Human growth hormone responses to repeated bouts of sprint exercise with different recovery periods between bouts

Keith Stokes,1 Mary Nevill,2 Jan Frystyk,3 Henryk Lakomy,2 and George Hall4

1Sport and Exercise Science Group, School for Health, University of Bath, Bath; 2School of Sport and Exercise Sciences, Loughborough University, Loughborough, Leicestershire, United Kingdom; 3Medical Research Laboratories, Aarhus University Hospital, Aarhus, Denmark; and 4Department of Anaesthesia and Intensive Care Medicine, St. George’s Hospital Medical School, University of London, London, United Kingdom

Submitted 5 August 2004; accepted in final form 19 May 2005

Stokes, Keith, Mary Nevill, Jan Frystyk, Henryk Lakomy, and George Hall. Human growth hormone responses to repeated bouts of sprint exercise with different recovery periods between bouts. J Appl Physiol 99: 1254–1261, 2005. First published May 26, 2005; doi:10.1152/japplphysiol.00839.2004.—This study examined the growth hormone (GH) response to repeated bouts of sprint cycling. Eight healthy men completed three trials consisting of two 30-s sprints on a cycle ergometer separated by either 60 min (Trial A) or 240 min (Trial B) of recovery and a single 30-s sprint carried out the day after Trial B (Trial C). Trials A and B were separated by at least 7 days. Blood samples were obtained at rest and during recovery from each sprint. In Trial A, GH was elevated immediately before sprint 2, and there was no further increase in GH following the second sprint [area under the curve: 460 (SD 348) vs. 226 min (SD 1100), P = 0.05]. Free insulin-like growth factor I tended to be lower immediately before sprint 2 than sprint 1 (P = 0.06). Serum free fatty acids were not different immediately before each of the sprints. In Trial B, there was a trend for a smaller GH response to the second sprint [GH area under the curve: 512 (SD 396) vs. 242 min (SD 190), P = 0.09]. Free insulin-like growth factor I tended to be lower (P = 0.06), and serum free fatty acids were higher (P = 0.01) immediately before sprint 2 than sprint 1. There was no difference in the GH response to sprinting on consecutive days (Trials B and C). In conclusion, repeated bouts of sprint cycling on the same day result in an attenuation or even ablation of the exercise-induced increase in GH, depending on the recovery interval between sprints.

Address for reprint requests and other correspondence: K. Stokes, Sport and Exercise Science Group, School for Health, Univ. of Bath, Bath, BA2 7AY, UK (e-mail: k.stokes@bath.ac.uk).

REPEATED ADMINISTRATION of pharmacological stimuli has been found to result in an attenuation of the growth hormone (GH) response in rats (27, 28) and humans (15). In addition, a repeated 10-min bout of high-intensity submaximal exercise has been shown to result in a dramatic attenuation of the exercise-induced GH response (4). These findings support the notion that GH can regulate its own secretion via a negative feedback mechanism, although the exact nature of this regulation remains unclear. However, repeated bouts of submaximal exercise at 70% of maximum O2 uptake have been shown to result in an augmented GH response (22, 37), with greater augmentation of GH release when the recovery period between bouts of exercise is increased (22). Therefore, evidence regarding the effect of repeated bouts of submaximal exercise on the exercise-induced GH response is equivocal (39).

A single 30-s sprint on a cycle ergometer elicits a marked increase in serum GH (41, 42) that is at least as reproducible as pharmacological stimuli (40). However, when two sprints are performed separated by 60 min of recovery, the GH response to the second sprint is attenuated (41). Because serum GH remains elevated for between 90 and 120 min after a single 30-s sprint (42), it is possible that the suppression of the GH response to a second sprint is a result of GH autoinhibition at the level of the pituitary (41). It has been shown that inhibition of the GH response to GH-releasing hormone can occur independently of circulating plasma free fatty acid (FFA) and somatostatin release (35). However, it is not known whether the attenuation of the GH response to sprint exercise continues beyond the return of serum GH to resting levels.

