Maximal exercise limitation in functionally overreached triathletes: role of cardiac adrenergic stimulation

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Maximal exercise limitation in functionally overreached triathletes: role of cardiac adrenergic stimulation. J Appl Physiol 117: 214–222, 2014. First published June 12, 2014; doi:10.1152/japplphysiol.00191.2014.—Functional overreaching (F-OR) induced by heavy load endurance training programs has been associated with reduced heart rate values both at rest and during exercise. Because this phenomenon may reflect an impairment of cardiac response, this research was conducted to test this hypothesis. Thirty-five experienced male triathletes were tested (11 control and 24 overload subjects) before overloading (Pre), immediately after overloading (Mid), and after a 2-wk taper period (Post). Physiological responses were assessed during an incremental cycling protocol to volitional exhaustion, including catecholamines release, oxygen uptake (VO₂), arteriovenous O₂ difference, cardiac output (Q), and systolic (SBP) and diastolic blood pressure (DBP). Twelve subjects of the overload group developed signs of F-OR at Mid (decreased performance with concomitant high perceived fatigue), while 12 others did not [acute fatigue group (AF)]. VO₂max was reduced only in F-OR subjects at Mid. Lower Q and SBP values with greater arteriovenous O₂ difference were reported in F-OR subjects at all exercising intensities, while no significant change was observed in the control and AF groups. A concomitant decrease in epinephrine excretion was reported only in the F-OR group. All values returned to baseline at Post. Following an overload endurance training program leading to F-OR, the cardiac response to exhaustive exercise is transiently impaired, possibly due to reduced epinephrine excretion. This finding is likely to explain the complex process of underperformance syndrome experienced by F-OR endurance athletes during heavy load programs.

However, if the balance between appropriate training stress and adequate recovery is disrupted, an abnormal training response may occur and a state of functional overreaching (F-OR) may develop. This process is often used voluntarily when going on a “training camp” and will lead to a temporary performance decrement, which is followed by improved performance. Nevertheless, the evidence for a maximized supercompensation effect after deliberate periods of intensified training leading to F-OR is not abundant (24). Aubry et al. (1) have recently shown that developing F-OR may even reduce the performance supercompensation during a subsequent simulated taper phase. By contrast, the athletes who performed the same intensified training period while successfully avoiding F-OR during this study showed greater performance gains. Additionally, F-OR has been shown to be detrimental to the athlete’s performance, immune function, sleep, and mood (14, 24). Understanding the underlying mechanisms leading to F-OR may therefore be of particular importance for athletes, coaches, medical doctors, and scientists. However, critical reviews of existing scientific literature always concluded that the underlying cause(s) of F-OR in endurance athlete remains elusive (24).

A reduced chronotropic response has been observed during exercise in F-OR endurance athletes (12). Recently, Le Meur et al. (19) used a multifactorial analysis including physiological, cognitive, biomechanical, and perceptual parameters to show that the decrease in heart rate (HR) at submaximal and maximal intensities was the most discriminating response between F-OR athletes and control athletes. However, it remained unclear whether this modified chronotropic response was a sign of an impaired cardiac response to exercise in F-OR athletes. Additionally, some authors suggested that alterations in the autonomic response may be involved in the etiology of F-OR (22), but this hypothesis, which may explain the reduced chronotropic response to exercise, has never been tested.

The purpose of the present study was to monitor the cardiovascular response at rest and during exercise in endurance athletes progressively driven to F-OR by a prolonged period of overload training. In the light of past research, we hypothesized that cardiac response would be impaired during exercise in F-OR athletes. Additionally, we...
investigated whether this potential change in cardiovascular response would be accompanied by changes in catecholamine release at exercise.

