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Greater changes in metabolic hormones are associated with a smaller decrease in pulsatile LH secretion in response to short term moderate energy restriction in healthy, young women

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Background: Energy restriction may result in hypothalamic amenorrhea by inhibiting GnRH secretion and downstream pulsatile LH secretion. Energy restriction also leads to adaptive changes in metabolic hormones. We sought to determine whether metabolic changes in response to energy restriction predict or mitigate inhibition of GnRH secretion.

Methods: Nineteen healthy women, (mean age ± SD; 23.36 ± 2.08 yrs) with regular ovulatory cycles and no evidence of energy restriction or excessive exercise, underwent two 5-day dietary interventions with identical exercise in the early follicular phase of two menstrual cycles. A neutral energy availability (NEA; 45 kCal/kg*LBM/d) was followed by a deficient energy availability (DEA; 20 kCal/kg*LBM/d) diet. On day five of each intervention, body composition was analyzed (BodPod®), and blood was sampled between 0800 —1600 hours for LH, TSH and GH, every 10 min, cortisol every 30 min, T3, reverse T3 (rT3) and T4 every 60 min, free T3 (FT3), free T4 (FT4) and TBG at 0800 h and 1600 h. We correlated means of pulsatile LH pulse frequency (LHPF) with integrated metabolic hormone changes across the day in the subset of women with reduced or unchanged LHPF after DEA (n=10) using linear regression.

Results: In ~50% of healthy young women, LHPF decreased or was unchanged in response to short-term moderate energy deprivation. BMI and bodyweight declined after DEA in both groups while % fat mass was unchanged. TSH, T3, leptin, insulin declined, and T4 increased from NEA to DEA while glucose, cortisol and GH were unchanged.

In subjects with reduced/unchanged LHPF, % delta T3 correlated inversely with delta LHPF (r=-0.727, p=0.017). Similarly, non-fasting delta TSH correlated inversely with % delta LHPF (r=-0.643, p=0.045), and % delta AUC TSH (r=-0.642, p=0.045) correlated inversely with DEA LHPF.

Percent delta insulin (r= -0.722, p=0.018) and % delta insulin AUC (r= – 0.688, p=0.028) correlated inversely with delta LHPF. Percent delta insulin-glucose ratio (r=-0.772, p=0.009) and % change in AUC insulin-glucose ratio (r=-0.759, p=0.011) also correlated inversely with delta LHPF. This inverse relationship was preserved when insulin was normalized for caloric intake (n-insulin) was correlated with % delta LHPF (r=-0.722, p=0.018) and % delta AUC n-insulin correlated with delta LHPF (r= -0.631 and p= 0.050).

Delta AUC leptin (r=-0.684, p=0.029) and % delta AUC leptin (r=-0.670, p=0.034) also correlated inversely with delta LHPF.

Mean cortisol at NEA correlated inversely with LHPF during DEA (r=-0.816, p=0.007), implying that higher baseline cortisol levels may predict a greater relative fall in LHPF. Cortisol AUC in DEA also correlated inversely with LHPF in DEA (r=-0.722, p=0.028).

Conclusion: Our data suggest that greater changes in metabolic hormones may protect against the inhibitory effect of moderate energy deprivation on GnRH secretion in healthy young women with normal reproductive function.

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