

## **Effects of an acute bout of exercise on circulating extracellular vesicles: tissue-, sex-, and BMI-related differences.**

A. E. Rigamonti, V. Bollati, L. Pergoli, S. Iodice, A. De Col, S. Tamini, S. Cicolini, G. Tringali, R. De Micheli, S. G. Cella, A. Sartorio

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Background: Exercise is recognized to evoke multisystemic adaptations that, particularly in obese subjects, reduce body weight, improve glucometabolic control, counteract sarcopenia, and lower the risk of cardiometabolic diseases. Understanding the molecular and cellular mechanisms of exercise-induced benefits is of great interest due to the therapeutic implications against obesity.

Objectives and methods: The aim of the present study was to evaluate time-related changes in size distribution and cell origin of extracellular vesicles (EVs) in obese and normal-weight subjects who underwent a moderate-intensity exercise on a treadmill (at 60% of their VO<sub>2</sub>max). Blood samples were drawn before, immediately at the end of the exercise and during the postexercise recovery period (3 and 24 h). Circulating EVs were analyzed by a nanoparticle tracking analysis and flow cytometry after labeling with the following cell-specific markers: CD14 (monocyte/macrophage), CD61 (platelet), CD62E (activated endothelium), CD105 (total endothelium), SCGA (skeletal muscle), and FABP (adipose tissue).

Results: In all subjects, acute exercise reduced the release of total (i.e., 30-700 nm) EVs in circulation, predominantly EVs in the microvesicle size range (i.e., 130-700 nm EVs). The postexercise release of microvesicles was higher in normal-weight than obese subjects; after exercise, circulating levels of exosomes (i.e., 30-130 nm EVs) and microvesicles were, respectively,

lower and higher in females than males. In all experimental subgroups (males vs. females and obese vs. normal weight subjects), acute exercise reduced and increased, respectively, CD61 + and SCGA + EVs, being the effect on CD61 + EVs prolonged up to 24 h after the end of the test with subjects in resting conditions. Total EVs, exosomes, and CD61 + EVs were associated with HOMA-IR.

Conclusions: Though preliminary, the results of the present study show that a single bout of acute exercise modulates the release of EVs in circulation, which are tissue-, sex-, and BMI specific, suggesting that the exercise-related benefits might depend upon a complex interaction of tissue, endocrine, and metabolic factors.

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