**METHODS**

**Subjects**

Forty well-trained male triathletes volunteered to participate in this study. During the experimental period, five subjects did not follow the protocol due to injury or personal obligations and were excluded from subsequent analyses. The final sample was included in analysis was \( n = 35 \). The experimental design of the study was approved by the Ethical Committee of Saint-Germain-en-Laye (Acceptance No.12048) and was done in accordance with guidelines set forth in the Declaration of Helsinki. Before participation, subjects underwent medical assessment with a cardiologist to ensure that they presented normal electrocardiographic patterns and could participate in this study. After comprehensive verbal and written explanations of the study, all subjects gave their written informed consent to participate.

The subjects were randomly assigned to either the control group (\( n = 11 \)) or the overload training group (\( n = 24 \)) according to a matched group experimental design based on peak power output determined during a familiarization test (PPO_fam, see description below), maximal oxygen uptake (V\( \dot{O}_2 \)max), and past experience in endurance sports.

**Study Design**

The protocol is illustrated in Fig. 1. The training of each triathlete was monitored for a period of 9 wk, which was divided into four distinct phases. The two first phases were similar for all participants. The first phase consisted of 3 wk during which the subjects completed their usual training. The second phase consisted of 1 wk of moderate training load during which the subjects were asked to reduce their habitual training volume by \(~50\%\) while maintaining the training intensity, according to the guidelines provided by Bosquet et al. (5) concerning optimal tapering strategies. During the third period, the overload training group completed a 3-wk overload program designed to deliberately overreach the subjects: the duration of each training session of the classic training period was increased by 30%. The control group repeated its usual training program during this period. Thereafter, all the participants completed a 2-wk taper period, during which they were asked to decrease their normal training volume by \(~50\%\). During the first phase, the subjects completed a maximal performance test to be familiarized with the testing used during the protocol (described below). At the end of phases II and III, the triathletes performed a maximal incremental cycling test. For each participant, the test was completed systematically the same day of the week at the same hour. To ensure that performance variations during the maximal incremental tests were due to the global training regimen and not to the training session(s) performed the day before each test, the subjects were required to respect a training day off before each testing session. During the 48 h before each test, the triathletes were also required to follow a nutritional and hydration guidelines to ensure adequate muscle glycogen store resynthesis and a well-hydrated state on each testing day. They were instructed to eat until satiety was reached during each meal. Breakfast consisted of a variety of macronutrients from both solid and liquid energy sources. The selected foods included an assortment of cereals, bread, fruit, yogurt, milk, juice, ham, and cheese. For lunch and dinner, the subjects consumed a mixed salad as starter and then white meat during lunch and fish during dinner. The side plate consisted of a mixed of 50% carbohydrates (i.e., pasta, rice, and noodles) and 50% of vegetables (i.e., green beans, broccoli, and tomatoes). One piece of fruit and 125 ml of yogurt were added as dessert at both lunch and dinner. To ensure the subjects were well-hydrated on each testing day, they were instructed to follow a hydration plan with two glasses and 500-ml intake of water, during and between each meal, respectively. They were asked to drink more if they observed their urine to be dark. The participants were reminded of these recommendations before each test by e-mail or phone call.

![Fig. 1. Schematic representation of the experimental protocol. Bicycle symbols represent maximal incremental cycling tests.](http://jap.physiology.org/ by 10.220.33.4 on April 5, 2017)
Measurements

Mood state. Before exercise testing, subjects were asked to complete the profile of mood state (POMS) questionnaire to assess specific mood states including vigor and fatigue (23).

Performance and VO₂max. VO₂max was tested on an electronically braked cycle ergometer (Excalibur Sport, Lode). Positions of the handlebars and seat height were adjusted to the measures used by the athletes on their own bike. The test was performed until complete exhaustion to determine VO₂max and PPO. The completion of the test was confirmed with a plateau in VO₂max despite an increase in power output or a respiratory exchange ratio value of 1.15 (15). The exercise protocol started with a warm-up of 5 min at a workload of 100 W, followed by 5 min at 150 W and 5 min at 200 W. Thereafter, further increments of 25 W were added every 2 min until volitional exhaustion was confirmed with a plateau in VO₂max despite an increase in power output. Heart rate (HR) was measured every 5 s during each testing session over the entire protocol. The endurance time distribution was subsequently calculated for each athlete.

