Treadmill Running Reduces Parathyroid Hormone Concentrations During Recovery Compared With a Nonexercising Control Group

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Context: Lower PTH concentrations reported in the hours after acute, endurance exercise compared with preexercise levels might be influenced by factors such as circadian fluctuations.

Objective: The objective of the study was to compare postexercise PTH concentrations with a nonexercising control group.

Design and Setting: A laboratory-based study with a crossover design, comparing a 60-minute (at 10:30 AM) bout of treadmill running at 65% of the maximal rate of oxygen uptake (exercise) with semirecumbent rest (CON). Blood samples were obtained immediately before (baseline 10:15 AM) and after (11:30 AM) exercise and during recovery (12:30 AM, 1:30 PM, and 2:15 PM).

Participants: Ten physically active men (mean ± 1 SD, age 26 ± 5 y; body mass 78.3 ± 5.8 kg; maximal rate of oxygen uptake 57.3 ± 6.9 mL/kg^{-1} · min^{-1}) participated in the study.

Main Outcome Measures: PTH, albumin-adjusted calcium, and phosphate concentrations were measured.

Results: PTH concentrations increased (+85%, $P < .01$) during exercise and were higher than in CON immediately at the end of exercise (4.5 ± 1.9 vs 2.6 ± 0.9 pmol/L^{-1}, $P < .05$). In the postexercise period (12:30–2:15 PM), PTH was not different compared with baseline but was lower compared with CON at 1:30 PM (−22%; $P < .01$) and tended to be lower at both 12:30 PM (−12%; $P = .063$) and 2:15 PM (−13%; $P = .057$). Exercise did not significantly affect the albumin-adjusted calcium concentrations, whereas phosphate was higher than CON immediately after exercise (1.47 ± 0.17 vs 1.03 ± 0.17 pmol/L^{-1}, $P < .001$) and was lower at 1:30 PM (−16%: $P < .05$).

Conclusions: Lower PTH concentrations after acute endurance running compared with a rested control condition suggest a true effect of exercise. **(*J Clin Endocrinol Metab* 99: 1774–1782, 2014)**

Bone is a highly dynamic tissue that is constantly in flux, fulfilling a range of critical roles within the human body. Beyond its obvious roles of internal organ protection and a scaffold to support movement, bone serves as both a sink and reservoir for calcium, an ion essential for cellular metabolism and function, whereas the marrow

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Abbreviations: ACa, albumin-adjusted calcium; Ca^{2+}, ionized calcium; ET, endurance trained; $\%HR_{max}$, percentage of maximum heart rate; PO_4, phosphate; RA, recreationally active; RER, respiratory exchange ratio; VO_2, oxygen uptake; VO_{2max}, maximal rate of oxygen uptake.

cavity provides an essential source of hematopoietic, mesenchymal, and endothelial stem cells. Bone also needs to be capable of adapting to the biomechanical challenges placed upon it while simultaneously making components of its structure accessible in response to subtle changes in the systemic environment.

Bone achieves some of these tasks through the process of remodeling, in which bone is removed by osteoclast resorption and new bone is formed by osteoblasts in its place. The action of PTH is of prime importance because its secretion is key to accessing the calcium reservoir. Simultaneously, secretory activity of PTH is regulated by the systemic presence of calcium in the form of ionized calcium (Ca^{2+}), which is sensed by the calcium-sensing receptor on the parathyroid gland (1). A decrease in Ca^{2+} increases PTH secretion, which, in turn, stimulates osteoblasts to produce chemical triggers, particularly receptor activator of nuclear factor-κB ligand, stimulating osteoclastogenesis, bone resorption, and the mobilization of bone calcium. Consistent with this mode of action, chronic elevation in the systemic PTH concentration and loss of the circadian rhythm in PTH is associated with increases in biochemical markers of bone resorption (2), bone loss (3, 4), and increased risk of fracture (5, 6).

Despite its recognition as a proresorptive factor, evidence of bone formation effects of PTH have existed since the late 1920s (7). The dual effects of PTH on bone appear dependent on its mode of administration and the signaling mechanism, with prolonged elevations as a result of continuous infusion and transient spikes through repeated injections of PTH (8), producing bone resorption or formation, respectively (9). The primary determinant of whether PTH has anabolic effects appears to be the length of time concentrations remain above baseline levels (10).

