Characterising the impact of lipid-rich diets on the endocrine profile of C57 mice during progressive weight gain resulting in the development of obesity

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Obesity develops from an imbalance between energy consumption and energy output. While this addresses the overall change in energy homeostasis (resulting in weight gain), it does not consider physiological disruptions resulting in an inability to regulate energy demand or output. The endocrine system is central to the regulation of appetite, breakdown of dietary components for storage or use, and overall maintenance of body composition. Weight gain and obesity are associated with multiple disruptions in the normal endocrine profile. For example, secretion of ghrelin, growth hormone and adiponectin all decline with increased adiposity, whereas obesity is associated with prolonged elevation of leptin and the development of central leptin resistance. In order to characterize the impact of obesity on endocrine function it is necessary to first identify suitable animal models that closely correlate to endocrine disruptions associated with human obesity. In this study we assessed the effectiveness of three commercial diets (sourced from Specialty Feeds, Western Australia) in inducing obesity: a very high fat, low sucrose diet (VHFLS diet - 60% kcal contribution from fat, 106g/kg sucrose), a high fat moderate sucrose diet (HFMS diet - 23% kcal contribution from fat, 201g/kg sucrose), and a high fat high sucrose diet (HFHS diet - 23% kcal contribution from fat, 405g/kg sucrose). Four week old male C57 mice were fed on either diet for a period of 12 weeks, and analysis of weight gain and consequential effects on endocrine function were assessed at 4, 8 and 12 weeks of feeding. Age-matched control mice were maintained on standard mouse chow. Animals had free access to food and water for the duration of the experiment, with the exception of two days prior to sacrificing when animals were fasted overnight for a glucose tolerance test. We found that a diet rich in fat and sucrose is sufficient to induce obesity in mice by 12 weeks of feeding. By contrast, animals maintained on the VHFLS diet did not become obese. A characteristic shift in the endocrine profile was observed in all animals maintained on a high fat diet. However, development of glucose intolerance by week 12 of dietary intervention only occurred in HFHS diet-fed mice. These results confirm that a diet rich in fat and sucrose is essential to induce a characteristic shift in endocrine profile in C57 mice to that observed in human obesity. We will utilize this animal model to further characterize the impact of obesity on endocrine profile disruption.