After the test, breath-by-breath values were visually controlled and averaged over 30 s. The highest average value was determined to be VO₂max. PPO was calculated as PPO = Wcompl + 25 × (t/120) (18), where Wcompl is the last completed workload and t is the number of seconds in Wcompl.

Cardiac parameters. An impedance cardiography device (Physioflow Enduro, Manatec) was used in this study to determine HR, stroke volume (SV), and cardiac output (Q) during rest and exercise. The Physioflow was carefully calibrated before each test according to the manufacturer recommendations. This device has been previously validated against the direct Fick method during rest and submaximal and maximal incremental exercise (7, 28). In similar experimental conditions to those employed in the present study (exercise protocol and subjects fitness level), the coefficients of variations for SV and at peak exercise using the Physioflow during repeat cycle ergometer VO₂max test spaced at least 2 days apart were 3.6 and 3.5%, respectively (n = 20, VO₂max: 60.5 ± 8.6 ml·min⁻¹·kg⁻¹) (16).

Arteriovenous O₂ difference. The arteriovenous O₂ difference was estimated by rearrangement of the Fick equation:

\[(a - \bar{v})O_2\text{diff} = VO_2/Q\]

Arterial pressures. Diastolic (DBP) and systolic blood pressures (SBP) were measured in the arm at rest (cycling position) and for each protocol started with a warm-up of 5 min at a workload of 100 W, followed by 5 min at 150 W and 5 min at 200 W. Thereafter, further increments of 25 W were added every 2 min until volitional exhaustion. O₂ and CO₂ concentration in the expired gas was continuously measured and monitored as breath-by-breath values (Quark, Cosmed). The gas analyzers and the flowmeter of the applied spirometer were calibrated before each test.

Blood lactate concentration. Fingertip blood samples (5 µl) were collected to determine [La⁻]ₜ values at the end of each cycling step, immediately at exercise cessation, and every 90 s until [La⁻]ₜ began to decrease (Lactate Pro; ARKAY) (27). The accuracy of the analyzer was verified before each test using standards.

Blood volume and catecholamines. A 22-G catheter was inserted into an antecubital vein while the subjects rested quietly in a chair ~30 min before the maximal cycling test to measure hemoglobin concentration. The relative changes in blood volume (BV) at rest from Pre were calculated according to the following equation (9):

\[
BV(\%_{Pre}) = \left(100 \times \frac{Hb_{Pre}}{Hb_{Mid}}\right)
\]

where Hb represented the blood hemoglobin concentration.

Subjects then rested for 10 min after catheterization to allow for normalization of catecholamine levels because of the catheter insertion. Approximately 6 ml of blood were obtained and placed into ethylenediaminetetraacetic acid tubes at rest and during the last 30 s of each subsequent work stage: ~40% PPOmax (i1), ~60% PPOmax (i2), ~80% PPOmax (i3), and immediately after exercise cessation (Max). i1, i2, and i3 were calculated relative to the PPOmax and used before overloading (Pre), immediately after overloading (Mid), and after a 2-wk taper period (Post). This way, plasma norepinephrine ([NEp]) and epinephrine ([Ep]) concentrations were determined for the same absolute power output values at rest, i1, i2, and i3 throughout the experiment to abolish the confounding effect of exercise intensity on these parameters. The tubes were immediately placed on ice and centrifuged within 5 min of collection. The plasma and the serum samples were aliquoted and stored at −80°C until analysis. [NEp] and [Ep] were determined using high-performance liquid chromatography with electrochemical detection. All samples were analyzed the same day for each participant. The within-day coefficients of variation were <5% for both [NEp] and [Ep].

