A multi-factorial assessment of elite paratriathletes’ response to two weeks of intensified training

Original Investigation

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Running head: Intensified training in elite paratriathletes

Abstract word count: 220
Text-only word count: 3315
Figures: 3
Tables: 3
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Abstract

Purpose: In able-bodied athletes, several hormonal, immunological and psychological parameters are commonly assessed in response to intensified training due to their potential relationship to acute fatigue and training/non-training stress. This has yet to be studied in Paralympic athletes.

Methods: Ten elite paratriathletes were studied for five weeks around a 14-day overseas training camp whereby training load was 137% of pre-camp levels. Athletes provided: six saliva samples (one pre-camp, four during camp, one post-camp) for cortisol, testosterone and secretory immunoglobulin A; weekly psychological questionnaires (POMS and RESTQ-S); daily resting heart rate and subjective wellness measures including sleep quality and quantity.

Results: There was no significant change in salivary cortisol, testosterone, cortisol:testosterone ratio or secretory immunoglobulin A during intensified training ($p \geq 0.090$). Likewise, there was no meaningful change in resting heart rate or subjective wellness measures ($p \geq 0.079$). Subjective sleep quality and quantity increased during intensified training ($p \leq 0.003$). There was no significant effect on any POMS subscale other than lower anger ($p = 0.049$) whilst there was greater general recovery and lower sport and general stress from RESTQ-S ($p \leq 0.015$).

Conclusions: There was little to no change in parameters commonly associated with the fatigued state which may relate to the training camp setting minimising external life stresses and the careful management of training loads from coaches. This is the first evidence of such responses in Paralympic athletes.

Key words: overreaching, monitoring, disability, triathlon, mood disturbance
Introduction
Athletes often undergo short periods of intensified training (IT), commonly in the form of training camps, purposely designed to provide an overload stimulus whereby significant acute increases in training load (TL) are observed. Whilst periods of IT may result in improved performance, there is the possibility athletes may be at risk of acute fatigue. Meeusen et al. define acute fatigue as the first state experienced as a result of IT and its associated stressors. If the accumulation of physical and/or non-physical stress were to continue, the development of overreaching (OR) may ensue whereby decrements in sporting performance are evident. Testing for performance in fatigued athletes raises inherent issues such as providing a further taxing stimulus or disruption to the normal training regime. To circumvent this, less physically demanding and disruptive methods of detecting fatigue and excessive stress after periods of IT have been sought. This may be particularly pertinent in heterogeneous cohorts and/or complex, multi-modal sports, such as paratriathlon.

Due to the effect of IT on the hypothalamic axes, and their ease of measurement in saliva, resting levels of cortisol and testosterone are commonly measured parameters. It is reported that IT results in increases in biologically active, free cortisol with a concomitant decrease in free testosterone, thus an increase in cortisol:testosterone ratio, representing a greater catabolic state in the body. Studies have supported this, displaying increases in salivary cortisol (sC) or decreases in salivary testosterone (sT) as a result of IT. Additionally, Coutts et al. proposed that salivary secretory immunoglobulin A (sIgA) may also be a sensitive marker in response to IT. This is due to longitudinal prospective studies evidencing athletes experiencing depressions in sIgA during periods of high TL. Although the responses to IT of other stress markers, such as resting heart rate (RHR) or sleep quality/duration, have yet to show uniformity, subjective psychological states do seem to produce consistent results. Although the effects of IT have been studied in many types of athletes, triathletes have received particular attention, this is partly due to their habitually high TLs. Despite the extensive research focusing on able-bodied (AB) triathletes, little is known about how paratriathletes respond to IT. As in studies of Mujika et al. and Stephenson et al., paratriathletes are likely to be undertaking high TLs, placing them at risk of acute fatigue. Furthermore, there is no published literature regarding any hormonal, immunological, physiological or psychological effects of IT in Paralympic endurance athletes. Thus, it is not evident how this population may differ to AB athletes regarding markers of physical and/or psychological stress. This topic is of particular relevance as Paralympic athletes may be at greater risk of excessive stress due to physical impairments causing movement inefficiencies, thus heightening the internal load of movement, with impairments increasing the demands of daily life. Consequently, the aims of the present study were to elucidate how paratriathletes respond to IT in the form of a 14-day overseas training camp to permit a comparison with literature from AB athletes.

