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Plasma LEAP-2 after a Low-Calorie Diet with or without Exercise in Women with Obesity

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Gut-derived factors regulate food intake and body mass. Recently, liver expressed antimicrobial peptide-2 (LEAP-2) has been identified to decrease caloric intake, in part, through lowering acylated-ghrelin (AG). Exercise reduces post-prandial AG and favors fullness while dieting may raise hunger and AG. However, it is unclear if LEAP-2 changes after a low-calorie diet with interval exercise (LCD+INT) compared with LCD in relation to weight regulation. **PURPOSE:** Assess if LCD+INT raises LEAP-2 more than LCD in relation to appetite, AG, and metabolic health. **METHODS:** Twenty-five women with obesity were randomized to either 2-wks of LCD (n=13, 46.2±3.3yrs, 37.5±1.5kg/m², VO₂max=18.9±1.2ml/kg/min; ~1200 kcal/d) or LCD+INT (n=12, 50.8±3.3yrs, 37.7±2.1kg/m², VO₂max=17.6±1.1ml/kg/min; 60 min/d of supervised INT alternating 3min of 90% and 50% HR_{peak}). LCD+INT were fed 350kcal post-exercise to equate energy availability. AG and LEAP-2 were measured at 0, 30, and 60min of a 75g OGTT. Glucose and insulin were obtained at 0, 30, 60, 90, 120, and 180min to estimate insulin sensitivity (Matsuda index) and glucose effectiveness (GE). Fasting appetite was assessed via visual analogue scales. **RESULTS:** LCD reduced BMI (-0.8±0.1 vs. -0.4±0.1kg/m²; P=0.03) and fat mass (-1.2±0.2 vs. -0.4±0.2; kg P=0.03) compared with LCD+INT, but only LCD+INT increased VO₂max (1.0±0.6 vs. -0.6±0.4ml/kg/min; P=0.04). Both treatments tended to raise insulin sensitivity (0.9±0.5 vs. 0.2±0.2; P=0.06) and FFA tAUC_{180min} (P=0.001), with no effect on GE (P=0.32). LCD+INT tended to preserve fasting fullness (1.7±7.9 vs. -16.1±5.1mm; P=0.07) and raise fasting AG compared to LCD (3.2±3.3 vs. -7.4±4.1ng/dl; P=0.06). Although there was no treatment effect on fasting LEAP-2 (P=0.41), LEAP-2 tAUC_{60min} tended to decrease (P=0.07). Further, low LEAP-2 tAUC_{60min} correlated with low post-trial body fat (r=0.45, P=0.03) as well as high VO₂max (r=-0.41, P=0.05) and AG tAUC_{60min} (r=-0.45, P=0.03). **CONCLUSION:** Short-term LCD+INT does not alter LEAP-2 versus LCD alone. However, low LEAP-2 correlated with low body fat, VO₂max, and AG. These data suggest LEAP-2 responds to lifestyle-mediated energy deficit. Further working examining LEAP-2 mechanisms on weight regulation is warranted.