Assessment of the F-OR Syndrome

To determine the reproducibility of performance during the maximal running test and to identify F-OR athletes in the overload group, the typical error in performance was calculated in the control group (i.e., change in performance divided by \sqrt{2}). To be diagnosed as F-OR, athletes of the overload group had to reveal 1) a performance decrement higher than this threshold (OR threshold), 2) a concomitant high perceived fatigue, and 3) a performance supercompensation from Pre during the subsequent taper (20).

Training Monitoring

Training volume and intensity were calculated on the basis of recordings from HR monitors (Polar, Kempele, Finland). For all subjects, HR was measured every 5 s during each training session over the entire protocol. The endurance time distribution was subsequently calculated for each athlete.
calculated using three HR zones: 1) ≤HR at 2 mmol/l, 2) between HR at 2 mmol/l and HR at LT, and 3) HR values superior to HR at lactate threshold (LT). Given that the relationship between [La\(^{-}\)]\(_{b}\) and HR values during exercise can be influenced by a heavy training load program (19), the reference HR values were reassessed after each incremental cycling test.

**Data Analysis**

All cardiovascular and metabolic parameters were subsequently averaged for each cycling intensity. Given that interindividual differences in PPO were observed, the relationship between each variable and exercise intensity was used to determine the value of this parameter for the following intensities: 0, 70, 80, 90, and 100% of peak power output achieved after the overload period (PPO\(_{\text{max}}\)). We used PPO\(_{\text{max}}\) to abolish the confounding effect of exercise intensity on the variables measured at exercise. This way, within-group change in each variable was analyzed for the same absolute power outputs (except PPO and peak values of VO\(_{2}\), Q, HR, SV, (a-v)O\(_{2}\) difference, and [La\(^{-}\)]\(_{b}\)), while respecting similar relative intensities for all the participants.

**Table 2. Mean values ± SD at baseline, after the overload period, and after the 2-wk taper period in the 3 experimental groups**

