of genes related to inflammation and plasticity was determined via reverse transcription polymerase chain reaction (RT-PCR) and the fecal microbiota was quantified via high-throughput sequencing of the 16S ribosomal RNA. Weight gain and energy intake were comparable across the diets. Rats consuming the SFA and Sugar diets were impaired on hippocampal-dependent place recognition memory compared to Controls and PUFA rats. All rats performed comparably on the perirhinal-dependent object recognition task. Hippocampal and hypothalamic inflammatory and neuroplasticity genes were not substantially affected, but each of the diets significantly altered the microbial composition in distinct ways. Specifically, the relative abundance of 89 taxa differed between groups with the majority of changes accounted for by the Clostridiales order and within that, *Lachnospiraceae* and *Ruminococcaceae*. These taxa showed a range of macronutrient specific correlations with place memory. In addition, Distance based Linear Models found relationships between memory, a cluster of hippocampal inflammation-related genes and gut microbiota composition. In conclusion, our study shows that even in the short-term the macronutrient profile of the diet is crucial for diet-induced memory deficits and suggests a possible link between diet, gut microbiota and hippocampal inflammatory genes. Longer term studies are warranted.

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AMPK-ACC signalling is required for increasing appetite under conditions of metabolic stress

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Activation of AMP-activated protein kinase (AMPK) during increased energy demand promotes food intake and reduces brown fat thermogenesis to shift the organism to neutral energy balance. The underlying molecular interactions are not entirely understood.

The acute effects of AMPK on lipid metabolism are mediated by phosphorylation of acetyl-CoA carboxylase (ACC) 1 at Ser79 and ACC2 at Ser212, thereby inhibiting fatty acid synthesis and promoting fatty acid oxidation. To investigate the physiological impact of this regulation on whole body energy balance, we generated mice with Ser79Ala/Ser212Ala knock-in mutations (ACC double knock-in, ACC DKI). ACC DKI mice have increased ACC1/2 activity in peripheral tissues and a propensity for increased lipid synthesis. Despite deregulated lipid metabolism, ACC DKI mice do not gain more weight when compared to wild type control mice and, in contrast, show a tendency for reduced body weight from 15 weeks of age.

Food intake measurements showed that ACC DKI mice have reduced appetite in response to metabolic stress, such as overnight fasting or cold exposure. Furthermore, while ACC DKI mice are able to maintain normal body temperature under cold stress, they compensate for reduced energy intake by utilising lipids as preferred energy source. Cold exposure and overnight fasting are accompanied by increased plasma levels of the orexigenic hormone ghrelin in ACC DKI mice. Importantly, we demonstrate that feeding in response to ghrelin is attenuated and ghrelin-induced expression of the orexigenic neuropeptides NPY and AgRP is inhibited, indicating that the anorexic phenotype of ACC DKI mice may be due to ghrelin insensitivity.

These results show that AMPK regulation of ACC is an important physiological mechanism in the control of body weight regulation, whereby the lipid accumulating effects in the periphery are outweighed by anorexic effects in the hypothalamus.

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Invited talk: Executive dysfunction in obese individuals

Evelyn Smith

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Research has indicated that individuals with obesity have neurocognitive deficits, especially in executive function, which may in turn impact on weight loss and maintenance. In this talk I will review the evidence of this relationship, highlighting some of the mechanisms, and limitations of the literature. I will then present data on our latest randomised controlled trial which examined efficacy of a manualised cognitive remediation therapy for obesity (CRT-O) in terms of improving executive function, reducing binge eating behaviour and helping with weight loss. 80 adults with obesity (body

mass index >30 kg/m^2), 70% binge eaters, received three weekly sessions of group Behavioural Weight Loss (BWL) and then were randomised to 8 sessions of individual CRT-O or to a no-treatment control group. Mixed-effects model analyses revealed that the CRT-O group had a significant improvement in executive function at post-treatment and 3-month follow-up compared to the control group (Cohen's $d = 0.96$ to 2.1). 68% of those in the CRT-O group achieved a weight loss of 5% or more at follow-up compared to only 15% of the controls. Individuals in the CRT-O group lost on average 6.6% of the weight at 3 month follow up (Cohen's $d = 1.4$). Changes in executive function predicted changes in weight ($p < .05$). Binge eating reduced in the CRT-O group compared to the control (Cohen's $d = 0.80$). CRT-O seems to be a promising treatment for obesity and binge eating. CRT-O studies with longer follow-ups, pairing it with longer BWL programs and examining the mechanisms are currently underway in Australia and Germany.

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Invited talk: Interactions between insulin resistance and bone health

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The contribution of insulin resistance vs. adiposity in determining bone mineral density (BMD), bone turnover and fracture risk in humans remains unclear. Bone mineral density (BMD) predicts fracture risk, and obesity is associated with higher BMD. People with both type 1 and type 2 diabetes have increased fracture risk, despite many people with type 2 diabetes being overweight or obese, with normal BMD. Factors that contribute to increased fracture risk in diabetes are insulin use, increased risk of falls due to neuropathy and retinopathy, inflammation, glycation of collagen, use of PPAR-y agonists and poor bone quality related to poor nutrition. Fracture risk in diabetes does not appear to be associated with BMD, and so must occur at a cellular level.

Bone turnover markers are lower in people with the metabolic syndrome, and in diabetes, and is associated with insulin resistance rather than adiposity.

This talk will review published data looking at fracture rates and bone turnover marker levels in people with obesity, insulin resistance and diabetes. Data will be presented from studies looking at bone turnover markers performed locally. These data suggest that increased visceral adiposity and higher fasting insulin levels in insulin-resistant states is associated with lower fasting OC and CTx, and failure to further suppress with more insulin. This raises the possibility that diabetic osteopathy may be considered another complication of diabetes.

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Invited talk: Is the increased exposure to antidepressants a key contributor to the obesity pandemic?

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Major depressive disorder (MDD) and obesity are both common heterogeneous disorders with complex aetiology, with a major impact on public health. Antidepressant prescribing has risen nearly 400% since 1988. In parallel, adult obesity rates have doubled since 1980, from 15 to 30%, while childhood obesity rates have more than tripled. Are these two facts related? Despite the concomitant rise of antidepressant use and of the obesity rates in Western societies, the association between the two, as well as the mechanisms underlying antidepressant-induced weight gain, remain under explored. Our recently developed animal paradigm shows that the combination of stress and antidepressants followed by long-term high-fat diet results, long after discontinuation of antidepressant treatment, in markedly increased weight, in excess of what is caused by high-fat diet alone. On the basis of existing epidemiological, clinical and preclinical data, we have generated the testable hypothesis that escalating use of antidepressants, resulting in high rates of antidepressant exposure, might be a major contributory factor to the obesity epidemic, particularly in Western countries.

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