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FACULTY OF SPORT AND HEALTH SCIENCES UNIVERSITY OF JYVÄSKYLÄ, FINLAND

Jukka Hintikka [1], Raakel Luoto [2], Olli Ruuskanen [2], Johanna K. Ihalainen [1], Matti Waris [3], Olli J. Heinonen [4], Maarit Valtonen [5], Satu Pekkala [1]

[1] Faculty of Sport and Health Sciences, University of Jyväskylä
[2] Department of Pediatrics and Adolescent Medicine, Turku University Hospital
[3] Institute of Biomedicine, University of Turku
[4] Paavo Nurmi Centre, Department of Health and Physical Activity, University of Turku
[5] Finnish Institute of High Performance Sport KIHU, Jyväskylä

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UNIVERSITY OF TURKU

SERUM CYTOKINES IN ELITE ATHLETES ASSOCIATE WITH TRIGLYCERIDE METABOLISM

BACKGROUND

- **Regular bouts of vigorous exercise combined with other stressors and lack of sufficient recovery can cause a sustained pro-inflammatory response, leading to low-grade systemic inflammation.**
- **Inflammatory cytokines regulate several factors in glucose and lipid metabolism and increase in response to metabolic diseases.**
- **During training and competition season, elite athletes are predisposed to increased levels of energy expenditure, stress and low-grade inflammation and are at an increased risk of infections.**
- **We studied the serum inflammatory markers and metabolome of elite cross-country skiers and age matched controls. Samples were collected at the end of an exhaustive training and competetive season.**

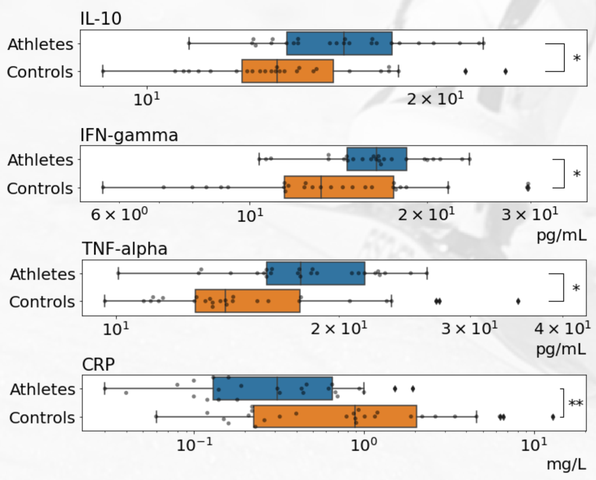
METHODS

The study included 27 athletes belonging to Finland´s National Nordic Ski Team competing at an international level. For every athlete, one healthy and moderately-exercising (<6 hours/week) control subject was recruited. Blood samples were collected a day before the start of the National Championships, an event at the end of the skiers' competition season.

Serum cytokines were analyzed with a 4-plex cytokine ELISA kit (Quansys, Logan, USA): Interleukin 10 (IL-10), interferon gamma (IFN-gamma), interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-alpha). Serum C-reactive protein (CRP) concentrations were measured with a high-sensitivity ECLIA assay (Immulite 2000, Siemens, LA, USA). Glycoprotein acetyls (GlycA) and serum metabolites were analyzed using a high-throughput ^{1}H NMR metabolomics and lipidomics platform (Nightingale Health, Helsinki, Finland).

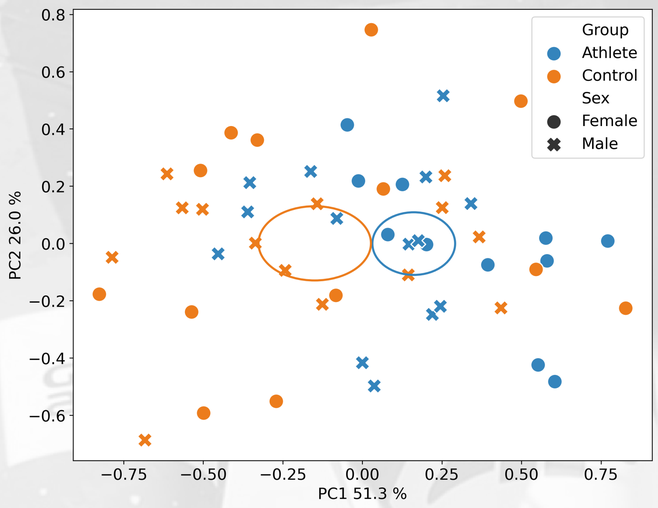
RESULTS

THE ATHLETES HAD HIGHER CYTOKINE LEVELS BUT LOWER CRP THAN THE CONTROLS



*Boxplots of cytokines and CRP. Rank-sum p value * <0.05 ** < 0.01*

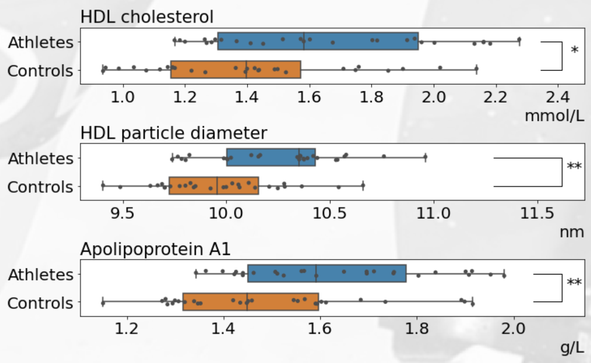
We set the cytokines on a principal component analysis to reduce data dimensionality. Athletes and particularly female athletes had higher scores along the first component (PC1), corresponding to pro-inflammatory cytokines.