<table>
<thead>
<tr>
<th>Variables/Groups</th>
<th>Pre</th>
<th>Mid</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPO, W</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>352 ± 26</td>
<td>355 ± 25</td>
<td>357 ± 27</td>
</tr>
<tr>
<td>AF</td>
<td>357 ± 26</td>
<td>364 ± 28</td>
<td>372 ± 26(\dagger)</td>
</tr>
<tr>
<td>F-OR</td>
<td>366 ± 36</td>
<td>358 ± 35(\dagger)</td>
<td>372 ± 35(\dagger)</td>
</tr>
<tr>
<td>Perceived fatigue, AU</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>3 ± 3</td>
<td>6 ± 4</td>
<td>4 ± 3</td>
</tr>
<tr>
<td>AF</td>
<td>4 ± 3</td>
<td>9 ± 5(\dagger)</td>
<td>6 ± 6</td>
</tr>
<tr>
<td>F-OR</td>
<td>4 ± 4</td>
<td>13 ± 5(\dagger)</td>
<td>4 ± 5(\dagger)</td>
</tr>
<tr>
<td>VO(<em>{2})(</em>{\text{max}}), mlO(_{2})/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>4,292 ± 342</td>
<td>4,389 ± 354</td>
<td>4,330 ± 391</td>
</tr>
<tr>
<td>AF</td>
<td>4,424 ± 488</td>
<td>4,490 ± 437</td>
<td>4,480 ± 450</td>
</tr>
<tr>
<td>F-OR</td>
<td>4,472 ± 409</td>
<td>4,317 ± 367(\dagger)</td>
<td>4,368 ± 452</td>
</tr>
<tr>
<td>Q(_{\text{max}}), l/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>29.6 ± 6.1</td>
<td>30.3 ± 5.7</td>
<td>29.0 ± 4.7</td>
</tr>
<tr>
<td>AF</td>
<td>31.8 ± 4.2</td>
<td>32.3 ± 4.6</td>
<td>31.9 ± 4.4</td>
</tr>
<tr>
<td>F-OR</td>
<td>32.8 ± 5.4</td>
<td>29.3 ± 6.9(\dagger)</td>
<td>31.8 ± 5.4(\dagger)</td>
</tr>
<tr>
<td>HR(_{\text{max}}), beats/min</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>184 ± 6</td>
<td>183 ± 4</td>
<td>183 ± 7</td>
</tr>
<tr>
<td>AF</td>
<td>182 ± 10</td>
<td>181 ± 8</td>
<td>182 ± 9</td>
</tr>
<tr>
<td>F-OR</td>
<td>182 ± 6</td>
<td>177 ± 6(\dagger)</td>
<td>181 ± 6(\dagger)</td>
</tr>
<tr>
<td>SV(_{\text{max}}), ml</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>161 ± 33</td>
<td>166 ± 31</td>
<td>159 ± 25</td>
</tr>
<tr>
<td>AF</td>
<td>175 ± 28</td>
<td>179 ± 28</td>
<td>177 ± 29</td>
</tr>
<tr>
<td>F-OR</td>
<td>180 ± 30</td>
<td>166 ± 40(\dagger)</td>
<td>176 ± 33(\dagger)</td>
</tr>
<tr>
<td>(a-v)O(_{2}) diff, ml/dl</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>14.9 ± 2.6</td>
<td>14.8 ± 2.1</td>
<td>15.2 ± 2.1</td>
</tr>
<tr>
<td>AF</td>
<td>13.8 ± 2.1</td>
<td>13.8 ± 2.1</td>
<td>13.9 ± 2.2</td>
</tr>
<tr>
<td>F-OR</td>
<td>13.8 ± 1.5</td>
<td>15.2 ± 2.6(\dagger)</td>
<td>13.9 ± 1.9(\dagger)</td>
</tr>
<tr>
<td>[La(^{-})](_{b}), mmol/l</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>12.2 ± 1.5</td>
<td>12.3 ± 0.8</td>
<td>11.9 ± 1.5</td>
</tr>
<tr>
<td>AF</td>
<td>12.0 ± 1.7</td>
<td>11.2 ± 2.1</td>
<td>12.3 ± 2.9</td>
</tr>
<tr>
<td>F-OR</td>
<td>12.7 ± 2.3</td>
<td>10.7 ± 2.1(\dagger)</td>
<td>12.3 ± 2.2</td>
</tr>
</tbody>
</table>

Mean values ± SD at baseline (Pre), after the overload period (Mid), and after the 2-wk taper period (Post) in the 3 experimental groups (control, n = 11; AF, n = 12; F-OR, n = 12). PPO, peak power output; Q\(_{\text{max}}\), maximum cardiac output; HR\(_{\text{max}}\), maximum heart rate; SV\(_{\text{max}}\), maximum stroke volume; (a-v)O\(_{2}\) diff, arteriovenous oxygen difference; [La\(^{-}\)]\(_{b}\), blood lactate concentration; AU, arbitrary units. *P < 0.05, †P < 0.05, ‡P < 0.05, significant difference between Pre and Mid, between Mid and Post, and between Pre and Post, respectively.

**Statistical Analysis**

The normality of data was tested using a Kolmogorov-Smirnov test. When data were skewed (i.e., [Ep], [NEp]), data were log transformed. Two-way ANOVAs [time (Pre, Mid, Post) × group (control, acutely fatigued (AF), F-OR)] with repeated-measures were applied to the energy index value, PPO, and peak values for VO\(_{2}\), Q, HR, SV, (a-v)O\(_{2}\) difference, and [La\(^{-}\)]\(_{b}\). Three-way ANOVAs [time (Pre, Mid, Post) × group (control, AF, F-OR) × intensity (0, 70, 80, 90, and 100% PPO\(_{\text{max}}\))] with repeated-measures were performed on all parameters at submaximal intensities. When the sphericity assumption in repeated-measures ANOVAs was violated (Mauchly’s test), a Greenhouse-Geisser correction was used. The post hoc analysis was performed using Bonferroni’s test. For all tests, the significance level was set at P < 0.05. Analyses were performed with Statistica Version 7.1 (StatSoft).