Subcutaneous bolus injection of recombinant human GH (rhGH), eliciting similar peak, but longer lasting elevations in circulating GH levels as those seen following sprint exercise, has been shown to increase serum levels of free as well as total insulin-like growth factor I (IGF-I) within 4 h and for up to at least 24 h (29). It may be speculated that an exercise-induced increase in circulating GH will have a similar effect. Conversely, circulating IGF-I (in particular free IGF-I) may participate in the feedback control of GH secretion (7) at various levels: IGF-I increases somatostatin and reduces GH-releasing-hormone synthesis and secretion in the hypothalamus, and inhibits GH synthesis and release in the pituitary (2, 6, 16, 17, 20, 44). At the time of writing, the role of circulating IGF-I in the regulation of the GH response to repeated exercise is not clear. In this context, exercise has been reported to increase serum levels of IGF-binding protein (IGFBP)-1, which is one of six high-affinity IGFBPs (9, 21, 24). Although the IGFBPs are reported to stimulate as well as to inhibit IGF-I mediated actions, the role of IGFBP-1 is predominantly inhibitory. On a molar basis, IGFBP-1 constitutes only a minor fraction (~10%) of the total IGF-binding capacity in plasma, but, nevertheless, IGFBP-1 has achieved considerable interest due to its unique properties. IGFBP-1 is the only binding protein that shows a marked diurnal variation. This is explained by its tight inverse relationship with insulin, which rapidly suppresses the hepatic IGFBP-1 synthesis and secretion. Furthermore, in numerous conditions, IGFBP-1 shows a tight inverse relationship with levels of free IGF-I. This observation indicates that IGFBP-1 acts through sequestration of free IGF-I, and currently IGFBP-1 is considered to be a key regulator of free IGF-I levels in vivo (11). At the time of writing, it remains unknown whether the exercise-induced increase in IGFBP-1

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affects the IGF-I mediated feedback inhibition of the somatotrophs.

The aim of the present study was to determine whether the GH response to sprint exercise is altered by the recovery interval between bouts when repeated sprints are performed. This investigation tested three hypotheses: 1) that following 60 min of recovery from a single 30-s sprint on a cycle ergometer, the GH response to a second sprint would be attenuated due to elevated serum GH; 2) that following 240 min of recovery, GH levels would have returned to baseline, whereas serum IGF-I would be elevated, which would attenuate the GH response to a second sprint performed at this time; and 3) that resting serum IGF-I might be altered the day after sprint exercise, which may affect the GH response to a sprint performed on the second day.

MATERIALS AND METHODS

Subjects. Eight nonobese, healthy male volunteers, aged 19–26 yr [23 yr (SD 2)], gave their written, informed consent for this study, which conformed to the standards set by the Declaration of Helsinki and had the approval of the local ethics committee. All subjects were physically active (taking part in physical training between three and six times per week) but were not specifically trained for a particular sport. Body mass was 82.7 kg (SD 11.5), height was 180.2 cm (SD 6.9), and body mass index was 25.4 kg/m² (SD 2.5).

Equipment. The exercise tests were carried out on a modified friction-loaded cycle ergometer (Monark 864), which was interfaced to a microcomputer (BBC). This allowed instantaneous power output, corrected for flywheel acceleration, to be monitored and recorded accurately. Performance data were averaged over 1-s intervals. Lakkomy (26) has described the equipment used in detail. A restraining harness was also placed around the subjects’ waists to prevent them from rising out of the saddle, thereby concentrating movement in the lower limbs. The same harness setting and saddle height were used for each trial. Toe-clips and tape held the subjects’ feet securely in the pedals.

Protocol. After familiarization, the subjects arrived at the laboratory in the morning after an overnight fast on three separate occasions, completing one trial on each visit (Fig. 1). Trails A and B were carried out in a random order, separated by at least 7 days. Trial C was always completed the day after Trial B. On arrival at the laboratory, a cannula was placed in an antecubital forearm vein under local anaesthetic (1% lignocaine) for intermittent blood sampling during each trial. A standardized, submaximal warm-up consisting of cycling for 4 min at 60 W, 30 s at 80 W, and then 30 s at 100 W was then performed followed by a 5-min rest period. Subjects then completed an all-out 30-s sprint from a stationary start against an applied resistance equivalent to 7.5% (75 N/kN) of their body mass. Venous blood samples were then taken while subjects rested in a seated position. In Trial A, the rest period following the first sprint was 60 min, and then the warm-up routine was repeated followed by a second all-out 30-s sprint, against the same applied resistance (Fig. 1). Subjects then rested on a couch for a further 60 min. In Trial B, the rest period following the first sprint was 240 min before the warm-up routine, followed by performance of a second all-out 30-s sprint. Subjects then rested on the couch for a further 90 min while further blood samples were taken. Trial C was carried out the day after Trial B and followed the same procedure as the other two trials. However, in Trial C, subjects only completed one sprint before resting on the couch for 120 min while blood samples were taken. Subjects were instructed to sprint maximally for the duration of each sprint and were encouraged verbally while sprinting.

