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Plasma IL-6 responses to high-intensity cycling exercise

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BACKGROUND

Interleukin-6 (IL-6) belongs to a family of cytokines, which are proteins secreted from various cell types in response to stimuli[1]. IL-6 is typically reported as a pro-inflammatory[2] cytokine, but it has also been seen to partially mediate an anti-inflammatory response[3]. In metabolism, IL-6 increases the availability of blood glucose and free fatty acids by increasing lipolysis in adipose tissue and glycogenolyis in the liver[4]. It is believed that IL-6 expression and release from contracting skeletal muscle may play a vital role in systemic metabolism by its regulation of substrate availability and use[5] (Figure 1). Such coordination has important implications for defining how physical activity protects against, and inactivity promotes, the development of chronic metabolic disorders. The exercise-induced elevation of plasma IL-6 has created an interest for its role in initiating biochemical signaling pathways in skeletal muscle, regulating metabolism in healthy individuals, as well as the potential for altered IL-6 function in states of metabolic disease such as type 2 diabetes and obesity[6]. However, IL-6's influence on specific aspects of energy metabolism remains a topic of considerable debate[6].

Because IL-6 is produced in and released from skeletal muscle during exercise, some scientists have termed it a "myokine." As a result, skeletal muscle is now seen in a new role: an endocrine organ that produces and secretes myokines in response to exercise[6]. Exercise intensity is known to be an important factor in plasma IL-6 concentrations[2]. Higher intensity levels elicit higher concentrations of IL-6, but the specific mechanisms and reasons for this finding remain a topic of debate. Peak levels of IL-6 are reached at the end of the exercise, or shortly thereafter[7]. Although several studies have evaluated the IL-6 response to endurance exercise[8, 9], the literature lacks a thorough study of how repeated bouts of high-intensity exercise affect IL-6.

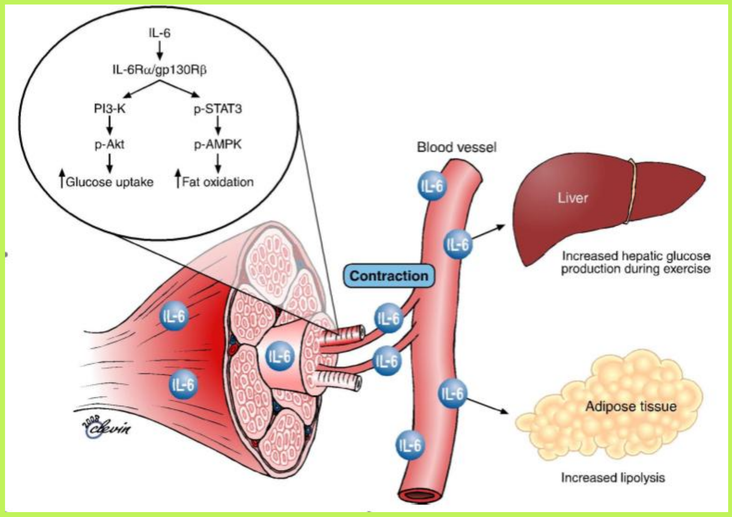

Figure 1. Proposed actions of muscle-derived IL-6 in response to muscle contraction. IL-6 acts as a myokine as it enters the circulation and mobilizes fat stores. IL-6 increases lipolysis in adipose tissue and stimulates glucose production and output by the liver. Locally, IL-6 has autocrine/paracrine actions on the active muscle cells to increase glucose uptake as well as fat oxidation[6].

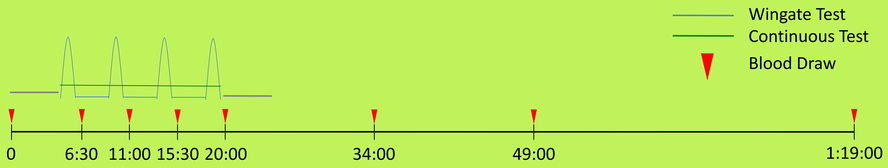

Figure 2. Blood draw schedule during for exercise bouts with running clock. Graph begins at the warm-up and concludes with the 60-min post-exercise sample.