Methods
Participants
Ten (seven males, three females) elite paratriathletes (age 30 ± 8 y, body mass 66.1 ± 7.6 kg, cycling $\dot{V}O_{2\text{peak}}$ 57.6 ± 6.4 ml·kg$^{-1}$·min$^{-1}$) of mixed impairments (amputation $n=6$, spinal cord injury $n=1$, cerebral palsy $n=1$, lower leg impairment $n=1$, visual impairment $n=1$), volunteered
to participate in this study. All provided written informed consent and the procedures were
approved by the Loughborough University Ethical Advisory Committee. All participants
regularly competed at an international level for 2-7 y with nine athletes racing in the 2016
Paralympic Games.

Study design
Athletes were studied over the course of five weeks which consisted of one week pre-IT, two
weeks IT plus two weeks post-IT (Figure 1). IT took place during the months January-February
in Lanzarote, Spain (mean daily temperature 18.7 ± 0.9°C). During IT, average weekly training
volume was 137 ± 33% (mean ± standard deviation) of pre-IT levels.

Training load
Changes in TL during the study period were as prescribed by participants’ coaches. All
followed a similar periodised plan with deliberate overload intended during the IT phase. To
assess the changes in TL, training was quantified by the methods of Cejuela-Anta and Esteve-
Lanao whereby total training minutes for swim, bike and run were multiplied by intensity
factors of 0.75, 0.5 and 1, respectively, and summated.16,19

Saliva analysis
Participants provided saliva samples on days 2, 9, 12, 16, 19 and 30. These sampling days were
chosen, based on athletes’ schedules, to provide the most consistency with regards to the
preceding day’s training. Each sample was collected in the morning (06:00-07:00) before
training, ten minutes after last fluid intake and whilst in a fasted state. These measures were
taken to limit any cofounding effects of circadian rhythm, hydration status and salivary
stimulating effects of food.11 A passive unstimulated saliva sample was collected over a period
of three minutes into a pre-weighed sterile plastic container with minimal orofacial movement.
SC and ST concentrations were determined in duplicate using commercially available enzyme
linked immunosorbent assay kits (Salimetrics Europe Ltd, Newmarket, UK). SIgA was
analysed using techniques described by Leicht et al.10 Mean intra-assay coefficients of
variation were 1.5%, 2.0% and 3.2% for SC, ST and SIgA, respectively. On days where
participants provided saliva samples, a questionnaire of illness symptoms was also completed,
as used by Gleeson et al.,20 for determination of upper respiratory tract illness (URI) incidence.
When URI was present, requirement for training modification was noted.

Psychological questionnaires
Participants completed the POMS and RESTQ-S on five occasions (days 5, 12, 19, 26 and 33),
completed before athletes’ planned recovery day of the respective week. They were asked to
answer POMS questions with respect to how they have felt in the last seven days/nights.
Responses from the POMS were used to calculate a total mood disturbance by summation of
negative scales (fatigue, depression, tension, anger, confusion) and subtraction of the positive
vigour scale. Additionally, scales were analysed individually to see any effect of IT on specific
mood states. When completing the RESTQ-S, participants rated how often they experienced
general and sport-specific stress or recovery orientated activities in the last three days or nights.
RESTQ-S responses were used in the calculation of total stress score via summation of stress-
related scales. Likewise a total recovery score was calculated in the same manner using
recover-related scales. Additionally, general stress, sport-specific stress, general recovery and
sport-specific recovery scores were produced using the appropriate scales.

Daily wellness measures
Upon waking every morning, participants provided several wellness measures. Similar to the
questionnaire used by Buchheit et al.,21 on a six-point, Likert scale participants rated their
energy levels, motivation, muscle soreness, sleep quality whilst providing sleep duration in hours. Additionally, participants recorded their RHR using their personal heart rate monitor whilst supine for at least five minutes. Participants’ daily RHR and subjective wellness measures were averaged over five discreet periods: day 1-7, 8-14, 15-21, 22-28 and 29-35.

**Statistical analyses**

All statistical analyses were conducted using IBM SPSS Statistics 23.0 software (IBM, New York, USA). Statistical significance was set at $p<0.05$. Data were checked for normal distribution using the Shapiro-Wilk test and homogeneity of variance using Levene’s test. Where sphericity could not be assumed, the Greenhouse-Geisser correction was used. Changes in TL, sC, sT, salivary cortisol:testosterone ratio (sC:T), sIgA, POMS and RESTQ-S scales plus daily wellness measures over time were assessed via one-way within-measures analysis of variance (parametric) or Friedman’s test (nonparametric). The Bonferroni post-hoc test was used to evaluate pairwise comparisons of time points.

