Macrophages and tissue remodelling following acute nutritional modulation in humans

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In diet-induced and genetically obese rodent models, adipose tissue is associated with macrophage infiltration, and increased secretion of pro-inflammatory cytokines that induces the development of insulin resistance, and type 2 diabetes. In humans with obesity, macrophage infiltration, and a pro-inflammatory phenotype and insulin resistance are also noted. However, macrophages are also required for healthy adipose expansion during weight gain in mouse models. Our past work suggests little evidence of macrophage infiltration of subcutaneous adipose tissue during acute overfeeding and weight gain in humans, although we have noted changes in markers of tissue remodelling evident in muscle. We have recently completed a physiological study examining the metabolic impacts of weight loss induced by severe intermittent fasting *versus* a moderate daily calorie restriction (CR) in women with obesity, and in mouse models, for 8 weeks. New findings from these studies highlight the effects of acute changes in nutrition on adipose tissue and skeletal muscle remodelling, and associations with changes in insulin sensitivity. Clinically, intermittent fasting produced slightly more weight loss and improvements in HOMA-IR, and as we expected, higher levels of non-esterified fatty acids, and ketones on fasting days. However no difference in peripheral insulin sensitivity was noted between groups following fed days. The molecular data suggest that tissue specific responses may also exist in response to a period of severe intermittent *versus* moderate daily energy deprivation in humans, and potentially as a result of the marked increases in lipolysis in the fasting states. Whether this translates to differences in health over longer periods are as yet, unclear.