

CHARACTERIZATION OF THE PROLACTIN RESPONSE TO PROLONGED ENDURANCE EXERCISE

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ABSTRACT

This study characterized the blood prolactin responses to a prolonged endurance exercise bout in comparison to a resting, control period with no exercise. Six healthy exercise trained males completed both a 90 minute cycle exercise (70% VO_{2max}) and a rest-control experimental session under standardized conditions. Blood samples were collected at – 15, 0 (exercise start), 15, 30, 45, 60, 75, 90 (exercise end), 105, and 120 minute time points in the exercise and rest-control sessions. Prolactin concentrations were analyzed using radioimmunoassay procedures and tested for significant changes with ANOVA analysis. In the exercise session, prolactin concentrations from 45 to 120 minutes were significantly greater than the 15 minute concentration before exercise ($p < 0.01$). Furthermore, the exercise concentrations at 45 to 120 minutes were also significantly greater than the concentrations observed at the comparable rest-control time points ($p < 0.01$; approximately 300% elevation). The frequent blood sampling protocol used in this study clearly portrays the magnitude, time-line, and extend of the prolactin response to prolonged endurance activity. The mechanism and role for the prolactin response was not the focus of this study, but relative to the latter, it is speculated the hormonal change could pertain to signaling energy usage-status within the body and, or prompting immune system activation.

Key words: hormones, stress, endocrine, methodology

INTRODUCTION

Prolactin is a hormone released primarily by the anterior pituitary in humans [1]. Across several species its release and physiological function has been linked to stress reactivity, water balance, immune system activation and reproductive function [1, 2, 4, 7, 12]. A vast majority of the research on prolactin relates to this last topic due to the fact that prolactin has long been associated with lactation in women [1] and in excessive quantities to gonadal suppression in both men and women [1, 13].

Copious research indicates physical exercise (e.g., sports training and competitions) results in a significant and substantial increase in the circulating levels of prolactin [3, 5, 8, 9]. However, there appears to be a major methodological limitation in much of the available research on prolactin and exercise. Specifically, many exercise studies have typically looked at prolactin responses to exercise with too infrequent of blood sampling protocols and, or without a non-exercise control assessment of the hormone [e.g., 3, 8]. Regrettably, these methodological constraints have compromised the validity of exercise studies attempting to determine and quantify the prolactin response to specific exercise sessions.

For the above reasons, the present study was undertaken, the purpose being to characterize the prolactin responses to an exercise bout in comparison to a rest-control period with no exercise. In this study a 90 minute intensive exercise bout (70% maximal oxygen uptake [$\text{VO}_{2\text{max}}$]) was utilized due to previous research demonstrating this would result in substantial prolactin responses [5, 8].

METHODS AND PROCEDURES

The subjects for this study were six healthy male endurance athletes who had been involved with exercise training for > 5 years. Each subject gave written informed consent and all research procedures were reviewed and approved by university ethical and human research safety committees.

Subjects reported to the laboratory on two occasions: (1) a rest-control session and, (2) an exercise session. The time of day for each experimental session was standardized and controlled. The order of

session administration was randomized and in each situation subjects were asked to report 8 hours post-prandial, having refrained from physical activity (24 hours before) and to have avoided excessive stressful personal situations or events. Furthermore, the ambient environment conditions were replicated in the exercise and rest-control sessions and were thermally neutral (20–25°C, low relative humidity) as excessive heat exposure promotes prolactin release [8].

Aspects of the exercise protocols to determine the subjects VO_{2max} and the submaximal exercise protocols have been reported elsewhere [3, 5]. However, briefly the subjects completed a graded incremental cycle exercise test (3 minute stages, 50 W workload increases, continuous respiratory gas analysis) to exhaustion to determine their VO_{2max} . These results were used to calculate the submaximal workload to elicit ~70% of VO_{2max} for their 90 minute cycle exercise session. The exercise and, or rest-session occurred within 2 weeks of the completion of the VO_{2max} testing. All exercise was performed on a mechanically braked cycle ergometer (Monark, Sweden) and at 15 minute intervals throughout the exercise VO_2 (i.e., respiratory gases; Rayfield, USA), heart rate, and rating of perceived exertion were monitored.