Physical exercise is associated with bone formation, particularly at load-bearing sites, with mechanical loads imposed by muscle contractions and gravity in excess of those habitually encountered positively influencing the size, shape, and internal structure of the skeleton (11). These adaptive responses are thought to be mediated by osteocytes, acting as mechanosensors, and to result from regulation by the Wnt signaling pathway (12). Osteocytes may coordinate the osteogenic response to mechanical force by suppressing sclerostin and thereby up-regulating locally Wnt signaling (13). In turn, sclerostin is also regulated by hormonal stimuli, including PTH, with elevations, both intermittent and continuous, down-regulating sclerostin expression in osteocytes in mice (14) and decreasing systemic levels in humans (15).

Several studies report that PTH concentrations increase with acute, endurance exercise (16–19) and some (16, 18, 19), which have taken multiple measurements of PTH, suggest that this increase is transient, returning to preexercise levels within 30 minutes of its termination. Exercise training has been shown to decrease basal PTH concentrations (20), which would have the effect of increasing the difference between PTH levels at rest and during exercise, conditions suggested to have the most favorable effects on the skeleton (21). In two studies, PTH was monitored in the 3 hours after endurance exercise (18, 19), and the rapid decrease in PTH concentrations reported with the termination of exercise (16) continued in the postexercise period to levels significantly below baseline. The significance of these PTH changes induced after exercise remains unconfirmed because PTH measurements were taken in the late morning during the nadir of its known circadian rhythm (22–24).

The current study examines the temporal pattern of PTH during and after treadmill running comparing the profile of changes to a nonexercising control.

Materials and Methods

Participants

Ten healthy, physically active men [(mean ± 1 SD), age 26 ± 5 y; height 1.79 ± 0.05 m; body mass 78.3 ± 5.8 kg; maximal rate of oxygen uptake (VO_{2max}) 57.3 ± 6.9 $mL/kg^{-1} \cdot min^{-1}$] were recruited to participate in the study, which was approved by the QinetiQ Research Ethics Committee. Participants were included if they were nonsmokers, had not suffered a bone fracture in the previous 12 months, were free from musculoskeletal injury, and were not taking any medication or suffering from any condition known to affect bone metabolism. Compliance with these inclusion criteria was confirmed from a medical screening questionnaire and examination. All subjects provided written informed consent prior to taking part in the study.

Experimental design

This study comprises an analysis of a subset of the data collected in a study as previously described (25). The aim of the original study was to compare the bone turnover marker response to two bouts of exercise separated by different recovery periods. As such, the analysis focused on the response to the second bout of exercise in both conditions. However, as a result of the different recovery durations between the two bouts and the regular blood sampling, the data also provided an opportunity to compare the calcium metabolism response to exercise with a rested control group, a comparison that has received little attention, despite the known circadian fluctuations in PTH. In addition, the data also provided an opportunity to confirm that the lower (compared with baseline) postexercise PTH concentrations observed in several previous studies (18, 19) were in fact true effects of exercise.

In this study, participants completed two 9-day experimental protocols separated by at least 1 week. On days 1–3 of each protocol, participants refrained from physical activity and ate a prescribed diet. On days 4 and 5, participants performed two 60-minute bouts of treadmill running, completing either one on

day 4 and one on day 5 (separated by 23 h) or both on day 5 (separated by 3 h). On days 6–9, participants attended the laboratory for early morning follow-up analysis and continued to follow a controlled diet and refrain from physical activity. The order in which participants completed the two conditions was counterbalanced. For the purposes of this paper, only data from 8:00 AM up to and including 2:15 PM on day 5 were included in the analysis, during which participants either remained rested throughout (CON) or completed 60 minutes of treadmill running at 65% VO_{2max} starting at 10:30 AM (EX), followed by 3 hours of recovery. In both conditions, at least 17 hours had elapsed since participants had completed any exercise.

Trial procedures

After an overnight fast from 9:00 PM the previous evening, participants arrived at the laboratory at 7:30 AM and had their body mass measured (Mettler-Toledo ID7; Mettler-Toledo). Participants adopted a semirecombinant position and a cannula was inserted into a prominent forearm vein, and a baseline blood sample was collected at 8:00 AM. A standardized breakfast was provided at 8:15 AM, and participants remained semirecombinant until 10:15 AM when a further blood sample was collected.

