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Contextualising parasympathetic hyperactivity in functionally overreached athletes with perceptions of training tolerance

Running head: HRV and training tolerance in overreached athletes

Original Investigation

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Abstract

Purpose: Heart rate variability (HRV) as a measure of autonomic function may increase in response to training interventions leading to increases *or* decreases in performance, making HRV interpretation difficult in isolation. This study aimed to contextualise changes in HRV with subjective measures of training tolerance.

Methods: Supine and standing measures of vagal-related HRV (RMSSD), and measures of training tolerance (Daily Analysis of Life Demands for Athletes questionnaire, perception of energy levels, fatigue and muscle soreness) were recorded daily during 1 week of light-training (LT), 2 weeks of heavy-training (HT) and 10 days of tapering (T) in 15 male runners/triathletes. HRV and training tolerance were analysed as rolling seven day averages at LT, HT and T. Performance was assessed following LT, HT and T with a 5 km treadmill time-trial (5TTT).

Results: Time to complete 5TTT likely increased following HT (Effect size [ES] ± 90% confidence interval=0.16±0.06), and then almost certainly decreased following T (ES=-0.34±0.08). Training tolerance worsened after HT (ES≥1.30±0.41) and improved after T (ES≥1.27±0.49). Standing RMSSD very likely increased after HT (ES=0.62±0.26), and likely remained higher than LT at the completion of T (ES=0.38±0.21). Changes in supine RMSSD were possible or likely trivial.

Conclusions: Vagal-related HRV during standing increase in response to functional overreaching (indicating potential parasympathetic hyperactivity), and also to improvements in performance. Thus, additional measures such as training tolerance are required to interpret changes in vagal-related HRV.

Keywords: Overreaching, athletic performance, autonomic nervous system, cardiac regulation

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Introduction

Knowledge of athletic training status facilitates subtle adjustments in training load to optimise athletic performance at important time-points.[1] In well-trained athletes, a simple marker able to accurately assess training status would allow for the recognition of training-induced fatigue that may occur during periods of high training stress without appropriate recovery, resulting in functional overreaching, non-functional overreaching or overtraining.[2] Given that functional overreaching may facilitate supercompensatory performance improvements, provided there is appropriate interpretation of the *short*-term performance decrements and allowance of adequate recovery, it is important to identify this condition before periods of overload training give rise to non-functional overreaching or overtraining. These latter conditions are undesirable states of training since they result in long-term performance decrements without supercompensatory performance improvements.[2]

Recent research has investigated the potential for changes in autonomic nervous system (ANS) function to infer training status.[1] Since the ANS interacts with many physiological systems,[3] examining its responsiveness to changes in training load may indicate the ability to adapt to an exercise stimulus.[4] Furthermore, since the ANS regulates heart rate (HR), research has focussed on inferring training status through autonomic HR regulation as it provides a simple, non-invasive measure of ANS function.[5] HR variability (HRV) is a commonly used measure of autonomic HR regulation to infer training status. Studies investigating the effect of training interventions designed to induce improvements in performance on vagal-related indices of HRV have shown increases in these parameters,[6-10] indicating heightened parasympathetic modulation concurrent with increased physical performance. Greater discrepancy occurs in those studies investigating the effect of training interventions designed to induce a state of overreaching (i.e. a reduction in performance), with vagal-related indices of HRV shown to both increase and decrease.[11-14] These

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discrepancies may partly be the result of the naturally large day-to-day variation in measures of resting HRV (CV of ~12.5%[15]), potentially caused by subtle changes in environmental conditions,[16] sleep quality and quantity,[17] noise and light,[18] psychological stress[19] and acute fatigue.[20]

More recently, Le Meur at al.[17] utilised weekly averages of vagal-related HRV (i.e. average of recordings taken each day during a training intervention) to demonstrate an increase in parasympathetic modulation in response to heavy periods of training leading to functional overreaching. These weekly average values of HRV have been shown to be more sensitive to changes in training load in comparison to isolated measures (i.e. the recordings taken on the days pre- and post-intervention), as a result of attenuating the natural day-to-day variation in resting HRV.[21] Thus, it appears plausible that the lack of agreement in previous studies investigating the effect of heavy training leading to overreaching on resting HRV may be due to the utilisation of isolated measures, and consequently that average values should be employed to aid effective athletic monitoring. This lack of agreement between previous studies should not be ignored however, and it is important that the fatigue-induced increase in parasympathetic modulation shown by Le Meur at al.[17] when utilising weekly averages of HRV be further validated in athletes of various levels and sports, with different training protocols to ensure that it can be confidently applied to athlete management.

