Proceedings of the Nutrition Society (2022), **81 (OCE5)**, E199 doi:10.1017/S0029665122002324

Summer Conference 2022, 12–15 July 2022, Food and Nutrition: pathways to a sustainable future

Glucocorticoid ablation restores parameters of energy homeostasis in congenic obese LA/Ntul//-cp rats

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The expression of adrenal glucocorticoids on multiple parameters of energy metabolism are well recognised, where they may exert permissive actions at both membrane-linked and intracellular actions that may impact on the caloric efficiency (CE) of macronutrient utilisation and storage. Excess sensitivity to actions of glucocorticoids, by virtue of their ability among other actions, to impede the intracellular translocation of GLUT4 receptors from the endoplasmic reticulum to the plasma membrane may impair insulin sensitivity, thermogenesis and impair glucose uptake in peripheral tissues including skeletal muscle and adipose tissue.[(1–5)].The effects of glucocorticoid ablation via adrenalectomy (ADX) on typical insulin-mediated metabolic parameters including glycemic and thermogenic responses were determined in congenic obese LA/Ntul//-*cp* rats. groups (n = 6–12 rats/phenotype) of normally reared congenic lean and obese animals were fed a Purina chow diet from 6 to 9 weeks of age (WoA), and the Chow diet plus a highly palatable cafeteria diet (Café) from 9 to 12 WoA. Subgroups of obese animals were subjected to bilateral ADX at 6 WoA. Measures of oral glucose tolerance (OGT, 2.5G/kgBW) were obtained in the three treatment groups at 6, 9 and 12 WoA, and of noradrenaline-stimulated (NE) thermogenesis at thermal neutrality (VO2, 200 µg, s.c.) at 12 WoA. This study was approved by the USAT IBACUC committee. Daily caloric intake was greater of obese > lean rats and increased further with the Café diet. The CE of weight gain was greater in obese than in lean rats and increased further following adx + Café diet. Body weights of obese > lean, and ADX restored weight gain toward normal in obese rats. The OGT responses after 30 to 60 minutes were impaired consistent with moderate insulin resistance, but the obese animals remained non-diabetic at all ages compared to lean littermates. The effects of ADX on Insulin to glucose ratio (I: G) at 12 weeks of age were 5-fold greater in obese-rats and were partially normalized following ADX, consistent with moderate insulin resistance in the obese but not in the lean phenotype. ADX resulted in normalization of OGT in the obese phenotype at 9 and 12 WoA and normalization of the I:G ratio in ADX-obese rats. Resting and NE stimulated VO2 (200 ug, s.c.) was greater in lean than in obese at 6, 9 and 12 weeks of age. The NE-stimulated VO2 responses of obese rats were < lean, and ADX resulted in normalization of the thermic response to NE.These results are consistent with normalization of typical insulin-mediated components of glycemic and thermogenesis parameters following ADX of obese rats and suggest that the counterregulatory effects of insulin and glucocorticoid hormone actions may be contributory to the impaired glycemic and thermogenic responses in the obese phenotype of the LA/N//-*cp* (corpulent) rat.

Acknowledgments

Acknowledgements. The authors thank Ms C. Sandler for assistance in data collection, and Steven Dubin, DVM and his staff for assistance animal husbandry.

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