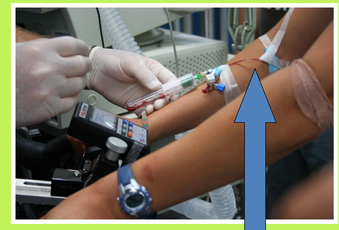

Table 1. Subject details. Values are displayed as mean (SD).

	Age (years)	Height (in)	Weight (lbs)	VO_2 Max (ml/kg/min)
Females (n=5)	20.6 (1.1)	65.9 (2.7)	154.8 (16.5)	41.1(7.0)
Males (n=5)	20.8 (0.8)	71.8 (3.5)	165.6 (33.0)	53.1 (6.9)
Total (n=10)	20.9 (0.8)	69.4 (4.1)	161.1 (26.6)	48.3 (8.8)

RESULTS:

*Time Interval Key:
1. Pre- to 1.5 min
2. Pre- to 6 min
3. Pre- to 10.5 min
4. Pre- to +1 min
5. Pre- to +15 min
6. Pre- to +30 min
7. Pre- to +60 min

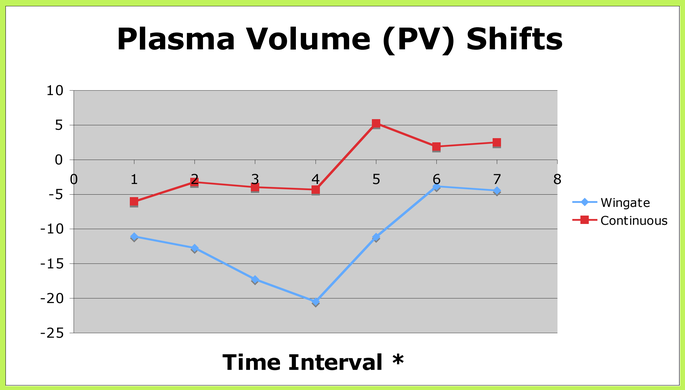

Figure 3. Plasma volume shifts during each time interval for both exercise bouts.

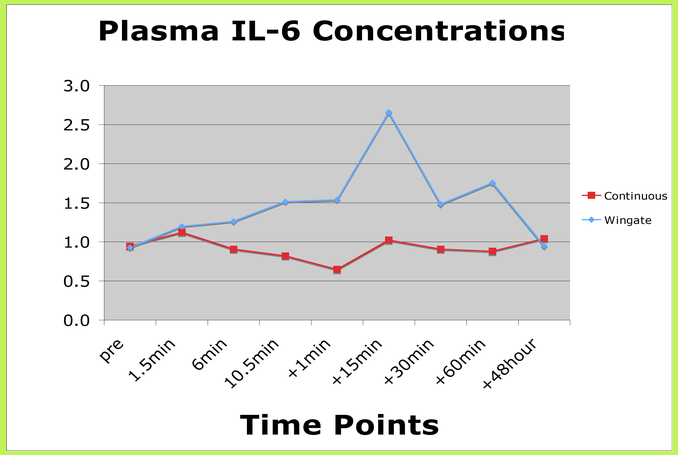

Figure 4. Mean plasma IL-6 concentrations at each time point for both exercise bouts.

PURPOSE:

The purpose of this study was to investigate the plasma IL-6 response to high-intensity cycling exercise.

METHOD:

Participants: 10 healthy college-aged students (n=5 females, n=5 males); see characteristics in Table 1.

Procedure:

1. VO_2max Test: Subjects first completed a graded exercise test using a cycling ergometer (Velotron; RacerMate Inc.), as VO_2 data was gathered with a metabolic cart (TrueMax 2400 Metabolic Measurement System; ParvoMedics). This test provided familiarization with equipment, as well as a quantitative measure of cardiovascular fitness.

2. Wingate Test: Using the protocol of Greer et al.[10], four 30-second Wingate cycling tests were performed. Each Wingate test was separated by 4 minutes of recovery, during which subjects cycled at 20 W. The total test duration was 24 minutes (5-min warm-up, 14-min test, and 5-min cool-down). The predetermined workload for the Wingate test was 7.5% body weight in kp.

3. Continuous Test: The continuous bout of exercise involved the same total work as performed during the Wingate intervals, but this workload was equally distributed over a 14-min duration (The same 5-min warm-up and cool-down were also included.)

