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Background: Intermittent energy restriction (IER) is gaining popularity as a weight-loss strategy. However, the effect of short-term energy restriction on thyroid hormone dynamics is not well characterized. **Methods:** Nineteen healthy women age 23.36± 2.08 yr (mean ± SD) with normal baseline thyroid function and negative anti-thyroid antibodies underwent two 5-day interventions of a prescribed diet and identical standardized exercise in the early follicular phase of two menstrual cycles - neutral energy availability (NEA) 45 kCal/kg*LBM/d followed by deficient energy availability (DEA) 20 kCal/kg*LBM/d. Energy requirements were estimated as previously described (doi.org/10.1210/jendso/bvaa046.1468) and were used to generate a diet and exercise regimen for each participant. On day 5 of both interventions, body composition was assessed by BodPod®. Standardized NEA or DEA breakfast and lunch were provided as appropriate as well as a standardized NEA snack on both sampling visits. Blood sampling was performed for 8 hours starting at ~0800 h with measurement of TSH and growth hormone (GH) every 10 min, cortisol every 30 min, total T3 (TT3), reverse T3 (rT3) and total T4 (TT4) every 60 min, free T3 (FT3), free T4 (FT4) and TBG at the beginning and end of sampling. Liquid chromatography-tandem mass spectrometry (LC-MS) was used for measurements of all thyroid hormones, with the exception of TSH and TBG which were measured by ELISA as were GH and cortisol. Data were analyzed using ANOVA-RM and linear mixed models. Results are presented as mean or least squared mean ± sem. **Results:** Body mass index, bodyweight and % fat mass were not different between interventions. GH and cortisol were unaffected by DEA (p=0.46, p=0.63). TBG was not affected by time of day or dietary intervention (p=0.95, p=0.41). However, compared with NEA, TT3 (89.15 ± 2.89 vs 95.55 ± 2.89 ng/dL for DEA and NEA, respectively; p<0.0001) and TSH (0.92 ± 0.08 vs 1.03 ± 0.09 µIU/mL; p=0.0011) were lower after DEA, while TT4 (6.26 ± 0.25 vs 6.06 ± 0.25 µg/dL; p=0.04), FT4 (3.37 ± 0.26 vs 2.94 ± 0.25 ng/d;, p=0.0052) and rT3 (11.77 ± 0.58 vs 8.85 ± 0.51 ng/dL; p<0.0001) were higher. Regardless of dietary intervention, FT3 (p=0.0005), TT3 (p<0.0001), TT4 (p<0.0001) and TSH (p<0.0001) decreased across the day. **Conclusion:** Using LC-MS for as a more robust measure of thyroid hormones, we have now shown that changes in thyroid hormone dynamics occur after only 5 days of 55% energy restriction in the absence of alterations in body composition, cortisol, GH, TBG or the circadian pattern of thyroid hormone secretion. The decrease in TSH combined with the decrease in TT3 and increase in rT3 support the contribution of both central and peripheral mechanisms to these changes. Taken together these results provide support for a multi-level adaptation in thyroid hormone dynamics to conserve energy expenditure in response to short-term energy restriction.

Thyroid

THYROID HORMONE METABOLISM AND ACTION

The Role of Nuclear Receptor Corepressors NCoR1 and SMRT on Physiologic Function in the Adult Mouse

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Thyroid hormone (TH) plays an essential role in maintaining homeostasis and regulating metabolism in all organ systems beginning with embryogenesis and continuing throughout life. TH action is mediated by the thyroid hormone receptor (TR), which is a nuclear receptor, and it's coregulators. The nuclear receptor corepressor 1 (NCoR1) and the silencing mediator of retinoid and thyroid hormone receptors (SMRT) are two critical corepressors of the TR that inhibit gene transcription in the absence of TH. Repression is mediated by complexing with histone deacetylase 3 (HDAC3), which is stabilized by NCoR1 and SMRT. NCoR1 and SMRT are critical for maintaining metabolic homeostasis and act to mediate energy expenditure, insulin sensitivity, and body weight. We sought to elucidate the roles of NCoR1 and SMRT in maintaining global physiologic function in the adult mouse. In order to study the post-natal role of these corepressors, we used a tamoxifen-inducible Cre recombinase (UBC-Cre-ERT2) to knock-out (KO) NCoR1, SMRT, or NCoR1 and SMRT together in adult mice because global deletion of either corepressor during embryogenesis is lethal. Mice were injected with tamoxifen at 8 weeks of age to KO either NCoR1 (NCoR1-KO; NKO), SMRT (SMRT-KO; SKO), or both NCoR1 and SMRT (double KO; DKO) and metabolic parameters were analyzed. While postnatal deletion of either NCoR1 or SMRT did not impact mortality, KO of both NCoR1 and SMRT resulted in a rapidly lethal phenotype heralded by weight loss, hypoglycemia and hypothermia. Metabolic phenotyping confirmed a loss of body mass and in particular fat mass in addition to a reduction in energy expenditure and increase in fecal caloric density. Further analysis showed the rapid development of hepatosteatosis and disturbances in lipid metabolism with a profound increase in beta-oxidation. We also found a reduction in HDAC3 protein levels in the DKO mice but no rapidly lethal phenotype in HDAC3 KO mice. Overall, we show that NCoR1 and SMRT together are critical for life as their deletion results in a rapidly lethal phenotype. While NCoR1 and SMRT are required to stabilize the corepressor complex, including HDAC3, HDAC3 KO resulted in a distinct and separate phenotype.

Thyroid

THYROID HORMONE METABOLISM AND ACTION

Thyroid Function in 3000 Cases of Patients With Atrial Fibrillation Treated With Catheter Ablation

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