Additionally, the increase in vagal-related indices of HRV under conditions of fatigue make the interpretation of changes in HRV following changes in training load difficult, since it appears that increases in HRV occur when athletic performance is improved in response to optimal training load, *and* attenuated following periods of overreaching. Thus supplementary markers of training tolerance (e.g. subjective questionnaires) may be required to put changes in HRV into context. Consequently, the aim of the present study was to determine the effect of overload training and subsequent taper on parasympathetic HR modulation and training

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tolerance, and assess whether these markers of training tolerance were able to put training-induced changes in parasympathetic HR modulation into context to facilitate effective monitoring of athletes in the field.

Methods

Twenty-two male runners or triathletes were recruited from local clubs in Adelaide, South Australia. The study was approved by the Human Research Ethics Committee of the University of South Australia in accordance with the Declaration of Helsinki, and all volunteers provided written informed consent prior to participating.

Pre-study familiarisation allowed participants to be habituated with the requirements of the study and testing procedures, and for determination of their peak HR during a maximal five kilometre treadmill time-trial (5TTT). Participants then had their 5TTT performance assessed on three separate occasions; after seven days of light training (LT; baseline), fourteen days of heavy training (HT; overreached state) and 10 days of tapering (T; recovered and adapted state). These assessments occurred the day after the last completed training session to avoid any effect of acute fatigue. The effect of this training on daily measures of HRV and markers of training tolerance were also investigated.

The time taken to run five kilometres on a motorised treadmill (Trackmaster TMX425CP, Full Vision Inc., Newton, KS, USA) was recorded as the measure of exercise performance during the 5TTT. Participants chose their preferred starting speed during familiarisation which remained constant across all experimental visits. Participants were blinded to running time and speed throughout the 5TTT, but were free to adjust the speed up and down as desired in order to complete the five kilometres in the fastest time possible. Reliability of the 5TTT in our laboratory in trained runners was determined to be excellent (CV=1.3%).

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RR intervals were recorded every morning at home upon wakening and after emptying the urinary bladder using a personal HR monitor (RS800CX, Polar Electro Oy, Kempele, Finland). RR intervals were measured for determination of HRV during three minutes of quiet rest in supine and standing postures. Although it has been postulated that supine measures of HRV are less sensitive to change than standing measures due to their ability to become saturated,[22] this has yet to be shown conclusively in overreached athletes,[17] and consequently, both measures were performed. Daily RR interval data were downloaded to Polar Protrainer 5 software (Polar Electro Oy, Kempele, Finland) where artefacts or ectopic heart beats were removed through Polar's automatic filtering. Data were then exported to HRV analysis software (Kubios HRV Analysis, version 2.0 beta 1, The Biomedical Signals Analysis Group, University of Kuopio, Finland) where any remaining artefacts or ectopic heart beats were manually removed, and the final two minutes of recording in supine and standing positions were ultimately analysed. The root-mean-square difference of successive normal R-R intervals (RMSSD) as an index of vagal-related HR modulation was analysed. This index was selected as it can be recorded over a short period of time[23] and has reduced sensitivity to respiration rates,[24] which makes it suitable for athletic monitoring in the field. RMSSD, RR interval and Ln RMSSD: RR interval were analysed as a rolling seven day average and presented as values on the final day of LT (LT7), the seventh day of HT (HT7), the 14th day of HT (HT14), the fifth day of T (T5) and the 10th day of T (T10).

Subjective measures of training tolerance were determined daily throughout the training intervention via a Daily Analysis of Life Demands for Athletes (DALDA) questionnaire, which has been shown to detect changes in mood resulting from periods of overload training in athletes.[25] The DALDA was scored on a three point scale (worse than normal, normal, better than normal). Perceptions of mood state, energy levels, stress, fatigue and muscle soreness were assessed using 10 point scales, where a score of 1 reflected negative

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adaptations with regard to mood and energy levels, but positive adaptations in stress, fatigue and muscle soreness, and the opposite for scores of 10.

