Using a triple glucose tracer technique to quantify postprandial glucose flux after acute exercise and exercise training

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Background: Under postprandial conditions, coordinated changes to glucose appearance (Ra), endogenous glucose production (EGP) and glucose disposal (Rd) limit excessive glycemic excursions in healthy individuals (Rizza *et al*., 2016). Understanding how lifestyle interventions can affect these parameters will enhance their therapeutic use in people with diabetes. However, much of the scientific knowledge regarding glucose metabolism is inferred from non-physiological measurement techniques that do not accurately represent the dynamic conditions associated with a postprandial state. The 'gold standard' for determining postprandial glucose flux is the triple tracer technique (Dalla Man *et al*., 2013), but so far it is underutilised in human research. Therefore, the aim of this study was to utilize the triple tracer technique to accurately quantify changes to glucose flux under postprandial conditions in response to a single bout of endurance exercise and then 4 weeks of endurance training.

Methods: Six healthy, lean, untrained males (22.8 ± 0.4 years) underwent the triple tracer technique using stable isotopes [U-13C6], [6,6-2H2] and [1-13C]glucose, at baseline, 20 ± 1hrs after a single bout of endurance exercise and then after 4 weeks of endurance training (1 h/day, 5d/wk). The exercise intensity for all sessions was 71.4 ± 0.1 % VO_2max. Glucose fluxes involving EGP, Ra and Rd were calculated using non-steady state equations as previously described (Basu *et al*., 2003). Data are in mean ± SEM.

Results: Preliminary data indicates that exercise significantly decreased glucose area under the curve (AUC) (1408 ± 61 *vs* 1268 ± 50 *vs* 1237 ± 45mmol.l^{-1} x h, p<.05, baseline *vs* acute exercise *vs* training, respectively) and peak glucose (8.44 ± 0.48 *vs* 7.38 ± 0.46 *vs* 6.83 ± 0.27mmol.l^{-1}, p<.05). However, insulin AUC (3966 ± 22 *vs* 2807 ± 9 *vs* 2437 ± 9 uU.ml^{-1} x h) and peak (43 ± 1 *vs* 35 ± 1 *vs* 26 ± 1 uU.ml^{-1}) were not significantly altered by acute exercise or exercise training.

Glucose, Ra and Rd were unchanged, while postprandial suppression of EGP was significantly reduced following both acute exercise and exercise training (61.4 ± 0.8 *vs* 52.4 ± 1.5 *vs* 48.9 ± 2.3% of AUC, p<.05). Peak suppression of EGP was not significantly altered by acute exercise or training when compared to baseline (3.1 ± 0.3 *vs* 3.3 ± 0.2 *vs* 3.5 ± 0.2μmol.kg.min^{-1}).

No significant difference between acute exercise and exercise training were observed for glucose, insulin, glucose Ra, Rd or EGP.

Conclusion: The improvement in glucose tolerance seen following exercise training is almost completely due to the effect of the last acute exercise bout and not the summative effect of training. Additionally, under physiological postprandial conditions, the glucoregulatory system is able to achieve the same rate of fluxes following acute exercise and exercise training despite lower prevailing glucose and no change in circulating insulin. However, the EGP nadir is more transient following exercise, demonstrating improved efficiency such that the system is more quickly able to return toward a steady regulatory state.

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