# Circadian ACTH release is enhanced while cortisol secretion is normal in obese premenopausal women: reversal by Acipimox

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The endocrine environment is a powerful regulator of body fat storage. Altered activity of the hypothalamic-pituitary-adrenal (HPA) axis leads to profound changes of body composition. Several studies suggest that the HPA axis is hyperactive in obesity. Animal studies showed that increased circulating Free Fatty Acids enhanced secretory activity of the HPA axis. Human obesity is associated with high circulating FFAs. We hypothesized that spontaneous activity of the HPA axis is enhanced and that lowering of circulating FFAs by acipimox reduces spontaneous secretion of the HPA hormonal ensemble in obese humans. To evaluate these hypotheses, diurnal ACTH/ cortisol secretion was studied in 11 obese and 9 lean premenopausal women (BMI: obese 33.5 ± 0.9 *vs.* lean 21.2 ± 0.6 kg/m$^2$, P <0.001) in the early follicular stage of their menstrual cycle. Obese women were randomly assigned to treatment with either Acipimox (inhibitor of lipolysis, 250 mg orally four times daily) or placebo in a double blind cross-over design, starting one day prior to admission until the end of the blood-sampling period. Blood samples were taken during 24 h with a sampling interval of 10 min for assessment of plasma ACTH and cortisol concentrations. ACTH and cortisol secretion rates were estimated by multiparameter deconvolution analysis. Daily ACTH secretion was substantially higher in obese than in lean women (7950 ± 1212 *vs.* 2808 ± 329 ng/24 h, P=0.002), whereas cortisol was not altered (obese 36 362 ± 5639 *vs*. lean 37 187 ± 4239 nmol/24 h, P=0.912). Acipimox significantly reduced ACTH secretion in the obese subjects (Acipimox 5850 ± 769 ng/24 h, P=0.039 *vs.* placebo), while cortisol release did not change (Acipimox 33 542 ± 3436 nmol/24 h, P=0.484 *vs.* placebo). In conclusion, spontaneous ACTH secretion is enhanced in obese humans, whereas cortisol production is normal. Acipimox favourably affects this neuroendocrine anomaly in obese premenopausal women.

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Poster Session: Endocrinology