Training intensities were based on percentages of peak HR determined during familiarisation. LT required seven days of running exercise for 30 minutes per day at 65-75% of peak HR, with a rest day on day seven preceding post-LT testing, such that it would allow participants to be rested and recovered from any pre-study training prior to starting HT. HT required fourteen days of running exercise for 66 minutes per day, with 36% of the training performed above 88% of peak HR, and was intended to induce substantial fatigue from which participants would not recover by the day following the final training session. Details of the HT program are provided in Table 1. Tapering lasted 10 days with rest days one and nine. Seven of the eight training sessions during taper required 30 minutes per day at 65-75% of peak HR, with one interval session (four repeats of three minutes at 69-81% peak HR followed by two minutes at 88-92% peak HR) conducted on day seven to provide participants with variety in training during this training phase. HR data were recorded at 15 second intervals during training sessions to determine training load during each period, which was quantified using Training Impulse (TRIMP)[26] (duration in minutes multiplied by % of peak HR). Additionally, daily TRIMP for zones 4 and 5 (high-intensity training zones) were combined to determine the progressive effect of HT on the ability to perform high-intensity training.

**** *Insert Table 1 here* ****

Data were analysed using magnitude-based inferences as these analyses indicate the magnitude of an effect, which may be considered more relevant to practical detection of functional overreaching, non-functional overreaching or overtraining than statistically significant effects. Data were presented as mean ± standard deviation (SD), and also effect

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size (ES) with 90% confidence intervals. All data were log transformed before analysis to reduce bias arising from non-uniformity of error,[27] however non-HRV variables were presented in their natural form for ease of interpretation. Changes in variables after each training period (LT7, HT7, HT14, T5 and T10) were analysed using a modified statistical spreadsheet,[28] which calculates ES between time-points of interest using pooled standard deviation. Threshold values for ES statistics were ≤0.2 (trivial), >0.2 (small), >0.6 (moderate), >1.2 (large), >2.0 (very large), and >4.0 (extremely large).[27] Probabilities to establish whether the true (unknown) differences were lower, similar, or higher than the smallest worthwhile change (as calculated from each variable's CV) were also calculated. Chances of higher or lower differences were evaluated qualitatively as follows: <1%, almost certainly not; 1–5%, very unlikely; 5–25%, unlikely; 25–75%, possibly; 75–95%, likely; 95–99%, very likely; and >99%, almost certain. If the chance of higher and lower differences was >5%, the true difference was assessed as unclear. Inter-variable relationships were assessed using Pearson's correlation and presented as r value with 90% confidence intervals, where r values were evaluated as follows: 0.0-0.1, trivial; 0.1-0.3, small; 0.3-0.5, moderate; 0.5-0.7, large; 0.7-0.9, very large; 0.9-1.0, nearly perfect.

Results

Five of the 22 recruited participants did not complete the study due to injury or illness, or were unable to tolerate the demands of HT. Two of the 17 completed participants were excluded due to poor compliance with the study's testing and training commitments. Thus, data for 15 participants (age 35.1±7.0 years with body mass 76.5±8.6 kg) were included for analysis.

Daily TRIMP almost certainly increased from 1978±307 units at LT7 to 4833±983 units at HT14 (ES±90% confidence interval=4.63±0.5) and then almost certainly decreased to 2038±572 units from HT14 to T10 (4.99±0.76). Additionally, zone 4 and 5 TRIMP decreased

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by 99 units/day during HT (Figure 3a), meaning that there was a near perfect linear decline in the ability to maintain TRIMP based high intensity training during the 14 consecutive days of HT (r=-0.93 ± 0.08).

The time taken to complete 5TTT was 19:06±2:10 min:sec at LT7, which likely increased at HT14 (0.16±0.07), and then almost certainly decreased from HT14 to T10 (-0.34±0.08). Overall, these changes resulted in a very likely improvement from LT7 to T10 (-0.17±0.07; Figure 1a). Peak HR during 5TTT was 188±8 bpm at LT7, and was almost certainly decreased at HT14 (-1.24±0.28), before almost certainly increasing at T10 (in comparison to HT14; 0.97±0.23; Figure 1b).