**Results**

**Training load**

There was a significant difference in TL over time ($p<0.001$) as TL was higher during days 8-14 than all other time points ($p \leq 0.034$) and higher during days 15-21 than days 1-7 ($p=0.014$) (Figure 2).

**Salivary testosterone, cortisol and secretory immunoglobulin A**

Salivary cortisol displayed significant changes over the study period with a difference between day 2 and day 30 ($p=0.046$; Figure 3). There was no significant difference in sT, sC:T or sIgA over time ($p \geq 0.090$) (Figure 3).

**Illness incidence**

Analysis of illness symptom questionnaires revealed that four participants reported at least one URI during the study period. The URI incidence ranged from one to two participants reporting URI per time point (Figure 3). In 43% of cases, ability to train was impaired such that training was modified or cancelled.

**Daily wellness measures**

There was no significant difference over time in subjective ratings of motivation, muscle soreness and energy status, nor so RHR ($p \geq 0.131$). However, there were significant differences in subjective sleep duration and sleep quality. Specifically, reported sleep duration was higher on days 8-14 and 22-28 than days 1-7 and 29-35 ($p \leq 0.024$) and was also higher in days 8-14 than days 15-21 ($p=0.023$) (Table 1). Sleep quality was greater in days 22-28 than days 1-7, 8-14 and 15-21 ($p \leq 0.043$) whilst sleep quality was lower in days 15-21 than 8-14 ($p=0.023$) (Table 1).

**Psychological questionnaires**

There was a significant change in the POMS anger scale with scores higher on day 5 than days 12 and 19 ($p \leq 0.044$), whilst anger was also higher on day 33 than day 19 ($p=0.049$). There was no significant difference in any other scale or total mood disturbance during the study period ($p \geq 0.079$) (Table 2). There were significant differences in RESTQ-S scales for total stress, general stress, sport stress and general recovery. Specifically, total stress and general stress were higher on day 5 than days 12, 19 and 26 ($p \leq 0.019$) whilst sport stress was higher on day 5 than days 12, 19 and 33 ($p \leq 0.023$). General recovery was higher on days 12 and 19 than all other time points ($p \leq 0.025$) (Table 3).
Discussion

The present study is the first to assess the hormonal, immunological and psychological responses to a period of natural IT in a group of elite paratriathletes. IT resulted in no significant change to sC, sT or sIgA whilst lowering measures of stress and anger and increasing self-reported sleep parameters and perceived recovery.

Although TL during IT was, on average, 137% of normal training, it appears that athletes in the current study were not showing acute fatigue or excessive stress. This increase was as programmed by athletes’ coaches as an intentional overload period and is of a similar magnitude to previous studies reporting OR. Nonetheless, others have also shown similar findings. In their study of Australian Rules footballers, Buchheit et al. reported that a two-week training camp, comparable to the present study, resulted in no evidence of impaired performance or subjective wellness. In fact, the participants improved their performance during an intermittent running protocol. The authors propose this beneficial adaptation was due to the participants’ high-level training background and careful planning of training by the coaches to minimise the risk of excessive physical stress. Similarly, Slivka et al. reported no effect of a three-week cycling race, whereby exercise volume increased 418%, on any markers of acute fatigue. Specifically, 60 min time trial performance was not impaired nor was performance in a graded exercise test. Furthermore, there was no effect on sC, sT, sIgA or RHR with only minimal influence on the POMS vigour scale. This was proposed to be due to a minimisation of external life stresses.

Salivary cortisol and testosterone have previously been suggested as useful markers of stress/recovery after periods of IT due to their ease of analysis and their potential relationship to overreached states. Although in the current study there was an increase in sC from pre- to post-IT, indicative of cumulative stress, there was little change during the 14-day IT period. Also, sT and sC:T were unchanged, indicating the catabolic:anabolic hormonal balance was not meaningfully perturbed, despite sC:T tending to be higher during IT albeit not to the threshold of predefined significance (p=0.090). The responses of sC and sT to periods of IT have commonly been studied in AB athletes. However, there appears to be little support for the hypothesised increase in the catabolic milieu. For example, whilst some have shown increases in sC, most have reported no significant changes. Similarly, studies have reported negative effects of IT on sT, but others have found no change. Nonetheless, this is the first study to investigate these responses in Paralympic endurance athletes. It appears, based on the current findings, that the effects of IT on salivary hormones are not significantly disparate to AB athletes.