**RESULTS**

**Training Program**

Changes in weekly average training volume, the distribution of the relative training time spent in the intensity zones, and the number of training sessions per training phase in the three disciplines during the four phases of the protocol are presented in Table 1. All of the triathletes presented at least 94% compliance to the prescribed training sessions.

**Assessment of the F-OR Syndrome**

At baseline, all subjects reported low fatigue index at rest (i.e., “no fatigue” or “little fatigue” on the POMS scale at Pre), confirming that they were not already F-OR. At Mid, 12 overload subjects demonstrated a decrease in performance, followed by a supercompensation vs. Pre during the taper period (Table 2). For all of these 12 subjects, the decrease in performance at Mid (−2.5 ± 1.0%) exceeded the OR threshold (1.4%) and was associated with high perceived fatigue at Mid (i.e., “quite a bit” to “extremely” on the POMS fatigue item at Mid; Table 2). On this basis, these 12 triathletes were considered as F-OR. The 12 other subjects of the overload group, who maintained their performance level despite high perceived fatigue at Mid, were considered only AF and not F-OR. Thus the subsequent results are presented for 11 control subjects, 12 AF subjects, and 12 F-OR subjects. Their characteristics are presented in Table 3.

**Physiological Parameters**

**Cardiac parameters.** There was a time × group × intensity interaction for Q (P < 0.001) and HR (P = 0.02) and a time × group × intensity interaction for VO\(_{2}\) (P = 0.008) and SV (P = 0.003). Means are presented in Table 1.

**Table 3. Selected characteristics of the 2 experimental groups**

<table>
<thead>
<tr>
<th>Subject Characteristics</th>
<th>Control Group (n = 11)</th>
<th>Overload Training Group (n = 24)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>37 ± 6</td>
<td>34 ± 5</td>
<td>0.18</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.83 ± 0.06</td>
<td>1.80 ± 0.06</td>
<td>0.26</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>73 ± 8</td>
<td>73 ± 8</td>
<td>0.99</td>
</tr>
<tr>
<td>Past experience in endurance sport, yr</td>
<td>8 ± 5</td>
<td>7 ± 5</td>
<td>0.74</td>
</tr>
<tr>
<td>VO(<em>{2})(</em>{\text{max}}), ml/min</td>
<td>4,292 ± 342</td>
<td>4,448 ± 449</td>
<td>0.32</td>
</tr>
<tr>
<td>VO(<em>{2})(</em>{\text{max}}), ml/min·kg(^{-1})</td>
<td>59 ± 4</td>
<td>61 ± 5</td>
<td>0.23</td>
</tr>
<tr>
<td>PPO, W</td>
<td>352 ± 26</td>
<td>362 ± 31</td>
<td>0.38</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SD. No significant differences between both groups for all the parameters were reported.
group interaction for SV ($P < 0.01$). $\dot{Q}$ demonstrated significant change at exercise only in the F-OR group both at all exercise intensities. $\dot{Q}$ decreased in this group after the overload period and returned to Pre values at Post (Fig. 2). The reduced $\dot{Q}$ values in F-OR were associated with decreased HR and SV values at all exercise intensities at Mid. SV values were restored at Post in the F-OR group, while HR values during exercise remained lower at Post than Pre for all exercise intensities (Fig. 2).

Arterial blood pressures. There was a time $\times$ group interaction for SBP ($P = 0.04$). SBP demonstrated significant change during exercise only in the F-OR group (Fig. 3). SBP decreased in this group after the overload period and returned to baseline after Post. No significant time, time $\times$ group or time $\times$ group $\times$ intensity effect was observed for DBP ($P = 0.13$, $P = 0.20$, and $P = 0.28$, respectively).