**** *Insert Figure 1 here* ****

Standing values of RR interval, Ln RMSSD and Ln RMSSD: RR interval were 821±121 ms, 3.25±0.29 ms and 3.95±0.46 units, respectively, at LT7. Ln RMSSD very likely increased at HT14 in comparison to LT7 (0.62±0.26), and remained likely higher at T10 than LT7 (0.38±0.21; Figure 2b). Changes in RR interval and Ln RMSSD: RR interval throughout the intervention were assessed as likely trivial to almost certainly trivial (Figure 2a and c).

Supine values of RR interval, Ln RMSSD and Ln RMSSD: RR interval were 1159±170 ms, 4.04±0.53 ms and 3.50±0.47 units, respectively, at LT7. Figure 2 also shows the unclear, possible or trivial changes in these supine measures throughout the intervention.

**** *Insert Figure 2 here* ****

Figure 3 shows the day-to-day changes in rolling seven day vagal-related HRV during HT. Nearly perfect positive correlations were found between the 14 days of HT and changes in Ln RMSSD from LT7 in the standing position (r=0.98±0.03; Figure 3b), such that Ln RMSSD increased by 0.03 ms/day during HT. In comparison to LT7, changes in Ln RMSSD were

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222 possible at HT days 6-9, likely at days 10-12 and very likely at days 13 and 14. Changes in
223 Ln RMSSD from day 11 to day 14 were very likely to almost certainly trivial. Day-to-day
224 changes in Ln RMSSD were nearly perfectly correlated with zone 4 and 5 TRIMP during HT
225 (r=0.98±0.03; Figure 3c).

226 **** *Insert Figure 3 here* ****

227 Perceptions of fatigue, muscle soreness, energy levels, mood state, stress and the number of
228 'worse than normal' scores on the DALDA were 3.8±1.6, 3.1±1.3, 6.7±1.3, 7.2±1.3, 3.6±1.6
229 and 1.5±1.3, respectively, at LT7. Figure 4 shows the changes in these variables. Fatigue
230 (2.01±0.52), muscle soreness (2.25±0.51) and DALDA 'worse than normal' scores
231 (2.73±0.66) were almost certainly increased at HT14, while perceptions of energy levels were
232 almost certainly decreased (-1.30±0.41) at this time-point. Fatigue (-2.10±0.56), muscle
233 soreness (-2.12±0.67) and DALDA 'worse than normal' scores (-2.22±0.50) then almost
234 certainly decreased at T10, while energy levels almost certainly increased (1.27±0.49).
235 Changes in perceptions of mood state and stress throughout the intervention were assessed as
236 possible or very likely trivial.

237 **** *Insert Figure 4 here* ****

238 **Discussion**

239 The primary finding in the present study was that both decrements and improvements in
240 exercise performance induced by overload training and subsequent taper, respectively, were
241 accompanied by an increase in vagal-related HRV. These increases in parasympathetic
242 modulation during the different phases of training were able to be contextualised through
243 perceptions of training tolerance.

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The performance impairment induced by a period of HT was accompanied by a moderate increase in parasympathetic activity as assessed by RMSSD. This finding supports recent research by Le Meur et al.[17] who also demonstrated a moderate increase in RMSSD following a three week period of overload training, in which endurance performance was impaired. Le Meur et al.[17] interpreted this increase in RMSSD as a parasympathetic hyperactivity in the functionally overreached state, however the mechanism for this hyperactivity and why it concurrently occurs with attenuated performance is not well understood presently. Nonetheless, given that parasympathetic HR modulation may not be completely withdrawn even during high-intensity exercise,[29] hyperactive parasympathetic modulation may limit the ability to fully engage the sympathetic nervous system during maximal exercise, as evidenced by the reduction in peak HR following HT (a finding present in other overreaching studies[5]), leading to a reduction in maximal cardiac output and diminished performance. This hypothesis may be supported by the present study's correlation between RMSSD and zone 4 and 5 TRIMP during the fourteen consecutive days of HT, since this demonstrates that as the progressive parasympathetic hyperactivity (as a potential restraint of sympathetic nervous system engagement) occurred, the TRIMP based amount of high-intensity training, which is reliant on heightened sympathetic modulation, was reduced. Of course it needs to be acknowledged that parasympathetic hyperactivity may only in part contribute to attenuated sympathetic activity and cardiac output, since other factors, including reduced catecholamine excretion during exercise and/or desensitisation of cardiac beta-adrenergic receptors, have also been demonstrated.[30]

The present study also showed that the increase in parasympathetic modulation above LT7 levels began only after 6 days of HT (Figure 1b and c), and then reached a potential ceiling at day 11, such that changes were very likely to almost certainly trivial between days 11, 12, 13 and 14. The latter finding may indicate that athletes can tolerate additional days of HT after

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this point of stagnation and still remain in a functionally overreached state rather than progress to a non-functionally overreached state, although the exact amount of time that such tolerance may be sustained cannot be confirmed from the present study as HT was ceased after 14 days.