In EX, participants began exercising at 10:30 AM, running on a treadmill (XELG 70 ERGO; Woodway) for 60 minutes at 65% VO_{2max}, preceded by a 5-minute warm-up at 50% VO_{2max}, during which they consumed water ad libitum. Sixty-second samples of expired air (inspiration to inspiration) were collected at 14, 29, 44, and 59 minutes of the exercise session, and heart rate was recorded continuously (Vantage NV; Polar Electro Oy). On completion of exercise (11:30 AM), participants toweled dry, had their nude body mass measured, and returned to a semirecumbent position until 2:15 PM. The difference between pre- and postexercise body mass was calculated, and the participants consumed 1.5 mL of plain water for every gram change in body mass during the subsequent 3-hour recovery period. In CON, participants remained semirecumbent throughout. Further blood samples were collected at 11:30 AM (immediately after exercise in EX), 12:30 PM, 1:30 PM, and 2:15 PM.

On days 1–3, participants consumed a diet containing 6 g carbohydrate per kilogram fat-free $mass^{-1}$ and isocaloric with their habitual diet. On these days, participants provided their own food but were given instructions concerning the quantity, preparation, and timings of meals. On days 4 and 5, participants consumed a standardized diet (13.3 megajoules, 52% carbohydrate, 33% fat, and 15% protein) divided into four meals. Standardized meals were provided at 8:15 AM (after the first blood sample), 11:45 AM (after the first postexercise blood sample), and 3:45 PM, with participants taking a fourth meal home to be consumed at 7:00 PM. With the exception of the standardized breakfast, the meal at 11:45 AM, and plain water, no food or drink was consumed by participants until after the final blood sample was collected at 2:15 PM.

Metabolic measurements

Samples of expired air were collected into evacuated Douglas bags. The bags were emptied through a flow controller and volume counter and analyzed for fractions of oxygen (O_2) and carbon dioxide (CO_2) (Servomex 1400). The gas analyzer was calibrated using certified reference gases (100% nitrogen; 16% O_2, 5% CO_2; BOC Gases). To allow the conversion of gas volumes from ambient temperature and pressure saturated to body temperature and pressure saturated, measures of air temperature and pressure were also made.

Biochemical analysis

PTH was measured using a commercial immunometric assay (Nichols Institute), with a detection limit of 0.5 $pmol/L^{-1}$ and an inter- and intraassay coefficient of variation of less than 5% across the range 1–40 $pmol/L^{-1}$. Calcium (range of measurement in serum of 0.05–5.00 $mmol/L^{-1}$), albumin (range of measurement in serum of 10–70 g/L^{-1}), and phosphate (PO_4; range of measurement in serum of 0.10–6.46 $mmol/L^{-1}$) were measured using standard commercial assays (Roche) performed on a Roche modular analytical system. Because fluctuations in protein concentrations, especially albumin, may cause total calcium levels to change independently of the Ca^{2+} concentration, the calcium concentrations were corrected to give an albumin-adjusted calcium (ACa) value as follows: 0.8 mg/dL^{-1} was subtracted from the total calcium concentration for every 1.0 g/dL^{-1} by which the serum albumin concentration was less than 4 g/dL^{-1} or 0.8 mg/dL^{-1} was added to the total calcium concentration for every 1.0 mg/dL^{-1} by which the serum albumin concentration was greater than 4 mg/dL^{-1}. Lactate was measured (in duplicate) immediately after sample collection in whole blood (Yellow Springs Instruments 2300 Stat Plus; Yellow Springs Instruments Inc).

Statistical analysis

All data are presented as mean ± SD unless otherwise stated. Statistical significance was accepted at an alpha level of $P < .05$. Baseline (10:15 AM) biochemical concentrations in the two conditions were compared using a Student's *t* test for paired data. All data were subsequently analyzed using a linear mixed model, with the factors time (of sampling) and condition (EX vs CON) included and with participants as a random within-condition factor. Assumptions of the linear mixed model were investigated by examining the distribution of residuals and the pattern of residuals vs fitted values. Where nonnormality or nonconstant variance was observed, a transformation was applied to the data so that the assumptions were satisfied.