Prior to each experimental session an antecubital venous catheter was inserted into the non-dominant arm of the subjects, and they were allowed to rest quietly for 15 minutes in a supine position. Approximately 15 minutes (–15 min.) before beginning the 90 minutes submaximal exercise or rest-control session the first blood specimen (3 mL) was withdrawn. Then at 15 minute intervals afterwards specimens were withdrawn at; 0, 15, 30, 45, 60, 75, 90, 105, and 120 minutes (exercise was 0 to 90 minute). In the rest-control session the subjects sat upright and read or watch television. During both sessions the subjects consumed water *ad libitum*.

Blood specimens were collected into EDTA treated tubes and placed immediately on ice until preparation for storage. Blood collection tubes were later centrifuged at 3000 x g for 15 minutes at 4°C to separate plasma. For each tube the separated plasma was aliquoted into cyro-freeze tubes and stored at –80°C until hormonal analysis could be completed. Plasma was analyzed in duplicate for prolactin concentration using commercial radioimmunoassay procedures (DPC Inc., USA). Assay sensitivity was ~0.4 µg/L and all within and between coefficients of variation for the assays were less than 10%.

Statistical analyses were performed with the “Statistica” software package (version 6.0, USA). Data are reported as means plus or minus the standard error of the mean. Repeated measures analysis of variance was used to assess the hormonal concentrations for mean differences, with subsequent post hoc analysis being the Fisher *lsd* procedure. Statistical significance was set at $p \leq 0.05$.

RESULTS

The physical characteristics of the subjects were as follows: age = 23.5 ± 2.0 yr, height = 179.5 ± 2.5 cm and body mass = 76.0 ± 1.9 kg. The $VO_{2\max}$ of the subjects was 60.3 ± 3.9 mL/kg/min.

All subjects completed the 90 minute submaximal exercise session with no major difficulties. They displayed normal and expected steady-state cardiovascular responses for such demanding exercise (data not shown). There was a tendency in some subjects to display a slight degree of cardiac drift by the end of the exercise, however, profuse fluid intake minimize the magnitude of this phenomenon.

The prolactin concentrations during each of experimental sessions are displayed in Figure 1. During the rest-control session the prolactin concentrations varied over the blood sampling times, but no significant differences were noted. Conversely during the exercise session significant increases in prolactin were detected. The exercise session concentrations from minute 45 to 120 were significantly greater than the -15 minute concentration before exercise ($p < 0.01$). Furthermore, the exercise session concentrations at 45 to 120 minutes were also significantly greater than the concentrations observed at the comparable rest-control time points ($p < 0.01$).