Following the 10 day taper, performance was improved both in comparison to HT (indicating that the participants had been functionally overreached), and LT (indicating a supercompensatory performance adaptation). The increased RMSSD that was evident at the end of HT persisted following T, such that it was greater than at LT, and not different from the corresponding value at the completion of HT, although it should be noted that the magnitude of increase in parasympathetic modulation compared to baseline was greater in the fatigued state than in the supercompensated state, which may indicate a threshold for increases in parasympathetic modulation reflecting negative and positive training adaptations. This finding is in agreement with Le Meur et al.,[17] who showed that RMSSD was elevated from its baseline level following overload training and a subsequent seven day taper that allowed athletes to recover and adapt to the stimulus provided by the overload training. These findings suggest that a period of overload training and subsequent taper induce an overall increase in parasympathetic HR modulation that may represent a positive adaptation to training since there was an increase in performance in comparison to baseline levels following the taper. This overall increase in RMSSD following tapering is supported by studies showing increased parasympathetic modulation following training interventions designed to improve performance.[6-10]

The increased RMSSD following HT makes changes in this parameter difficult to interpret in isolation given that it was also increased following T (compared to LT) in this study and in the study by Le Meur et al.[17] These results demonstrate that training-induced increases in RMSSD may be indicative of both a positive (improved performance) *and* a negative

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294 (impaired performance) response to training, and thus that additional measures are required to
295 put these changes into context. Recently, Plews et al.[21] and Buchheit[1] have suggested that
296 presenting vagal-related indices of HRV as a ratio of RR interval length can provide insight
297 into underlying physiological mechanisms during training, and as such may be able to
298 differentiate between a positive and negative training response. A novel finding in the present
299 study however, was that the ratio of Ln RMSSD to RR interval was unchanged throughout
300 the intervention. Thus, this ratio of vagal-related HRV to RR interval length was not able to
301 contextualise the changes in vagal-related HRV in the present context of functional
302 overreaching.

303 The present study did however, show that subjective measures of training tolerance were able
304 contextualise the concurrent changes in vagal-related HRV. Perceptions of energy levels,
305 fatigue, muscle soreness and DALDA 'worse than normal' scores were almost certainly
306 altered in the expected direction following HT, and then returned to baseline levels following
307 T, demonstrating that they were able to differentiate between a positive and negative
308 adaptation in parasympathetic HR modulation in the present context. For example, should
309 RMSSD increase in response to training and be accompanied by large to very large negative
310 changes in measures of training tolerance, this increase is likely an indication of overreaching
311 leading to attenuated performance. Conversely, an increase in RMSSD in the absence of any
312 negative change in these variables likely indicates a positive training adaptation facilitating
313 improved performance. Perceptions of mood state and stress were unchanged during the
314 training intervention and these variables may therefore be insensitive to changes in training
315 status in the athletes involved in this study.

316 An important methodological finding in this study was that RMSSD assessed in the supine
317 position was less sensitive in detecting the parasympathetic hyperactivity following HT,
318 suggesting that standing measures of HRV are more appropriate in the present context. This

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is a somewhat similar finding to Le Meur et al.[17] who, despite showing an almost certain increase in supine RMSSD following HT, also demonstrated a reduced magnitude of change when comparing supine (ES=0.38) to standing (ES=0.62) values.

The present study may be considered somewhat limited by not utilising a control group, as the comparison of this group to a training group would allow definitive conclusion about the sensitivity of vagal-related HRV to increases and decreases in training load. However, since changes in HR and RMSSD in Le Meur et al.'s[17] control group fell within their natural day-to-day variability, it was assumed that changes in variables presented in this study would also fall within their respective day-to-day variability in a group of athletes *not* performing periods of overload training and subsequent taper, and thus a control group was not employed.