It has previously been demonstrated that TL or training duration displays an inverse relationship to sIgA measures over a prolonged period in Paralympic athletes. However, during IT there was no significant change in sIgA concentration in this study. Similarly, URI incidence was unchanged by IT. Coutts et al. had suggested that sIgA may be a sensitive measure in response to IT. This is due to the proposed relationship between high TL, sIgA and URI incidence. However, the studies of Papacosta et al. and Halson et al., in which participants were deliberately overreached via a period of IT, showed no significant changes in sIgA. Additionally, Slivka et al. noted no change in sIgA in a group who showed no signs of maladaptation after IT. Moreover, Born et al. recently stated that the mucosal immune system actually positively adapts to IT by increasing IgA measures. As such, there is currently little evidence to substantiate the claims of Coutts et al. that sIgA may show suppression as a result of IT. Here, we provide the first evidence in Paralympic athletes.
Participants in the current study perceived their sleep quality and duration to be higher during IT. Subjective sleep metrics were used due to their commonality in wellness monitoring of elite athletes because of the ease of use and limited associated cost compared to objective actigraphy. However, the use of subjective sleep parameters has been questioned. Hausswirth et al. note that in a group of overreached triathletes sleep quality was degraded, as measured via actigraphy, yet perceived sleep quality was unchanged. Furthermore, the authors state that changes in sleep variables are small and thus require extensive monitoring for the detection of acute fatigue or OR. Alternatively, others have supported the use of subjective sleep parameters and state they are sensitive to changes in TL. Nonetheless, due to the lack of objective information gathered on participants’ sleep, it is not possible to make comparisons between the aforementioned methods in the current athlete cohort. Future research should seek to further investigate the link between sleep and stress/recovery because, as stated in a recent review, sleep quality is typically impaired during training camps, unlike in the present study.

Resting heart rate in the present study was unchanged by IT, similar to previous studies. For example, Killer et al. reported no change in morning RHR after a nine-day IT period in trained cyclists, even with evidence of impaired performance. This is despite proposals that heart rate may be altered by IT due to a negative adaptation of the autonomic nervous system. One reason for the lack of relationship between RHR and IT may be due to the low signal:noise ratio reported by ten Haaf et al. Specifically, variation in self-recorded RHR, as a result of insufficient measurement control, may have masked any changes in response to IT.

It has previously been proposed that psychological and wellness measures are a sensitive marker in response to IT. Accordingly, in the current study where acute fatigue was not present, psychological measures showed either little change or slight improvements. There was no significant change in athletes’ self-reported motivation, muscle soreness or energy status. Similarly, there was very little change in athletes’ POMS profile over the study period. In fact, there was a decrease in the anger subscale during IT, whilst total mood disturbance tended to be lower during IT although not to the level of statistical significance ($p=0.079$). This again adds support to the lack of excessive stress as previous studies have found a relationship between increases in POMS negative scale scores and IT. Finally, responses to the RESTQ-S indicate that during IT there was a decrease in total, general and sport-specific stress with a concomitant increase in general recovery. The results for the RESTQ-S are particularly pertinent as it supports the notion that during IT, external life stresses were minimised despite the increase in TL. Hough et al. also employed the RESTQ-S to assess the responses of AB triathletes undergoing a 10-day training camp and noted no change in the subscales. The authors proposed that the triathletes were able to cope with the increased TL which is also likely the case in the present study due to coaches’ careful structuring of training and minimisation of life stresses.

This is the first study that has reported responses to IT in a group of Paralympic endurance athletes. Whilst the topic has been extensively researched in AB sports, little is known from those with physical impairments. Paralympic athletes may be at particular risk of physical stress due to factors that increase the likelihood of excessive overload such as movement inefficiencies. Although the population group in the current study only included one spinal cord injured athlete, there has previously been shown to be no significant difference in acute sC and sT responses to exercise compared to AB athletes, thus there is no reason why this athlete may obscure the results. Also, sIgA has been shown to display similar variance between Paralympic and AB athletes. Moreover, the use of the POMS questionnaire has been validated in male and female Paralympic athletes of mixed impairments although this is not yet the case for the RESTQ-S. Nonetheless, it can be assumed that all measures used in the...
present study were applicable to Paralympic athletes and that results were not confounded by participants’ impairments.