Where there was a significant main effect of time but no significant condition × time interaction, each subsequent time point was compared against baseline from a pooled mean using the least significant difference test. When the condition × time interaction was significant, within each condition, the least significant difference test was used to compare each subsequent time point against baseline and was also used to compare the two conditions at each time point. All statistical analyses were performed with the SPSS version 17 (SPSS Inc).

Results

Baseline biochemistry

There were no significant differences between the EX and CON groups at baseline (Table 1).

Cardiorespiratory variables and lactate levels during exercise

Oxygen uptake (VO_2), percentage of maximal rate of oxygen uptake, heart rate (percentage of maximum;

Table 1. Baseline Biochemical Concentrations in the Exercise (EX) and Control (CON) Groups

Measure	EX	CON	*P* Value (Student's *t* Test for Paired Data)
PTH, pmol/L^{-1}	2.6 ± 0.9	2.5 ± 0.7	.62
PO_4, mmol/L^{-1}	0.99 ± 0.1	0.97 ± 0.09	.71
Albumin, g/L^{-1}	43.3 ± 2.4	42.5 ± 2.4	.26
ACa, mmol/L^{-1}	2.36 ± 0.05	2.34 ± 0.08	.53

Data are mean ± SD.

$\%HR_{max}$), respiratory exchange ratio (RER), and lactate concentrations during exercise are shown in Table 2.

PTH response to exercise

Exercise significantly affected PTH concentrations (condition × time interaction, $P < .001$). In CON, PTH was not different from baseline at 11:30 AM or 12:30 PM but was significantly increased at 1:30 PM (+18%, $P < .05$) and 2:15 PM (+21%, $P < .01$) (Figure 1A). In EX, concentrations were increased (+85%, $P < .01$) with running and were higher than in CON at 11:30 AM (4.5 ± 1.9 vs 2.6 ± 0.9 pmol/L^{-1}, $P < .01$). From 12:30 PM to 2:15 PM, PTH concentrations were 90%–101% of baseline, resulting in lower concentrations in EX compared with CON at 1:30 PM (−22%; 2.2 ± 0.6 vs 2.9 ± 0.7 pmol/L^{-1}, $P < .01$), with concentrations also tending to be lower at 12:30 PM (−12%; $P = .063$) and 2:15 PM (−13%; $P = .057$).

PO_4 response to exercise

Exercise significantly affected PO_4 concentrations (condition × time interaction, $P < .001$). In CON, compared with before exercise, PO_4 was significantly increased at 11:30 AM (+7%, $P < .05$), 12:30 PM (+14%, $P < .05$), 1:30 PM (+25%, $P < .001$), and 2:15 PM (+27%, $P < .001$) (Figure 1B). In EX, concentrations were increased (+49%, $P < .001$) with running and were higher than in CON immediately at the end of exercise (1.47 ± 0.17 vs 1.03 ± 0.17 pmol/L^{-1}, $P < .001$). Thereafter, concentrations remained higher than baseline at 12:30 PM (+8%, $P < .05$), 1:30 PM (+7%, $P < .05$), and 2:15 PM (+22%, $P < .001$), and were lower than CON at 1:30 PM (1.06 ± 0.19 vs 1.19 ± 0.13, $P < .05$).

Table 2. VO_2, $\%VO_{2max}$, $\%HR_{max}$, RER, and Lactate Concentrations During 60 Minutes of Treadmill Running at 65% VO_{2max} in the Exercise Group

Variable	Value
VO_2, L/min^{-1}	2.86 ± 0.32
$\%VO_{2max}$	63.9 ± 1.8
$\%HR_{max}$	85 ± 4
RER	0.902 ± 0.025
Lactate, mmol/L^{-1}	1.0 ± 0.3

Values are mean ±1 SD.

Albumin and ACa response to exercise

Exercise significantly affected albumin concentrations (condition × time interaction, $P < .001$). Albumin concentrations were unchanged in CON (Figure 1C). In EX, concentrations increased ($P < .001$) with running and were higher than in CON immediately at the end of exercise (47.6 ± 2.2 vs 42.2 ± 1.9 g/L^{-1}, $P < .001$). Albumin concentrations had returned to baseline levels at 12:30 PM and were not different from CON in the postexercise period.