Conclusion

The results of this study suggest that RMSSD is increased in response to both a period of overload training leading to attenuated performance, and a period of taper allowing for supercompensatory performance improvements. Consequently, this study highlights the need for additional measures, such as subjective training tolerance, to put changes in RMSSD into context and allow for effective monitoring in the field. Additionally, supine measures of RR interval and HRV were unaffected by the training intervention utilised in the present study and may thus be considered less appropriate for effective athlete monitoring in this context.

Practical Applications

- Vagal-related HRV increases in response to decrements *and* improvements in performance.
- Subjective measures of training tolerance may be utilised to facilitate appropriate interpretation of HRV.

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- Appropriate HRV interpretation will allow coaches to accurately infer athletic training status, enabling the subtle adjustments in training load required to optimise performance at important time-points.

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435 **Tables**

436 **Table 1.** Heavy training program overview

Intensity (% Peak HR)	Duration (mins/day)
Zone 1: < 69	10
Zone 2: 69 - 81	16
Zone 3: 82 - 87	16
Zone 4: 88 - 94	16
Zone 5: > 94	8
Total Duration (mins/day)	**66**

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Figure legends

Figure 1. Percentage change in **a.** time to complete 5TTT and **b.** peak heart rate during 5TTT from LT7.

Data are mean ± 90% confidence level. Grey shaded areas represent the smallest worthwhile change for each variable. 5TTT, five kilometre treadmill time-trial; HR, heart rate; LT7, seventh day of light training; HT14, fourteenth day of heavy training; T10, tenth day of tapering; dotted circle, likely chance of practically meaningful difference in value from LT7; dashed circle, very likely chance of practically meaningful difference in value from LT7; continuous circle, almost certain chance of practically meaningful difference in value from LT7; continuous rectangle, almost certain chance of practically meaningful difference in value from HT14.

Figure 2. Percentage change in **a.** RR interval, **b.** Ln RMSSD and **c.** Ln RMSSD: RR interval from LT7.

Data are mean ± 90% confidence level. Grey shaded areas represent the smallest worthwhile change for each variable. Ln RMSSD, natural logarithm of the root-mean-square difference of successive normal R-R intervals; Ln RMSSD: RR interval, natural logarithm of the root-mean-square difference of successive normal R-R intervals normalised to RR interval; LT7, rolling seven day average on the seventh day of light training; HT7, rolling seven day average on the seventh day of heavy training; HT14, rolling seven day average on the fourteenth day of heavy training; T5, rolling seven day average on the fifth day of tapering; T10, rolling seven day average on the tenth day of tapering; dashed line, supine measures; continuous line, standing measures; dotted circle, likely chance of practically meaningful difference in value from LT7; dashed circle, very likely chance of practically meaningful difference in value

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from LT7; dotted rectangle, likely chance of practically meaningful difference in value from HT14.

Figure 3. a. Relationship between zone 4 and 5 training impulse and day of heavy training, **b.** Relationship between changes in standing 7 day rolling average Ln RMSSD from LT7 and day of heavy training and **c.** Relationship between changes in standing 7 day rolling average Ln RMSSD from LT7 and zone 4 and 5 training impulse during heavy training.

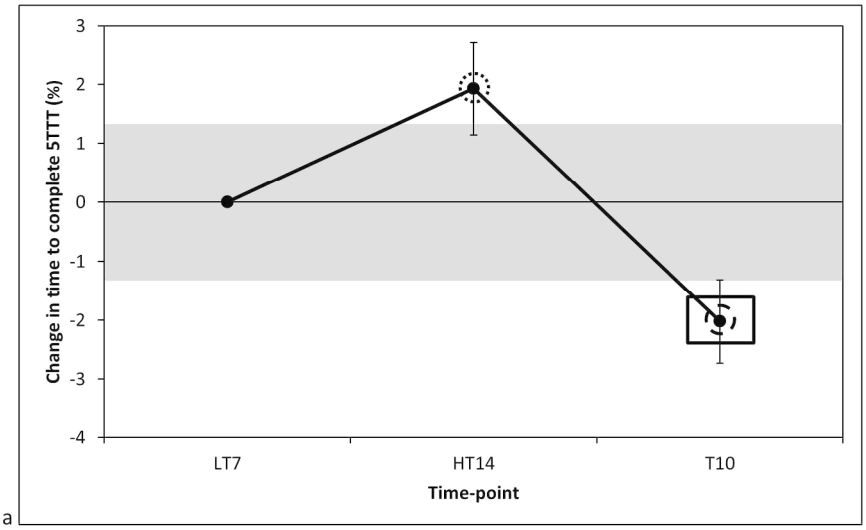
AU, arbitrary units; ms, milliseconds; Ln RMSSD, natural logarithm of the root-mean-square difference of successive normal R-R intervals; LT7, seven days of light training; TRIMP, training impulse; a, possible chance of higher values between days; b, likely chance of higher values between days; c, very likely chance of higher values between days.