**Practical Applications**

The present study aimed to report a range of responses to IT, previously linked to acute fatigue and excessive stress, in a group of elite paratriathletes. From the results, it is unlikely acute fatigue was present. This is hypothesised to be mediated by coaches’ careful management of TL, such as the deliberate inclusion of low TL days and the scheduling of training to maximise recovery time between sessions, and the camp environment minimising external life stressors. Consequently, those working with Paralympic athletes should seek to achieve the two aforementioned strategies to minimise the likelihood of fatigue or even OR post-IT. Nonetheless, inter-individual variation existed with response to IT. For example, there was evidence of lower sT with a concomitant elevation in subjective muscle soreness for one PTWC paratriathlete with a bilateral transfemoral amputation. Alternatively, a PTS5 athlete with a lower leg impairment displayed a large increase in sC with a simultaneous decrease in sleep quality during IT. Thus, coaches and practitioners should have an awareness of individualised responses, especially in a largely heterogeneous sport such as paratriathlon. Nonetheless, similar to research in AB athletes, it appears psychological states may be the best tool to determine the stress response to IT in paratriathletes. These may provide greater sensitivity and at a lower financial cost than hormonal or immunological analyses. Of note, a performance test was not included in the present study to minimise disruption to athletes’ pre-season training schedule. Additionally, the usefulness of performance tests was questioned due to the additive effect they can have on residual fatigue. Finally, a lack of control group prevented certainty that results were due to IT rather than seasonal variation; as such, this is a consideration for future research.

**Conclusion**

Despite increases in TL similar to previously published studies, the paratriathletes in the current study displayed no signs of acute fatigue or maladaptation. There was little to no change in hormonal, immunological or physiological parameters commonly associated with excessive stress; in fact, participants displayed positive psychological changes.
References


**Figure captions**

**Figure 1** Schematic of data collection. Grey blocks represent days on which saliva was collected for assessment of cortisol, testosterone and secretory immunoglobulin A. * represents days on which participants completed POMS and RESTQ-S. On all days, participants provided their resting heart rate plus subjective ratings of sleep quality and quantity, motivation, muscle soreness and energy levels.

**Figure 2** Training load (bars are mean values, lines are individuals’ values) during the study period. *Significantly greater than all other time points (p<0.034). †Significantly greater than day 1-7 (p=0.014).

**Figure 3** Salivary cortisol concentration (A), testosterone concentration (B), cortisol:testosterone ratio (C) and secretory immunoglobulin A (D) with illness incidence (bars) during the study period (mean ± SD). Shaded area signifies intensified training period. *Significantly greater than day 2 (p=0.048).
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Figure 3 Salivary cortisol concentration (A), testosterone concentration (B), cortisol:testosterone ratio (C) and secretory immunoglobulin A (D) with illness incidence (bars) during the study period (mean ± SD). Shaded area signifies intensified training period. *Significantly greater than day 2 (p=0.048).
Table 1 Subjective ratings of energy levels, motivation, muscle soreness, sleep quality and sleep duration plus resting heart rate over the study period (mean ± SD). *Significantly different to days 1-7 and 29-35 (p≤0.024). †Significantly different to days 15-21 (p≤0.023). §Significantly different to days 1-7, 8-14 and 15-21 (p≤0.043).

