

The effect of exercise intensity on circulating hepatokine concentrations in healthy men.

Scott A. Willis^{1,2}, Jack A. Sargeant^{1,2}, David J. Stensel^{1,2}, James A. King^{1,2}.

¹National Centre for Sport and Exercise Medicine, School of Sport, Exercise and Health Sciences, Loughborough University, UK

²NIHR Leicester Biomedical Research Centre, UK

Introduction: Hepatokines such as fibroblast growth factor 21 (FGF21), follistatin and leukocyte cell-derived chemotaxin 2 (LECT2) are liver-derived proteins which contribute to the regulation of whole-body glucose and lipid metabolism. Acute shifts in energy balance, through means such as exercise, modulate circulating concentrations of these hepatokines; however the influence of exercise intensity has not been fully explored. This study examined the effect of exercise intensity on circulating hepatokine concentrations in healthy men.

Methods: In a randomized, crossover design, 10 healthy men (see Table 1 for participant characteristics) completed three experimental trials, commencing with either a moderate-intensity run (55% peak oxygen uptake ($\dot{V}O_2$ peak); MOD), high-intensity run (75% $\dot{V}O_2$ peak; HIGH) or control period (rest; CON). The duration of MOD and HIGH differed (mean \pm SD: 57 \pm 8 vs 42 \pm 6 min, respectively) so that total energy expenditure was matched (target 600 kcal). After exercise, participants rested for 7 h, with standardised meals consumed at 2 and 6 h post-exercise. Venous blood samples were taken before exercise and at 0, 1, 2, 4 and 7 h post-exercise for measurement of plasma FGF21, follistatin and LECT2 concentrations (ELISA).

Results: Total energy expenditure was similar between the two exercise trials (MOD vs HIGH: 591 \pm 17 vs 595 \pm 14 kcal; $P = 0.46$). Two-way ANOVA revealed a significant trial main effect and trial-time interaction for FGF21 (both $P < 0.001$), indicating a greater increase in plasma FGF21 concentrations at 1, 2 and 4 h after HIGH compared to MOD (all $P < 0.03$; Figure 1A). A significant trial main effect and trial-time interaction for follistatin was also observed, indicating elevated plasma follistatin concentrations at 4 and 7 h after both MOD and HIGH vs CON (all $P < 0.01$; Figure 1B); however the response was similar between the two exercise trials. A significant trial-time interaction was found for LECT2, indicating an increase in plasma LECT2 concentrations immediately after MOD and HIGH

vs CON (both $P < 0.05$; Figure 1C); however there were no differences between the two exercise trials.

Discussion: The present study demonstrates that acute bouts of exercise transiently increase circulating concentrations of the hepatokines FGF21, follistatin and LECT2. Furthermore, the magnitude of the post-exercise increase in circulating FGF21 may be dependent on the intensity of the exercise, while responses in the other hepatokines appear to be independent of exercise intensity.

Table 1. Participant characteristics ($n = 10$).

	Mean \pm SD
Age (years)	26 \pm 2
Height (m)	1.77 \pm 0.07
Body mass (kg)	80.2 \pm 6.2
BMI (kg.m ⁻²)	25.6 \pm 1.7
Waist circumference (cm)	83.7 \pm 4.1
Body fat (%)	15.4 \pm 4.4
$\dot{V}O_2$ peak (ml.kg ⁻¹ .min ⁻¹)	49.8 \pm 5.3

BMI, body mass index; $\dot{V}O_2$ peak, peak oxygen uptake.

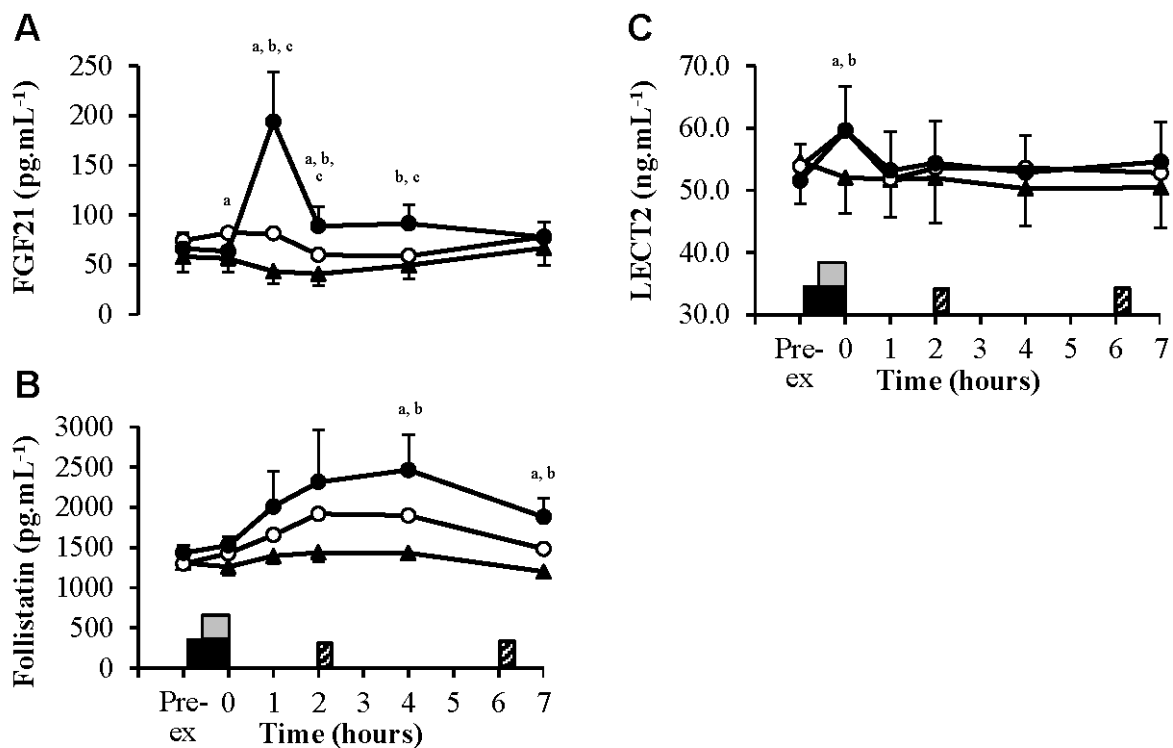


Figure 1. Circulating concentrations of FGF21 (A), follistatin (B) and LECT2 (C) during the control (▲), moderate-intensity exercise (○) and high-intensity exercise (●) trials. Data are presented as means \pm SEM for $n = 10$. Black rectangle indicates moderate-intensity exercise, grey rectangle indicates high-intensity exercise and hatched rectangles indicate test meals.

^aMOD significantly different from CON ($P < 0.05$); ^bHIGH significantly different from CON ($P < 0.05$); ^cHIGH significantly different from MOD ($P < 0.05$).