Exercise did not significantly affect ACa concentrations (condition × time interaction, $P = .645$). Pooled, mean ACa concentrations tended to be higher at 11:30 AM, but this did not reach statistical significance ($P = .06$) (Figure 1D). Concentrations were significantly lower than baseline at 12:30 PM (−1%, $P < .01$) and 1:30 PM (−1%, $P < .05$).

Discussion

The main findings from this study are the following: 1) PTH concentrations were significantly higher during and lower after running when compared with a nonexercising control and 2) in the exercise group, PTH was not significantly lower than baseline after the cessation of exercise.

The role of the transient increase in PTH with acute running is uncertain. It has been suggested (26) that PTH serves to liberate calcium from bone to counter its loss from the circulation as a result of sweating, but a relationship between dermal calcium losses and PTH concentrations has not been demonstrated (17). Alternatively, because the transient increase resembles, in its shape but not in concentration change, the spike in concentrations that occurs after a single injection of PTH (8) that, when administered daily, results in improvements in bone mass (27), the transient increase may contribute to an anabolic effect on bone. The increase in PTH may serve to suppress sclerostin (15) and inhibit the canonical Wnt/β-catenin signaling pathway (28), thus allowing load-induced bone formation (29). Such a mechanism might also explain the apparent sensitizing effect of PTH to the effects of mechanical loading (30, 31). If so, the rapid increase in PTH