An indwelling venous catheter was used to sample blood before, during, and after the exercise bouts at pre-test, 1.5, 6, and 10.5 minutes, as well as post-exercise at 1, 15, 30, and 60 minutes for both protocols (Figure 2). A 48-hr post-exercise blood draw was also taken after both exercise bouts.

Hemoglobin and hematocrit levels were determined to account for exercise-related changes in blood plasma volume. Plasma volume corrections[11] were made to analyze whether increased IL-6 concentrations were observed, or merely more concentrated due to a loss of plasma. Hemoglobin and hematocrit were calculated by routine cyanmethoglobin and microcapillary techniques, respectively (Lourdes Clinical Centrifuge; Lourdes Instrument Corporation). IL-6 concentrations were measured using chemiluminescent immunoassay (Immulite Analyzer; Diagnostic Products Corporation).

SUMMARY:

- The continuous bout of exercise provided a good control for the high-intensity Wingate protocol since both tests accomplished the same amount of work.
- Observed exercise-induced elevations of plasma IL-6 were relatively small and were quite close to normal resting values.
- Physical characteristics and fitness levels of subjects were variable and could have affected the results (especially due to values from one untrained subject).
- Greater plasma volume shifts were observed during the Wingate tests than during the continuous bout.
- Data from only 7 of 10 subjects has been analyzed, so this is a preliminary report.

CONCLUSION:

The relative contributions of the anaerobic and aerobic energy systems differ between the two exercise bouts: the Wingate tests are primarily anaerobic while the continuous bout is predominantly aerobic. It appears that brief stints of maximal cycling exercise (i.e Wingate tests) may be a stimulus for IL-6 release.

REFERENCES:

1. Pedersen, B. K., Ostrowski, K., Rohde, T., & Bruunsgaard, Helle. (1998). The cytokine response to strenuous exercise. *Can. J. Physiol. Pharmacol.,* 76, 505-511.
2. Ostrowski, K., Schjerling, P., & Pedersen, B. K. (2000). Physical activity and plasma interleukin-6 in humans – effect of intensity of exercise. *Eur J Appl Physiol,* 83, 512-515.
3. Petersen, A. M. W., & Pedersen, B. K. (2006). The role of IL-6 in mediating the anti-inflammatory effects of exercise. *Journal of Physiology and Pharmacology,* 57, 43-51.
4. Pedersen, B. K., Åkerström, T. C. A., Nielsen, A. D., & Fischer, C. P. (2007). Role of myokines in exercise and metabolism. *J Appl Physiol,* 103, 1093-1098.
5. Glund, S., & Krook, A. (2008). Role of interleukin-6 signalling glucose and lipid metabolism. *Acta Physiologica, 192*: 37-48. Fischer, C. P. (2006). Interleukin-6 in acute exercise and training: what is the biological relevance? *Exerc. Immunol. Rev.,* 12, 6-33.
6. Pedersen, B. K., & Febbraio, M. (2008). Muscle as an endocrine organ: focus on muscle-derived interleukin-6. *Physiol Rev,* 88, 1379-1406.
7. Fischer, C. P. (2006). Interleukin-6 in acute exercise and training: what is the biological relevance? *Exerc. Immunol. Rev.,* 12, 6-33.
8. Robson-Ansley, P., Barwood, M., Canavan, J., Hack, S., Eglin,C., Davey, S., Hewitt, J., Hull, J., & Ansley, L. (2008). The effect of repeated endurance exercise on IL-6 and sIL-6R and their relationship with sensations of fatigue at rest. *Cytokine,* 45, 111-116.
9. Ronsen, O., Lea, T., Bahr, R., & Pedersen, B. K. (2002). Enhanced plasma IL-6 and IL-1ra responses to repeated vs. single bouts of prolonged cycling in elite athletes. *J Appl Physiol,* 92, 2547-2553.
10. Greer, F., McLean, & Graham, T. E. (1998). Caffiene, performance, and metabolism during repeated Wingate exercise tests. *J Appl Physiol,* 85, 1502-1508.
11. Dill D.B., & Costill, D.L. (1974). Calculation of percentage changes in volumes of blood, plasma, and red cells in dehydration. *J Appl Physiol, 37,* 247-8.

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