Figure 4. Percentage change in **a.** DALDA 'worse than normal' score, **b.** fatigue, **c.** muscle soreness, **d.** energy levels, **e.** mood state and **f.** stress from LT7.

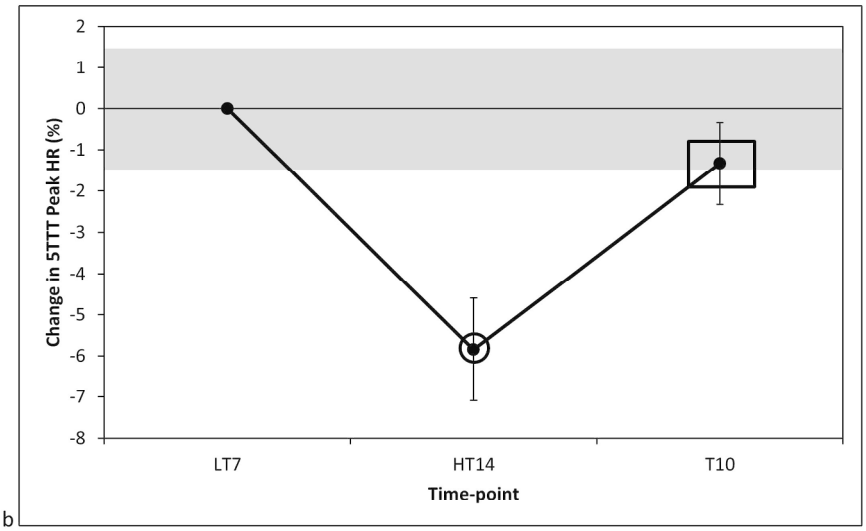
Data are mean ± 90% confidence level. Grey shaded areas represent the smallest worthwhile change for each variable. DALDA, Daily Analysis of Life Demands for Athletes questionnaire, LT7, rolling seven day average on the seventh day of light training; HT7, rolling seven day average on the seventh day of heavy training; HT14, rolling seven day average on the fourteenth day of heavy training; T5, rolling seven day average on the fifth day of tapering; T10, rolling seven day average on the tenth day of tapering; dotted circle, likely chance of practically meaningful difference in value from LT7; dashed circle, very likely chance of practically meaningful difference in value from LT7; continuous circle, almost certain chance of practically meaningful difference in value from LT7; dashed rectangle, very likely chance of practically meaningful difference in value from HT14; continuous rectangle, almost certain chance of practically meaningful difference in value from HT14.

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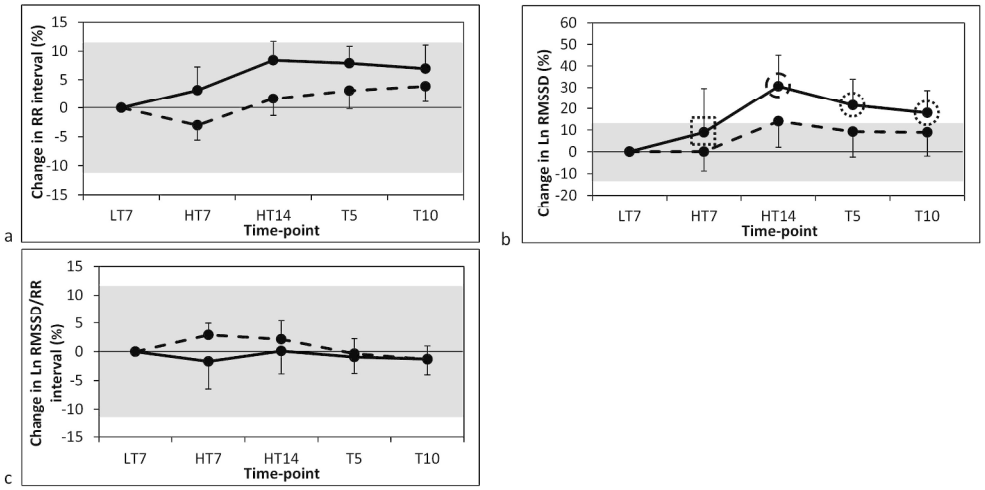