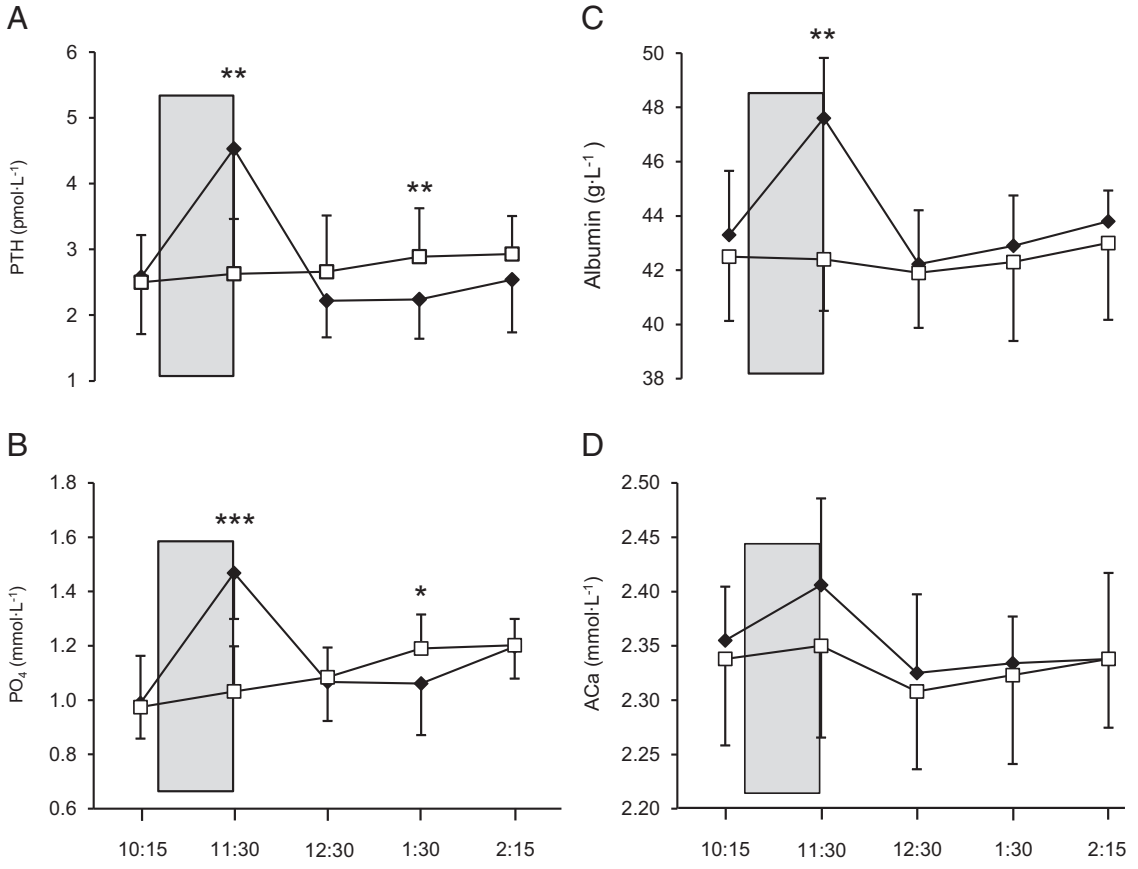

Figure 1. PTH (A), PO_4 (B), albumin (C), and ACa (D) in the EX (closed diamonds) and CON (open squares) groups. Gray bar denotes exercise (60 min at 65% VO_{2max}) in the EX group only. Data are mean ± SD. *, EX different ($P < .05$) from CON; **, EX different ($P < .01$) from CON; ***, EX different ($P < .001$) from CON.

concentrations with the onset of exercise might serve to maximize this effect (30).

Although the transient increase in PTH with exercise might resemble the shape of the spike in concentrations with a single injection of PTH, the maximum absolute concentrations are markedly lower, being 4.5 (range 2.1–7.9) pmol/L^{-1}, with a mean relative increase of 1.9 (1.1–4.2)-fold, compared with 79 and 39 pmol/L^{-1} after injections of PTH 1–84 and 1–34 (8) and relative increases of approximately 10-fold (32). Alone, this might suggest that the increase in PTH with exercise might be insufficient to elicit an anabolic effect in bone. That said, rather than the maximum concentration, the primary determinate of whether PTH has anabolic effects appears to be the length of time concentrations remain above baseline levels (10). For example, in rats, a transient increase in plasma PTH over 1–2 hours is optimal for bone formation (10, 33), whereas in humans, after the sc administration of 20 μg PTH 1–34, a time of maximum observed concentration of approximately 30 minutes and a duration of elevated PTH of up to 3 hours, lead to improved bone mineral density and decreased fracture risk in patients with osteoporosis (34).

Although endogenous increases in PTH are modest compared with those achievable with exogenous provision, in rats, EDTA-induced increases in PTH (3- to 6-fold) produce area under the curve values similar to those seen with a 5-μg/kg^{-1} injection of PTH, the latter of which results in bone formation (35). Transient, endogenous increases in PTH, achieved via short-acting calcium-sensing receptor antagonists (calcilytics), have also been shown to prevent bone loss and increase bone formation in animals (36, 37). In humans, these antagonists produce transient (several hours) increases in PTH of 1.9- to 6.0-fold in a profile consistent with sc PTH administration (36, 38). The mean relative increase in PTH with exercise in the current study was 1.9-fold, which is comparable with the 1.6- to 2.0-fold increases that we have observed previously with similar bouts of exercise (18, 19, 25, 39), although these increases are only at the lower end of the range reported with calcilytics. Because bone formation activity in humans with the chronic administration of calcilytics is yet to be confirmed, it remains uncertain whether the modest and transient increases in PTH with exercise might, if achieved repeatedly, have bone-formation effects.

We did not measure Ca^{2+} and, under normal conditions, the serum Ca^{2+} concentration is the key regulator of PTH secretion. Exercise can induce acidosis, which is known to affect Ca^{2+} concentrations, but lactate levels in

the present study were low (~1 mmol/L^{-1}), and therefore, the presence of a significant metabolic acidosis is unlikely. In addition, the routine measurement of Ca^{2+} is subject to numerous preanalytical considerations, including the requirement for blood to be sampled anaerobically, the impact of posture and delays in sample processing. As a consequence, the reproducibility of Ca^{2+} in clinical practice is poor. In the absence of acidosis, the total calcium concentration is considered a reliable indicator of Ca^{2+}, but exercise results in a hemoconcentration, as observed in the present study, which falsely elevates the total calcium levels. The measurement of ACa both accounts for the effect of hemoconcentration and has been shown to be a reliable indicator of calcium metabolism (40).