Blood sampling and analysis. The first blood sample was taken at least 15 min after the cannula was inserted. All blood samples were 10 ml in volume, and patency was maintained by displacing the blood contained in the cannula with isotonic saline. In Trial A, blood samples were taken in a seated position at rest (−10 min); post-warm-up (−4 min); and 5, 10, 20, 30, 40, and 60 min after each sprint. In Trial B, blood samples were taken at rest (−10 min); post-warm-up (−4 min); 5, 10, 20, 30, 40, 60, 90, 120, 180, and 240 min after the first sprint and post-warm-up; and 5, 10, 20, 30, 40, 60, and 90 min after each sprint. In Trial C, blood samples were taken at rest (−10 min); post-warm-up (−4 min); and 5, 10, 20, 30, 40, 60, 90, and 120 after the single sprint.

Samples were dispensed into two tubes. 1) One portion (4–5 ml) was placed into a lithium heparinized tube (Sarstedt LH/5 ml). Blood pH was measured immediately (Radiometer ABL5 pH/blood gas monitor), and thereafter 20-μl aliquots of blood were removed, deproteinized in 2.5% perchloric acid, and stored at −20°C for later determination of blood lactate concentrations (31). Further, aliquots were removed for the measurement of hematocrit by microcentrifugation (Hawksley) and hemoglobin concentration (by the cyanmethaemoglobin method for the calculation of percent change in plasma volume (10). 2) The remaining blood (4–5 ml) was allowed to clot for 1 h in a plain tube (Sarstedt Serum ZZ/5 ml). This was then centrifuged at 3°C for 15 min at a speed of 6,000 rpm (Burkard Koolspin), and the serum was removed and stored at −70°C for the determination of FFA, GH, total IGF-I, free IGF-I, binary complex IGF-I:IGFBP-I, and IGFBP-1 concentrations. Serum FFA was determined by using a commercially available assay kit (Wako Chemicals) with an intra-assay coefficient of variation (CV) of <2.7%. Serum GH was measured by ELISA (Medigenix GH-Biosource) with a sensitivity of 0.1 μg/l, an intra-assay CV of 2.1–3.6%, and an interassay CV of 6.8–7.1%.
Serum total (extractable) IGF-I was determined in acid ethanol serum extracts by an in-house double monoclonal time-resolved immunofluorometric assay with mean within and in-between assay CVs <5 and 10%, respectively (12). Serum-free IGF-I was determined after ultrafiltration by centrifugation at conditions approaching those in vitro (14). The lower detection limit of free IGF-I in the ultrafiltrates was 0.020 μg/l. Mean within and in-between assay CVs of free IGF-I were 15 and 20%, respectively. Serum IGFBP-1 was determined by an in-house radioimmunoassay (RIA) performed as described previously (46) with modifications (25). The RIA is based on a monoclonal IGFBP-1 antibody, which recognizes all isomers of IGFBP-1 in serum (clone 6303 from Medix Biochemica, Kauniainen, Finland). Within and in-between assay CVs of the IGFBP-1 RIA were <5 and 10%, respectively. The dimeric complex of IGF-I and IGFBP-1 was determined by an in-house time-resolved immunofluorometric assay (13). The dimeric complexes were captured by an IGFBP-1 antibody (clone 6306) and detected by an europium-labeled monoclonal IGF-I antibody. The assay is highly specific for the dimeric complex of IGF-I and IGFBP-1; thus no signal is obtained unless both peptides are present, and neither IGFBP-2, -3, -4, nor IGF-II causes any detectable cross reaction (13). The saturation of IGFBP-1 is defined as the molar concentration of the dimeric complex of IGF-I and IGFBP-1 relative to the molar concentration of IGFBP-1. The different IGF-related measurements were determined presprint and 5 min postspirt and only in five subjects due to limited serum sample volume.