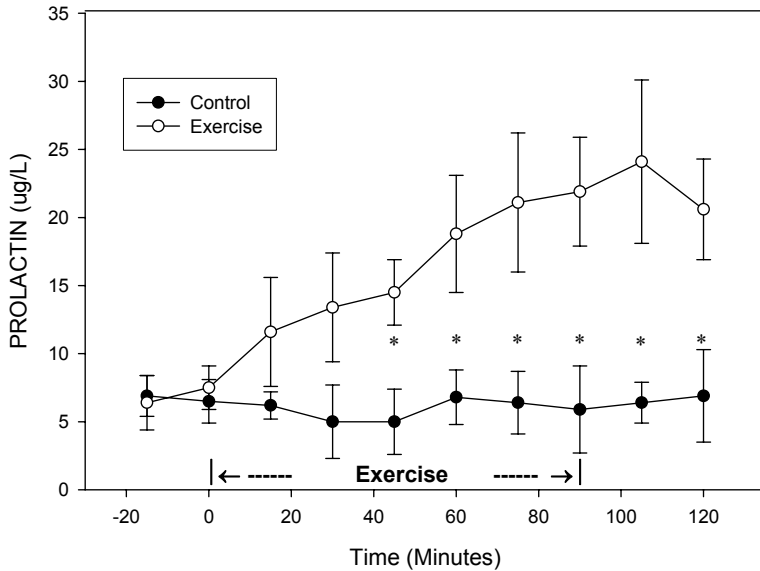


Figure 1. Prolactin concentrations in a resting, control session (filled circles) and a exercise session (open circles; 90 minutes duration, 70% VO_{2max}). All values are means \pm SEM. The * symbol denoted significant difference between each session at the specific time point ($p < 0.05$).

DISCUSSION

The intent of this study was to provide a more detailed characterization of the prolactin responses to exercise (i.e., prolonged endurance cycling) due to the limited number of such findings in the research literature which employed frequent blood sampling protocols. The present findings demonstrate that the strenuous form of exercise used induced significant and persistent elevations in prolactin concentrations. Many of the significant exercise prolactin concentrations approached a 300% elevation over the comparable rest-control session values. The prolactin concentrations became elevated during the exercise session by 45 minutes into the exercise bout. The magnitude of the increases and the time course of these changes are similar to those

reported previously (all be it, many such studies have used less frequent bloods sampling protocols) [5, 8, 9].

In contrast to most hormones, prolactin is apparently under chronic negative inhibition with dopamine serving as the inhibiting factor of secretion. Dopamine is secreted into portal blood by hypothalamic neurons, binds to receptors on lactotroph cells which produce prolactin, and inhibits both the synthesis and secretion of the hormone [1]. In addition to tonic inhibition by dopamine, prolactin secretion is positively regulated by several other hormones, including thyroid-releasing hormone, gonadotropins-releasing hormone and vasoactive intestinal polypeptide [1, 2]. In response to exercise, the elevations in prolactin concentrations seem brought about by the removal of the dopamine inhibition effect; although, further work is necessary to clarify and substantiate this point.

The role prolactin plays in responses to exercise is an issue of much debate and continued investigation. There are several possible explanations for why prolactin increases with exercise. First, it is well established that hyperprolactinemic states (acute or chronic) can have suppressive effects on the reproductive systems in men and women [1]. In humans as well as many other species, reproductive function is linked to energy reserves and availability [1, 2]. It is conceivable that prolactin elevations due to exercise serve as a means to signal for a reduction in reproductive function due to the reduced or limited energy available induced by strenuous activity [6, 10]. The exercise prolactin response is transient, but nonetheless is substantial and persistent enough in the early hours of recovery from exercise to perhaps signal such a status change [3]. On the other hand, it is also possible that prolactin is playing a key role in activation of the immune system following exercise. The prolactin receptor is widely expressed by immune cells, and some types of lymphocytes even synthesize and secrete prolactin [1, 2, 4]. These observations suggest that prolactin may act as an autocrine, paracrine as well as endocrine modulator of immune activity [4, 7, 12]. Thus the hormone may serve as a mediator to the post-exercise inflammatory process and as a means to initiate aspects of the process in order to allow recovery-regeneration and adaptation to exercise. The intention of this study was not to elucidate the mechanism or the role of prolactin release to exercise; but the above speculation present plausible explanations as to why the observe response occurred. Future research needs to address these issues much more closely.

To summarize, this study found that the hormone prolactin has a significant and robust elevation in the blood in response to prolonged endurance exercise. The blood levels in this study became significant increased by 45 minutes into the exercise bout and remained so throughout the remainder of the exercise as well as for 30 minutes into recovery. The role prolactin plays in response to exercise is unclear, but may relate to signaling energy usage-status within the body and, or as an immune system activator. Further research is necessary to address the question of what physiological role this hormone has in helping the body to accommodate and adjust to exercise.

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