$V_O_2$ and arteriovenous $O_2$ difference. No significant time, time $\times$ group or time $\times$ group $\times$ intensity effect was reported for $V_O_2$ at submaximal intensities ($P = 0.18$, $P = 0.58$, and $P = 0.30$, respectively). In contrast, a significant time $\times$ group effect was observed for $V_O_2_{max}$ ($P = 0.002$). This parameter decreased only in F-OR group at Mid ($P = 0.04$). There was a
significant time × group effect for the (a-\(\bar{v}\)) \(\text{O}_2\) difference (\(P < 0.001\)). This parameter demonstrated significant change at exercise only in the F-OR group (Fig. 4). (a-\(\bar{v}\)) \(\text{O}_2\) difference increased at all exercise intensities in this group after the overload period and returned to Pre values at Post.

**Blood variables.** There was a significant time effect for [La\(^-\)]\(_b\) (\(P < 0.01\)) with significantly reduced [La\(^-\)]\(_b\) at 90 and 100% PPO\(_{Mid}\) after the overload period, compared with baseline values. Nevertheless, no significant time, time × group, or time × group × intensity was observed for [La\(^-\)]\(_b\) at all submaximal intensities (\(P = 0.31\) and \(P = 0.14\), respectively). In contrast, a significant time × group effect was observed for peak [La\(^-\)]\(_b\) (\(P = 0.04\)). It decreased only in F-OR group at Mid (\(P = 0.01\)). No significant changes from Pre in estimated blood volume were reported at Mid and Post in the three experimental groups (changes < 2% from Pre values, \(P > 0.15\)). No time × group or time × group × intensity effect was observed for [NEp] (\(P = 0.39\) and \(P = 0.38\), respectively; Fig. 5). In contrast, a time × group × intensity effect was observed for [Ep] (\(P = 0.02\); Fig. 5). Between Pre and Mid,
[Ep] decreased at i3 ($P = 0.04$) and at exhaustion ($P < 0.001$). It returned to baseline level at Post.

**DISCUSSION**

This study provides novel information demonstrating that F-OR development in trained triathletes is associated with impaired cardiac response. Specifically, we show that the cardiac output is transiently decreased both at submaximal and maximal exercise intensities in triathletes led to F-OR after an overload training period. This alteration was reversed after completion of a 2-wk taper period. Furthermore, we showed that this cardiac response was likely due to reduced adrenergic response to intense exercise in F-OR athletes as indicated by the concomitant reduced epinephrine concentration.

To the best of our knowledge, this study is the first to show that the development of F-OR in trained triathletes is associated with transiently reduced Q during exercise. Several studies have reported that one prolonged, strenuous exercise bout lasting longer than 4 h can be associated with a transient impairment of the left ventricular function (25), but such observation has never been documented when considering chronic, heavy load endurance training programs. The reduced Q was confirmed in the present research by the similar evolution in the response of SBP to exercise during the overload period and during the subsequent taper period in the F-OR group. Because the use of impedance cardiography does not constitute the gold standard to measure Q, this similarity between Q and SBP responses at exercise confirmed that the reduced cardiac response in the F-OR group was not due to technical artifacts. Interestingly, a return of Q to baseline values was reported at all cycling intensities, and all F-OR athletes showed performance restoration or a supercompensation effect during the taper period. The lower values observed after overloading at all submaximal intensities suggested that this transient reduction in cardiac response was not a consequence of reduced performance but more likely a cause of F-OR development. In this perspective, we suggest that the decreased Q values observed after overloading in F-OR subjects may explain the lower $V\dot{O}_{2\text{max}}$ reported at the same period and the associated decreased performance. By applying the Fick principle, we reported that the decrease in Q observed in the F-OR athletes was associated with a concomitant increase in the arteriovenous oxygen difference at all exercise intensities. This finding showed that the F-OR subjects compensated their reduction in cardiac response with a greater fractional oxygen extraction at the muscular level. Nevertheless, this peripheral compensation for the reduced Q$_{\text{max}}$ value was insufficient to preserve $V\dot{O}_{2\text{max}}$. For this reason, we suggest that the performance decrement observed in the F-OR subjects at the end of the overload training period was related to a transiently lowered maximal capacity to resynthesize energy at the muscular level. This assumption was strengthened by the lower peak concentrations of lactate and epinephrine observed only in the F-OR triathletes, suggesting reduced rates of ATP production through glycolytic pathways. The lack of significant change in estimated blood volume during the overload period in the F-OR group demonstrated that these transiently decreased Q values were not associated with the development of a dehydrated state. Decreases in HR and SV values contributed to the reduction in Q in F-OR subjects at all exercise intensities. While HR decreased slightly in both control and AF athletes during the same period at submaximal intensities, no decrease in Q was observed in these groups due to the concomitant maintenance of SV. Additionally, no significant change in peak HR was observed at exhaustion in these two groups.