<table>
<thead>
<tr>
<th></th>
<th>Days 1-7</th>
<th>Days 8-14</th>
<th>Days 15-21</th>
<th>Days 22-28</th>
<th>Days 29-35</th>
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<tbody>
<tr>
<td>Energy levels (AU)</td>
<td>3.8 ± 0.7</td>
<td>4.1 ± 0.4</td>
<td>3.7 ± 0.6</td>
<td>3.6 ± 0.7</td>
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<td>Motivation (AU)</td>
<td>3.2 ± 0.5</td>
<td>3.2 ± 0.4</td>
<td>2.9 ± 0.6</td>
<td>3.0 ± 0.5</td>
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<td>Muscle soreness (AU)</td>
<td>2.6 ± 0.8</td>
<td>3.0 ± 1.1</td>
<td>3.0 ± 1.2</td>
<td>2.6 ± 1.0</td>
<td>2.7 ± 1.0</td>
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<td>Sleep quality (AU)</td>
<td>3.2 ± 0.5</td>
<td>3.1 ± 0.7†</td>
<td>2.8 ± 0.7</td>
<td>3.5 ± 0.6§</td>
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<td>Sleep duration (min)</td>
<td>432 ± 53</td>
<td>487 ± 53*†</td>
<td>460 ± 42</td>
<td>481 ± 49*</td>
<td>460 ± 57</td>
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<tr>
<td>RHR (beat min⁻¹)</td>
<td>50 ± 6</td>
<td>50 ± 5</td>
<td>49 ± 6</td>
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RHR – Resting heart rate.
Table 2 Results from POMS questionnaire subscales (mean ± SD). *Significantly different to day 5 (p≤0.044). †Significantly different to day 33 (p=0.049).

<table>
<thead>
<tr>
<th></th>
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<th>Day 12</th>
<th>Day 19</th>
<th>Day 26</th>
<th>Day 33</th>
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<tbody>
<tr>
<td>Anger</td>
<td>10 ± 9</td>
<td>5 ± 4*</td>
<td>5 ± 3*†</td>
<td>10 ± 9</td>
<td>11 ± 10</td>
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<td>Depression</td>
<td>13 ± 13</td>
<td>8 ± 11</td>
<td>9 ± 11</td>
<td>16 ± 15</td>
<td>18 ± 12</td>
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<tr>
<td>Tension</td>
<td>10 ± 6</td>
<td>8 ± 4</td>
<td>8 ± 5</td>
<td>12 ± 9</td>
<td>13 ± 7</td>
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<tr>
<td>Vigour</td>
<td>15 ± 7</td>
<td>16 ± 7</td>
<td>15 ± 7</td>
<td>14 ± 5</td>
<td>13 ± 6</td>
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<tr>
<td>Fatigue</td>
<td>9 ± 5</td>
<td>9 ± 5</td>
<td>10 ± 5</td>
<td>11 ± 5</td>
<td>11 ± 5</td>
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<tr>
<td>Confusion</td>
<td>7 ± 5</td>
<td>5 ± 4</td>
<td>6 ± 4</td>
<td>9 ± 7</td>
<td>11 ± 5</td>
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<tr>
<td>TMD</td>
<td>34 ± 39</td>
<td>19 ± 26</td>
<td>23 ± 28</td>
<td>45 ± 41</td>
<td>51 ± 39</td>
</tr>
</tbody>
</table>

TMD – Total mood disturbance.
Table 3 Results from RESTQ-S subscales (mean ± SD). *Significantly different to day 5 (p≤0.023). †Significantly different to days 5, 26 and 33 (p≤0.025).

<table>
<thead>
<tr>
<th></th>
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<th>Day 12</th>
<th>Day 19</th>
<th>Day 26</th>
<th>Day 33</th>
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<tr>
<td>Total stress</td>
<td>2.3 ± 0.9</td>
<td>1.5 ± 0.8*</td>
<td>1.7 ± 0.7*</td>
<td>2.0 ± 1.0*</td>
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<tr>
<td>Total recovery</td>
<td>2.2 ± 1.0</td>
<td>2.8 ± 0.9</td>
<td>2.7 ± 1.3</td>
<td>2.1 ± 0.6</td>
<td>1.9 ± 1.0</td>
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<td>General stress</td>
<td>2.3 ± 1.0</td>
<td>1.5 ± 0.8*</td>
<td>1.7 ± 0.7*</td>
<td>2.0 ± 1.1*</td>
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<td>General recovery</td>
<td>1.9 ± 0.9</td>
<td>2.6 ± 0.9†</td>
<td>2.6 ± 1.2†</td>
<td>1.8 ± 0.5</td>
<td>1.6 ± 1.0</td>
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<td>Sport stress</td>
<td>2.1 ± 0.9</td>
<td>1.6 ± 0.9*</td>
<td>1.8 ± 1.1*</td>
<td>2.1 ± 0.9</td>
<td>1.5 ± 1.1*</td>
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<tr>
<td>Sport recovery</td>
<td>2.6 ± 1.2</td>
<td>3.1 ± 1.1</td>
<td>2.8 ± 1.5</td>
<td>2.6 ± 0.9</td>
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