Statistical analysis. Paired t-tests were used to determine any differences in performance in each of the sprints. Two-way repeated-measures ANOVA was used to determine any differences in the blood lactate (n = 7), blood pH, and serum GH responses for 60 min following sprint 1 and sprint 2 in Trial A and in Trial B and also when comparing the first sprint in Trial B (day 1) with the sprint in Trial C (day 2). Two-way repeated ANOVA was also used to determine any differences in serum total IGF-I, free IGF-I, IGFBP-1, and IGF-I binary complex, and IGFBP-1 saturation (n = 5) before and immediately after sprints 1 and 2 in Trial A and in Trial B, and Trial B sprint 1 and Trial C. Paired t-tests were used to determine any differences in serum FFA concentrations (n = 7) before sprints 1 and 2 in Trial A and in Trial B, and Trial B sprint 1 and Trial C. Statistical significance was accepted at the P ≤ 0.05 level. Effect size (ES) was also calculated, and a large effect was taken when ES > 0.8. All results are expressed as means (SD). Peak values refer to the mean of the highest measured values for each individual.

RESULTS

Performance. Peak power (PP) was similar in both sprints in Trial A and in both sprints in Trial B (Table 1). However, PP was significantly greater in Trial B sprint 1 compared with a sprint completed 24 h later (Trial C). There were no other differences in sprint performance variables either between sprints in Trial A and Trial B, or between the first sprint in Trial B (day 1) and the sprint in Trial C (day 2, Table 1).

Metabolic responses. In Trial A, peak blood lactate concentrations were 11.8 (SD 1.6) and 11.5 mmol/l (SD 2.0) following sprints 1 and 2, respectively, with a different temporal pattern of response to each of the sprints (sprint main effect, P = 0.46; time main effect, P < 0.01; interaction effect, P = 0.01). Nadir blood pH was 7.18 (SD 0.04) and 7.19 (SD 0.05), with no differences in the response to sprint 1 and sprint 2 (sprint main effect, P = 0.41; time main effect, P < 0.01; interaction effect, P = 0.42). In Trial B, the overall blood lactate response to sprint 1 was greater than that following sprint 2 (sprint main effect, P = 0.03; time main effect, P < 0.01; interaction effect, P = 0.42), although nadir pH did not differ [7.20 (SD 0.04) vs. 7.21 (SD 0.05)]. There were no significant differences in blood lactate (sprint main effect, P = 0.20; time main effect, P < 0.01; interaction effect, P = 0.28) or blood pH (sprint main effect, P = 0.29; time main effect, P < 0.01; interaction effect, P = 0.13) responses to Trials B sprint 1 and Trial C (peak blood lactate: 10.9 (SD 2.3) vs. 11.0 mmol/l (SD 1.8); nadir pH: 7.20 (SD 0.04) vs. 7.20 (SD 0.04)). Preexercise serum FFA was not significantly different before sprint 1 and sprint 2 [0.29 (SD 0.20) vs. 0.15 mmol/l (SD 0.06), P = 0.11] in Trial A but was higher before sprint 2 than sprint 1 in Trial B [0.76 (SD 0.30) vs. 0.33 mmol/l (SD 0.25), P = 0.01] and before the sprint in Trial C than Trial B sprint 1 [0.46 (SD 0.29) vs. 0.33 mmol/l (SD 0.25), P = 0.03].

GH. In Trial A, sprint 1 resulted in a marked elevation of serum GH (Fig. 2A). Sprint 2 did not induce a further increase in serum GH, and peak GH concentrations [14.4 (SD 9.6) vs. 7.0 μg/l (SD 4.7), P = 0.02], as well as GH area under the curve (AUC) calculated for the first 60 min after each sprint [460 (SD 348) vs. 226 min·μg·1·1−1·1 (SD 182), P = 0.05], were significantly greater during recovery from sprint 1 compared with sprint 2. ES for GH AUC after sprint 1 and sprint 2 was 0.67. In Trial B, sprint 1 elicited a marked GH response, but GH returned to preexercise levels within 120 min (Fig. 2B). Sprint 2 resulted in a further GH response, although there was a tendency for a smaller response than that following sprint 1 (sprint main effect, P = 0.10), with lower GH AUC [512 (SD 396) vs. 242 min·μg·1·1−1·1 (SD 190), P = 0.09] and GH peak [18.2 (SD 12.7) vs. 8.3 μg/l (SD 7.1), P = 0.09] following