The present results suggest that the decreased cardiac output during exercise observed in the F-OR group was due to an adrenal insufficiency. A decrease in plasma epinephrine concentration was indeed reported both at $\sim$80% PPO and at exhaustion in the F-OR triathletes. At the same time, no significant change in plasma norepinephrine concentration was
observed at any exercise intensity in this group. This result was in line with the study of Uusitalo et al. (30), who reported a similar response in a group of trained female endurance athletes led to F-OR after a 4-wk program of intensive training. Because the adrenal medulla is the major contributor to circulating epinephrine, this result strengthened the hypothesis of the development of an adrenal insufficiency in F-OR endurance athletes rather than a downregulation of the sympathetic nervous system. In favor of a central origin for decreased sympathetic activity, Lehmann et al. (21) reported a decrease in nocturnal urinary norepinephrine and epinephrine excretion after an increase in training volume (21). The lack of significant changes in plasma epinephrine and norepinephrine concentrations at rest in the present study, also reported by others authors (8, 19, 30), did not confirm this hypothesis. Overall, the present results indicated that changes in the catecholamine response to exercise load are a more reliable sign of heavy training-induced stress and training maladaptations than changes in their resting levels. Moreover, the impaired cardiac response reported in the present study could be due to a downregulation of the sinus node’s β-adrenergic receptors. Prolonged exposure to elevated catecholamine concentrations as a result of intensified training would be sufficient to downregulate the sensitivity of these receptors and/or decrease their number (22, 31). This was observed after a single long-duration endurance exercise bout (2, 13), after chronic exposure to hypoxia (10), and after infusion of adrenergic agonists (29). Further investigation using provocation or blockade tests is required to determine whether such adaptations apply to F-OR endurance athletes. Lastly, the potential mechanisms responsible for the reported adrenal insufficiency remained unclear. Two possible underlying mechanisms could be at play: 1) an Addison-type syndrome, in which the adrenal glands are no longer able to synthesize cortisol and epinephrine despite normal stimulation by the adrenocorticotropic hormone (ACTH) (3, 4, 17); or 2) reduced adrenal responsiveness to ACTH stimulation (11, 22). As we did not measure ACTH or serum cortisol concentrations in the present study, we did not have the possibility to test these hypotheses.

Study Limitation

In the present study, the cardiac response was tested during a maximal cycling test, which has been shown to exert both high static and dynamic demands on the cardiovascular system at exercise (26). Because running is associated with lower static demands, it cannot be excluded that the alteration of the cardiac response would be different using a running test on a treadmill. Further investigations are required to test this hypothesis.

In conclusion, the results from the current study provide new information, demonstrating impaired cardiac response during exercise in trained triathletes led to F-OR after an overload training program. We showed that this cardiac response was induced by a reduced adrenergic response to intense exercise in F-OR athletes as indicated by concomitantly reduced catecholamine concentrations. These results highlight the importance of the interplay between cardiac response and F-OR development during an overload training program and represent an important message that merits consideration in the longitudinal medical follow-up of trained triathletes. The potential chronic persistence of this reduced cardiac response during exercise in athletes who enter the overtraining syndrome, the long-term forms of F-OR, represents a topic of future study.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


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