coaches should ensure that athletes maintain adequate rest and regenerative periods, and lifestyle and psycho-physiological health monitoring is undertaken. Further research may wish to focus on the identification of simple field-based psycho-physiological markers (and surrogates) which can be monitored regularly throughout the training calendar.

Declaration of interest

The authors report no conflicts of interest.

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Authors' contribution

A – Study Design

B – Data Collection

C – Statistical Analysis

D – Data Interpretation

E – Manuscript Preparation

F – Literature Search

G – Funds Collection