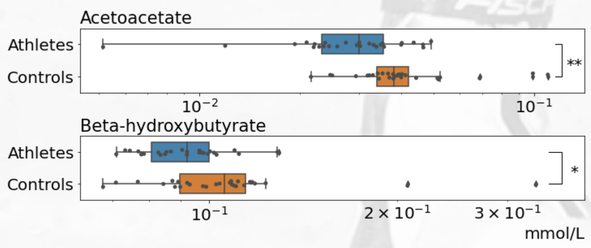
	IL-6	TNF-alpha	IFN-gamma	IL-10
PC1 (51 %)	**0.596**	**0.506**	**0.572**	0.249
PC2 (26 %)	-0.490	-0.063	0.754	-0.432

Principal component analysis (PCA) plot of the serum cytokines and associated loadings. Ellipses denote 95% confidence interval.

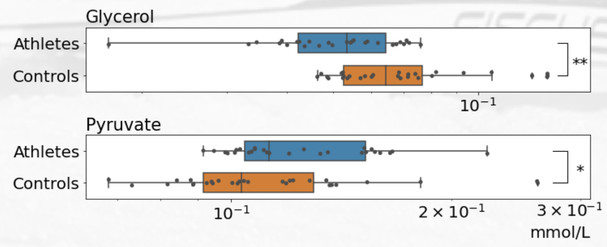
THE ATHLETES HAD HIGHER HDL CHOLESTEROL, HDL PARTICLE DIAMETER AND LOWER KETONE BODIES THAN THE CONTROLS — DIFFERENCES REMAINED AFTER ADJUSTING FOR BODY MASS INDEX



*Boxplots of HDL cholesterol, HDL particle size and apo-A1. 2-tailed t-test or kruskal-wallis p value * < 0.05 ** < 0.01*



*Boxplots of ketone bodies. 2-tailed t-test or rank-sum p value * < 0.05 ** < 0.01*

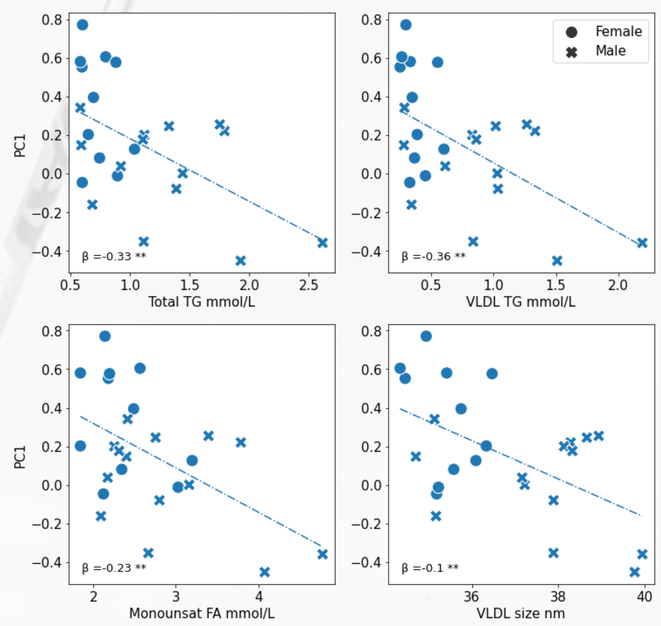


*Boxplots of glycolysis related metabolites. 2-tailed t-test or kruskal-wallis p value * <0.05 ** < 0.01*

PRO-INFLAMMATORY CYTOKINES WERE HIGHER IN FEMALE ATHLETES, BUT NOT IN CONTROLS, AND COVARIED WITH TRIGLYCERIDES, FATTY ACIDS AND VLDL

Associations of inflammatory component PC1, training load and lipids among the athletes. Color indicates statistically significant difference (2-tailed t-test) or correlation (Pearson).

	Sex	*Training load*	*PC1*
			Females ↑
Ketone Bodies			
Acetoacetate	**Males ↑**	0.041	-0.128
Beta-OH-butyrate		0.161	**-0.484**
Triglycerides (TG)			
Total TG	**Males ↑**	**0.428**	**-0.554**
VLDL TG	**Males ↑**	**0.454**	**-0.576**
Fatty acids (FA)			
Monounsaturated FA	**Males ↑**	**0.418**	**-0.527**
Lipoprotein sizes			
VLDL size	**Males ↑**	**0.431**	**-0.552**
Cholesterol			
VLDL cholesterol	**Males ↑**	0.287	**-0.523**
		Pearson corr coeff.	



*Regression plots of inflammatory component PC1 and lipids among the athletes. β indicates regression coefficient, p-value ** < 0.01*

DISCUSSION AND CONCLUSIONS

- **We found no clear evidence for low grade systemic inflammation in elite athletes induced by high training load**
- **The athletes had lower CRP, higher HDL cholesterol and larger cholesterol particles than the controls, which are markers of metabolic and cardiovascular health**
- **The sex differences in cytokine and lipid profiles could reflect higher triglyceride clearance rate in female athletes[1], induced by higher pro-inflammatory cytokines[2]**
- **Further, longitudinal, studies on the immuno-metabolism of elite athletes are recommended**

[1] Magkos F *et al.* 2007. Women Produce Fewer but Triglyceride-Richer Very Low-Density Lipoproteins than Men, *J. Clin. Endocrinol. Metab.* 92 (4):1311–1318
[2] Shi J *et al.* 2019. Cytokines and Abnormal Glucose and Lipid Metabolism. *Front. Endocrinol.* 10:703

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Background: FIS Cross-Country World Cup 2020/21 in Dresden, Sandro Halank, CC BY-SA 4.0