Table 1. Peak and mean power output, peak and mean pedal revolutions, total work done, and fatigue index in sprints 1 and 2 in Trial A and Trial B and the sprint completed in Trial C

| Trial A | | Trial B | | Trial C |
|---|---|---|---|
| | Sprint 1 | Sprint 2 | | Sprint 1 | Sprint 2 | | Sprint 1 | Sprint 2 |
| PPO, W | 1,538 (65) | 1,494 (70) | | 1,528 (85) | 1,487 (75) | | 1,464 (67)* |
| MPO, W | 719 (30) | 725 (32) | | 711 (32) | 699 (31) | | 709 (32) |
| PPR, rpm | 165 (4) | 164 (4) | | 163 (5) | 162 (5) | | 162 (4) |
| MPR, rpm | 122 (3) | 123 (3) | | 120 (3) | 119 (3) | | 120 (3) |
| Work done, J | 21,488 (944) | 21,757 (959) | | 21,311 (959) | 20,980 (940) | | 21,265 (953) |
| Fatigue index, % | 70 (2) | 68 (2) | | 70 (2) | 70 (1) | | 68 (2) |

Values are means (SD); n = 8 subjects. PPO, peak power output; MPO, mean power output; PPR, peak pedal revolutions; MPR, mean pedal revolutions. *Trial B sprint 1 vs. Trial C, sprint main effect, P = 0.04.
GH release, GH results for the five subjects for whom IGF-I data are available are presented here. In Trial A, there was a tendency for both GH AUC [376 (SD 216) vs. 216 min·µg⁻¹·l⁻¹ (SD 134), P = 0.10] and GH peak [13.8 (SD 8.3) vs. 7.3 µg/l (SD 4.4), P = 0.08] to be greater following sprint 1 than sprint 2. In Trial B, there were no differences in GH AUC [591 (SD 446) vs. 291 min·µg⁻¹·l⁻¹ (SD 225), P = 0.19] or GH peak [20.9 (SD 16.1) vs. 10.1 µg/l (SD 8.0), P = 0.17]. When comparing Trial B sprint 1 with Trial C, there were no differences in GH AUC [591 (SD 446) vs. 568 min·µg⁻¹·l⁻¹ (SD 540), P = 0.91] or GH peak [20.9 (SD 16.1) vs. 17.1 µg/l (SD 16.4), P = 0.55].

IGF-I. There were no significant differences in serum total IGF-I pre- to 5 min postexercise or before sprint 1 and sprint 2 in any of the trials (Fig. 3A; n = 5), although there was a tendency for total IGF-I to be higher 5 min post- than pre-exercise.

sprint 2. ES for GH AUC after sprint 1 and sprint 2 was 0.68. There was no difference between the GH responses to Trial B sprint 1 and Trial C [Fig. 2C; GH AUC, 512 (SD 396) vs. 464 min·µg⁻¹·l⁻¹ (SD 453), P = 0.69; GH peak, 18.2 (SD 12.7) vs. 13.6 (SD 13.8), P = 0.35]. ES for GH AUC on day 1 and day 2 was 0.11. To provide homogenous data for the discussion of the putative role for IGF-I in modulating exercise-induced
exercise in Trial C (time main effect, \( P = 0.06 \)). ES for Trials A, B, and C for pre- vs. 5 min postexercise was 0.90, 0.43, and 0.40 and for pre-sprint 1 vs. pre-sprint 2 was 0.42, 0.13, and 0.04, respectively. Five minutes after exercise, serum-free IGF-I was not different from preexercise in any of the trials (Fig. 3B, \( n = 5 \)). ES for pre- vs. 5 min postexercise was 0.01, 0.34, and 0.01 for Trials A, B, and C, respectively. In Trials A and B, serum-free IGF-I tended to be lower for sprint 2 than sprint 1 (Trial A, sprint main effect, \( P = 0.06 \); Trial B, sprint main effect, \( P = 0.06 \)). Serum-free IGF-I was significantly lower in Trial C than Trial B sprint 1 (sprint main effect, \( P = 0.04 \)). ES for pre-sprint 1 vs. pre-sprint 2 was 0.76, 0.64, and 0.80 for Trials A, B, and C, respectively.