a



b

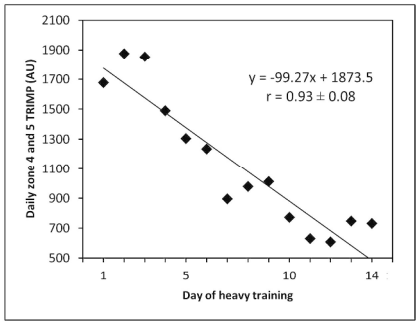
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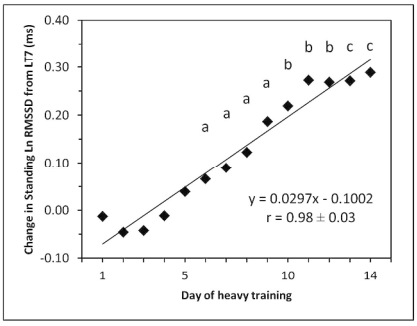
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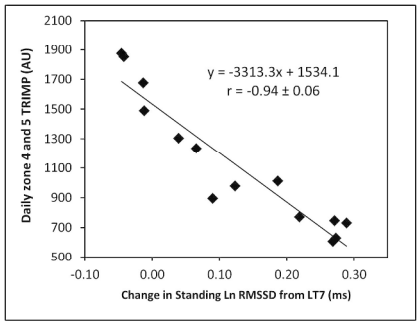
a.



b.

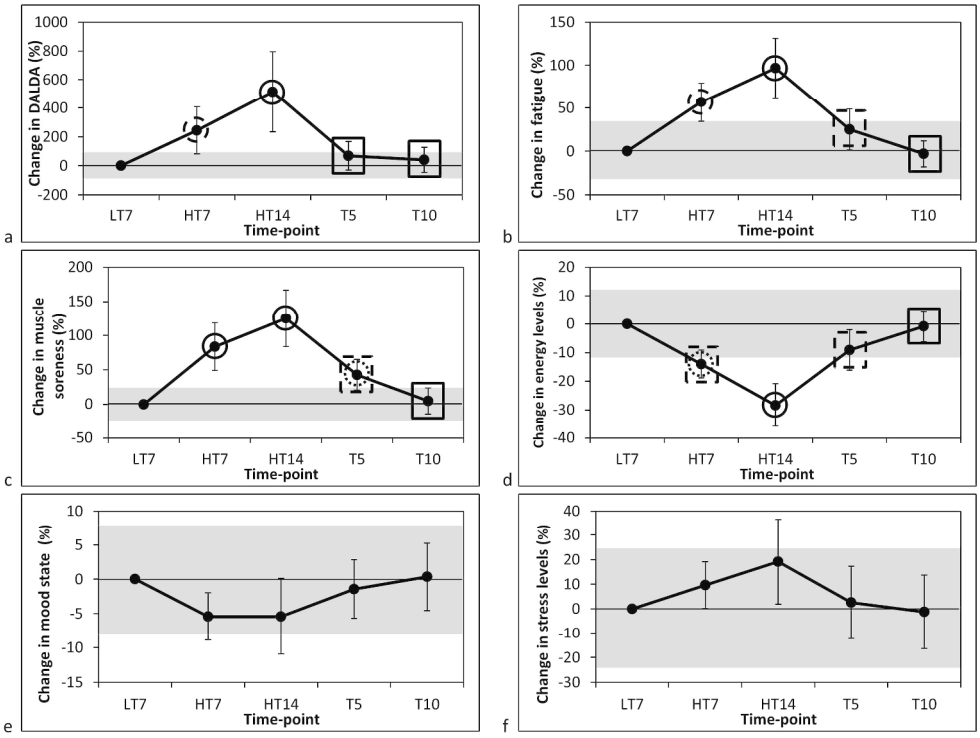


c.



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