Given the normal relationship between PTH secretion and systemic calcium concentrations, the increased PTH at the termination of exercise might be expected to be accompanied by reduced ACa levels. However, in contrast, there was a tendency for them to be slightly higher than preexercise concentrations. This phenomenon has been observed in a previous study (39), and marked increases in both PTH and ACa have also been reported (18, 19). The increased ACa may be a result of PTH-stimulated calcium reabsorption in the kidney and then osteoclastic resorption of bone, but the persistent elevation in PTH at the end of exercise (concomitant with increased ACa) suggests that, during exercise, PTH secretion is not regulated by the systemic calcium concentration. If so, it is possible that PTH is required to fulfill a function during exercise that overrides normal systemic calcium regulation. What this function is, however, remains to be determined.

Results from our previous studies have suggested that PTH concentrations decrease after acute, endurance exercise, with postexercise concentrations reduced by 7%–37% compared with preexercise values (18, 19). These studies did not, however, include a nonexercising control condition, and in both studies, exercise took place at 8:30 AM, with postexercise measures in the late morning (19) or late morning and early afternoon (18). Lower postexercise concentrations, therefore, may simply reflect the circadian rhythm of PTH, which reaches its nadir around the same time of day (22, 23). In the present study, PTH concentrations in the nonexercising control condition increased by approximately 20% between 10:15 AM and 14:15 PM, which compares favorably with a previous circadian rhythm study of healthy, young men, in whom the nadir in PTH concentrations occurred at approximately 10:30 AM (23). Although the PTH circadian rhythm results in only a relatively small change in PTH from the late morning to the early afternoon, which is markedly less than the postexercise decreases observed in previous studies (18, 19), we confirm, by comparing postexercise responses with a control condition, that the circadian rhythm does not completely account for the lower postexercise PTH concentrations.

Given the bone formation and bone resorption effects of transient and chronic increases in PTH, Brahm et al (21) have suggested that the most favorable effects of PTH on the skeleton would be achieved with low basal levels and large increases during exercise. Others (20) have proposed that the reduction in basal PTH levels after a physical training program would serve to exaggerate transient increases during exercise, thus producing a more potent osteogenic effect. In a similar manner, the significant reduction in postexercise PTH concentrations confirmed by the present findings might serve to accentuate the transient nature of the increase that precedes it, maximizing the relative difference in concentrations.

Postexercise PTH concentrations were not significantly different from those at baseline, which is in contrast to our previous studies in which the exercise finished earlier (9:30 AM) in the morning (18, 19) but consistent with the percentage reduction (≤10%) in PTH in a study with the same running intensity, duration and finish time in fasted participants (39) (Table 3). These findings might be explained by the nadir in the circadian rhythm of PTH (23) that occurs later in the morning. The timing of exercise and recovery would not, however, fully explain the marked changes observed in endurance-trained runners during prolonged, exhaustive exercise (18) that finished later in the morning (10:30–11:30 AM) (Table 3).

This leads to the question of the mechanism behind the postexercise decrease in PTH. The decrease might be a rebound effect related to the prior increase in the concentrations during exercise. However, in our previous study of exercise intensity (19), there was no change in PTH during exercise at 55% and 65% VO_{2max}, but concentrations were still reduced by 11%–21% from baseline in the first 3 hours after exercise. The data in Table 3 might suggest that the overall metabolic demand of exercise influences the postexercise PTH concentrations, with the decrease in PTH tending to be greater with increasing exercise intensity (19) and more marked in endurance-trained (ET) men who ran for 50% longer than their recreationally active (RA) counterparts during exhaustive exercise (18).

Postexercise changes in PTH in these studies might also be explained by calcium concentrations. After exhaustive exercise, the more marked decrease in postexercise PTH in ET compared with RA men was accompanied by a tendency for a greater increase in postexercise ACa (~+8% vs ~+4%) from 0 to 3 hours after exercise (18). Additionally, the tendency for lower postexercise PTH concentrations with increasing exercise intensities [63%–70% of

Table 3. Comparison of Postexercise (First 3 Hours) Changes in PTH Concentrations in the Present Study and Previously Published Data

			Postexercise PTH Concentration, % Before Exercise				
Study	**Condition**	**Start/Finish of Exercise**	**+0.5 h**	**+1 h**	**+1.5 h**	**+2 h**	**+3 h**
Present study	EX	10:30/11:30 AM		91		90	101
Scott et al (18)[a]	RA	~08:30/~10:30–11:30 AM	105	83[b]	90[b]	93[b]	
	ET	~08:30/~10:30–11:30 AM	84	70[b]	73[b]	76[b]	
Scott et al (19)[c]	Low	8:30/9:30 AM	101	82		84	89
	Mod	8:30/9:30 AM	103	79[d]		80[d]	81[d]
	High	8:30/9:30 AM	100	70[b]		63[b]	70[b]
Scott et al (39)[e]	Fast	10:30/11:30 AM		102		96	97
	Fed	10:30/11:30 AM		106		114	110

Abbreviation: Mod, moderate. Data are mean percentage of preexercise concentrations.