There were no significant differences in serum IGFBP-1 (sprint main effect, \( P = 0.38 \); time main effect, \( P = 0.26 \); interaction effect, \( P = 0.20 \)) or IGFBP-1-bound IGF-I (binary complex; sprint main effect, \( P = 0.96 \); time main effect, \( P = 0.20 \); interaction effect, \( P = 0.78 \)) pre- to 5 min postexercise in Trial A (Table 2). After exercise in Trial B, serum IGFBP-1 was higher (sprint main effect, \( P = 0.43 \); time main effect, \( P = 0.02 \); interaction effect, \( P = 0.83 \)) and binary complex was higher in four of the five subjects (sprint main effect, \( P = 0.43 \); time main effect, \( P = 0.08 \); interaction effect, \( P = 0.49 \)). The binary complex was higher after exercise in Trial C (sprint main effect, \( P = 0.98 \); time main effect, \( P = 0.04 \); interaction effect, \( P = 0.52 \)). ES for IGFBP-1 pre- vs. 5 min post sprint was 0.43, 0.20, and 0.13 for Trials A, B, and C, respectively. Postexercise IGFBP-1 saturation (Trial A, sprint main effect, \( P = 0.60 \); time main effect, \( P = 0.22 \); interaction effect, \( P = 0.26 \); Trial B, sprint main effect, \( P = 0.34 \); time main effect, \( P = 0.25 \); interaction effect, \( P = 0.29 \); Trial C, sprint main effect, \( P = 0.38 \); time main effect, \( P = 0.50 \); interaction effect, \( P = 0.17 \)) was not significantly different to preexercise in any of the trials, and there were no significant differences in serum IGFBP-1, IGF-binding complex, or IGFBP-1 saturation immediately before sprint 1 and sprint 2 in any of the trials.

Changes in plasma volume. All of the sprints in Trials A, B, and C resulted in a change in plasma volume [mean estimated changes in plasma volume 5 min postexercise: Trial A, sprint 1, −17.3% (SD 3.5); sprint 2, −14.1% (SD 3.0); Trial B, sprint 1, −13.4% (SD 3.4); sprint 2, −10.0% (SD 4.7); Trial C, −14.8% (SD 2.2)]. Estimated plasma volume had returned to preexercise levels by 20 min postexercise in all trials. Data for circulating hormones have not been corrected for estimated changes in plasma volume.

Table 2. Mean serum IGFBP-1 and IGF-I binary complex and IGFBP-1 saturation before and 5 min after sprint 1 and sprint 2 in Trials A, B, and C

<table>
<thead>
<tr>
<th>Trial</th>
<th>Sprint 1</th>
<th>Sprint 2</th>
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<th>Sprint 2</th>
<th>Trial 3</th>
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<td></td>
<td>Pre</td>
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<td>Pre</td>
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<tr>
<td>IGFBP-1, µg/l</td>
<td>26.8 (2.3)</td>
<td>24.1 (3.2)</td>
<td>24.5 (4.0)</td>
<td>34.0 (7.3)</td>
<td>28.8 (6.9)</td>
<td>32.4 (6.7)*</td>
<td>31.6 (6.0)</td>
<td>36.2 (5.6)*</td>
</tr>
<tr>
<td>IGF-I binary complex, µg/l</td>
<td>15.0 (1.9)</td>
<td>16.8 (3.4)</td>
<td>14.4 (3.8)</td>
<td>17.1 (4.2)</td>
<td>16.4 (4.9)</td>
<td>17.5 (5.5)†</td>
<td>16.4 (4.1)</td>
<td>19.8 (5.0)</td>
</tr>
<tr>
<td>IGFBP-1 saturation, %</td>
<td>58.2 (8.8)</td>
<td>74.2 (14.6)</td>
<td>62.2 (12.5)</td>
<td>63.4 (14.6)</td>
<td>70.6 (15.1)</td>
<td>55.2 (10.3)</td>
<td>55.8 (9.5)</td>
<td>55.5 (10.6)</td>
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</table>

Values are means (SD); \( n = 5 \) subjects. IGFBP-1, insulin-like growth factor binding protein-1; IGF-I, insulin-like growth factor I. *Trial B, time main effect, \( P = 0.02 \). †Trial C, time main effect, \( P = 0.04 \).

**DISCUSSION**

The results of the present study demonstrate an attenuation of the GH response to repeated bouts of sprinting on a cycle ergometer separated by 60 min of recovery. When the recovery period was 4 h, the GH response to exercise was still not fully restored. However, the GH responses to sprints completed at the same time on consecutive days were similar.

In agreement with previous findings (40–42), a single 30-s sprint on a cycle ergometer elicited a marked GH response, and serum GH remained elevated for 60 min of recovery. However, in accordance with previous findings (41), there was no GH increase following a second sprint completed at 60 min. Because GH levels were still elevated immediately before the second sprint, the absence of an increase in GH may be a result of GH autoinhibition, although circulating IGF-I and FFA are alternative candidates that might be involved in feedback inhibition of GH secretion.

In the present study, serum-free IGF-I levels were lower before sprint 2 than sprint 1 after 60 min of recovery (\( P = 0.06 \)). This suggests that circulating IGF-I is not responsible for attenuating the GH response to the second sprint in Trial A. However, it has been proposed that negative feedback of IGF-I on GH release may be exerted via either blood-borne IGF-I or IGF-I produced in the pituitary itself (33). Because it is not possible in vivo to distinguish between the contribution of locally produced vs. systemic IGF-I to the regulation of GH synthesis and secretion, it cannot be excluded that IGF-I produced in the pituitary itself may be involved in the regulation of the GH response to repeated exercise. It has previously been demonstrated that FFA may block GH secretion directly at the pituitary gland (5). However, in the present study, FFA levels were not elevated before the second sprint in Trial A, making it unlikely that changes in FFA are responsible for the altered GH response.

In Trial B, serum GH had returned to preexercise levels within 2 h of recovery, and after 4 h of recovery the GH response to a second sprint was suggestively, but not statistically, smaller (\( P = 0.09 \)) than following the first sprint. This observation suggests that, 4 h after the first sprint, there is still some inhibition of GH release, although it is not as great as that seen after 60 min of recovery. However, because serum GH was at preexercise levels immediately before the second sprint in Trial B, it is unlikely that systemic GH played a direct role in the inhibition of its own secretion.

GH administration increases serum IGF-I levels within ~4 h (29). Therefore, it was hypothesized that, in Trial B, the
increase in GH following the first sprint would result in elevated circulating IGF-I levels. When considering the GH data for the five individuals for whom IGF-I data are available, there were no significant differences in either GH AUC or GH peak, although both of these measures were lower in four of the five subjects following the second sprint. However, neither serum total nor serum-free IGF-I concentrations were elevated immediately before sprint 2. The disparity between the effects of exercise and rhGH administration-induced elevations may be attributable to the different time course of the respective GH responses. In the present study, circulating GH peaked ~40 min after exercise and returned to preexercise levels within 2 h, whereas rhGH administration resulted in an elevation in GH levels within 60 min that peaked 3 h postadministration and remained elevated for up to 12 h (29), representing a supraphysiological response. In any case, because serum total IGF-I was not elevated, and free IGF-I tended to be suppressed, before the second sprint in Trial B, it seems unlikely that circulating IGF-I could be responsible for any alteration in the GH response to the second sprint following 4 h of recovery.

In contrast, serum FFA was elevated immediately before the second sprint in Trial B. This is consistent with the finding that the most immediate effect of rhGH administration in humans is a dose-dependent increase in FFA reflecting stimulation of lipolysis (34). The increase in lipid intermediates associated with rhGH administration persists for at least 300 min (43). It is, therefore, likely that increased serum FFA concentrations could be at least partly responsible for the tendency for a lower GH response to the second sprint in this trial. This raises the possibility of at least a two-phase refractory period for the GH response to sprint exercise, with an initial period of GH autoinhibition, followed by later inhibition of GH release via the actions of FFA at the pituitary. In addition, the finding that the second sprint in Trial B elicited a GH response, despite elevated circulating FFA, suggests that sprint exercise is a potent enough stimulus to at least partially overcome FFA inhibition of GH release.

There were no differences in the preexercise levels of serum total IGF-I for Trial B sprint 1 and Trial C. This is in agreement with the finding that serum total IGF-I remained unchanged 24 h after brief high-intensity, submaximal exercise (4). Resting IGF-I might reflect the pattern of nocturnal GH secretion, correlating better with pulsatile than basal GH secretion (30). Moderate-intensity exercise has been found to alter the temporal pattern of nocturnal GH secretion without affecting total GH secretion, with specific disruption to peak GH secretion in early sleep (23). In the present study, there were no differences in resting IGF-I levels between Trial B sprint 1 and the sprint in Trial C, suggesting that sprint exercise completed during the morning or early afternoon does not disturb nocturnal GH secretion. PP was lower during the sprint in Trial C than in Trial B sprint 1, although there were no other differences in performance parameters. The difference in PP is difficult to explain, because sprint performance had recovered following 60 and 240 min of recovery in Trials A and B and is known to recover to 97% of unfatigued PP when repeated cycle ergometer sprints are separated by 300 s of recovery (8). Furthermore, impaired muscle function due to muscle damage is unlikely, due to the almost exclusive concentric nature of muscle contraction when performing cycle ergometer exercise. However, 30 s of cycle ergometer sprinting have been shown to induce oxidative stress (1), which could, theoretically at least, impair skeletal muscle function in a similar way to that seen in myocardial stunning following ischemia (32). Despite this small difference in sprint performance, the GH response to the sprint in Trial C was similar to the GH response to the first sprint in Trial B, showing that sprint exercise on the previous day does not alter the GH response to exercise after overnight recovery.