[a] Sixty minutes of treadmill running (fasted) at 65% VO_{2max} followed by intermittent running to exhaustion at 70% VO_{2max} in RA and ET men, with statistical analysis performed on pooled data from the RA and ET groups.

[b] Different ($P < .001$) from before exercise.

[c] Sixty minutes of treadmill running (fasted) at 55% (low), 65% (mod), and 75% (high) VO_{2max}, with statistical analysis performed separately on the three individual groups.

[d] Different ($P < .05$) from before exercise;

[e] Sixty minutes of treadmill running at 65% VO_{2max} after an overnight fast (fast) or a standardized breakfast fed at 8:15 AM (fed), with statistical analyses performed on pooled data from fast and fed.

baseline (75% VO_{2max}), vs 82%–89% (55% VO_{2max})] was also accompanied by a larger increase in ACa [+5% (75% VO_{2max}) vs +2% (55% VO_{2max})] (19). Consistent with this idea, when little or no decrease in postexercise PTH is observed, the ACa concentrations are also unchanged (39). Similarly, in the present study, in which the postexercise PTH concentrations were not different from those before exercise, the ACa concentrations were not increased significantly in the postexercise period.

In animals, both ingestion and iv infusion of PO_4 increases circulating PTH concentrations (41, 42), whereas in circadian rhythm studies in humans, changes in serum PO_4 precede those in PTH (24). In the case of iv infusion, circulating levels of both PO_4 and PTH are increased after only 10 minutes without detectable alterations in plasma Ca^{2+} (42), suggesting that acute increases in PO_4 rapidly stimulate PTH secretion. Conversely, when animals adapted to a high-PO_4 diet are provided with a low-PO_4 meal, both PO_4 and PTH concentrations decrease within 2 hours (42), whereas in humans with secondary hyperparathyroidism, PTH levels are normalized within 1 day of switching to a low-PO_4 diet (43). In the present study, PO_4 was significantly lower in EX compared with CON at 1:30 PM when PTH was also lower, whereas in a previous study comparing exercise at 55%, 65%, and 75% VO_{2max}, the largest decrease (from preexercise levels) in PTH after exercise (−37% at 2 h after exercise at 75% VO_{2max}) was accompanied by the largest decrease (17%) in PO_4 (19). Although changes in PO_4 do not explain all the changes in PTH during exercise (19), taken together, these data might suggest a role for PO_4 in the postexercise regulation of PTH concentrations. It is possible that the relative changes in both ACa and PO_4 together determine the extent of changes in PTH.

Finally, the present study specifically used male volunteers to avoid the potential confounding factor of fluctuations in the reproductive hormones on bone metabolism. However, the role of physical activity in female bone health is of considerable interest for numerous reasons, including acute (44) and chronic (45) interactions between energy availability, sex steroid levels and bone metabolism, the change in bone mechanosensitivity that occurs in women as a function of the decline in estrogen receptor-α number (46), and the high rates of stress fractures in physically active females (47). There is also evidence that in female long-distance runners, the PTH response to exercise may be associated with bone mineral density, suggesting an alteration to homeostatic control mechanisms (48). With carefully controlled studies comparing the calcium metabolism (and bone turnover marker) response with acute exercise in males and females currently lacking, further studies with female volunteers are warranted to confirm the findings from the present study.

In conclusion, compared with a rested control condition, PTH concentrations were decreased after acute endurance running. These data suggest a true effect of exercise on PTH concentrations after exercise. The lower PTH concentrations are not fully explained by increased ACa but might be related to decreased PO_4 concentrations or a combination of ACa and PO_4. Further larger studies

may elucidate the nature of postexercise changes in PTH and the mechanism(s) controlling these changes.

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