The role of the GH response to exercise is unclear. It is attractive to look toward GH as one of the mediators of adaptation to exercise training, particularly with reference to a role in hypertrophy in response to resistance training. This assumes that GH has an important role in protein synthesis, either in isolation or via the release of IGF-I from hepatocytes. However, pituitary GH is not essential for exercise-induced muscle hypertrophy (18), and recent evidence points toward a possible role for locally produced variants of IGF-I in this process (19). Additionally, the fact that all forms of exercise appear to result in GH release (39) suggests that hypertrophy is not the only potential role for exercise-induced GH release. An alternative role might be that of altering substrate metabolism during exercise and recovery (36). Given the time course of the GH response to exercise, it is possible that GH has a “glycoener-sparing” effect, either during prolonged exercise or during recovery from brief exercise. This might have important implications when considering the recovery period between bouts of exercise. Unfortunately, at the present time, the relationship among GH concentrations in the serum, GH signaling pathways, and longer term changes in body composition or exercise performance is not well understood. It is hoped that, as these relationships become clearer, the role of exercise-induced GH release will be better defined.

Conflict results have been reported regarding the acute effect of exercise on serum IGF-I. Brief, high-intensity submaximal exercise has been suggested to elicit acute increases in serum total IGF-I, independent of GH release, as well as GH-dependent IGF-I release with a longer time course (4, 38). However, acute increases in serum total IGF-I were not identified following prolonged exercise at 60% maximum O2 uptake (21), and a marathon run was found to result in a decrease in serum total IGF-I (24). The differences in these findings are not surprising, as they employed very different exercise protocols. In the present study, sprint exercise did not result in an acute increase in serum total IGF-I in Trial A and Trial B. However, it appears that exercise not only influences total IGF-I levels but also has a role in regulating IGF-I binding (38). There is general consensus that circulating IGFBP-I increases following exercise (9, 21, 24). In the present study, serum IGFBP-I was significantly higher 5 min postexercise than preexercise in Trial B but was not significantly altered in Trial A. However, small effects suggest that robust alterations in serum IGFBP-I do not occur in response to sprint exercise.

The results of studies examining the acute effect of exercise on serum-free IGF-I are equivocal. An incremental rowing exercise test followed by a single-stage maximal rowing exercise test resulted in reduced serum-free IGF-I with a nadir 60 min after the end of exercise (9). In contrast, resistance exercise has been shown to result in a ~90% increase in free IGF-I in elderly individuals (3), whereas 30 min of cycling exercise did not elicit any changes in serum-free IGF-I (45). In the present study, sprint exercise did not result in any immediate
alterations in free IGF-I. However, moderate-large effects between sprint 1 and sprint 2 in Trials A and B and between Trial B sprint 1 and Trial C indicate that serum-free IGF-I tended to be lower 60 min, 240 min, and even the day after an initial bout of sprint exercise.

In conclusion, this study has provided further evidence for direct GH autoinhibition when bouts of sprint exercise are separated by 60 min of recovery. It appears that this inhibition is potent enough to override other stimuli for GH release. However, a longer recovery period does not fully restore the GH response to sprint exercise, despite a return of serum GH to preexercise levels. This divergence between the GH response and preexercise GH levels suggests the presence of another mechanism for the inhibition of GH in response to repeated exercise with longer recovery intervals. Serum-free IGF-I tended to be lower immediately before a second sprint performed 4 h after the first. However, there was an increase in circulating FFA 4 h after the first sprint. Because circulating GH was not elevated at this time, suggesting that GH autoinhibition was not preventing GH release, the observed increase in circulating FFA may have been at least partly responsible for the apparent attenuation of the GH response to the second sprint after 4 h of recovery.

ACKNOWLEDGMENTS

The authors thank Peter Sørensen for valuable advice regarding IGF-I analysis and Joan Hansen, Kirsten Nyborg, and Susanne Sørensen for performing the IGF-I, IGFBP-I, and binary complex analyses.

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