Results: Frequent consumption of SSBs was associated with increased risk of T2DM in women, but not in men at both the four (SSB intake 1—6 times per week OR = 1.7, 95% confidence intervals (CI) 1.3—2.4 and >1 per day-OR = 2.5, 95%CI 1.5—4.1) and eight year follow-ups (SSB intake 1—6 times per week OR = 1.7, 95%CI 1.2—2.3 and >1 per day OR = 3.1, 95%CI 2.0—5.0). The addition of both weight gain and body mass index (BMI) to the full regression model only slightly attenuated these effects. Having a BMI of 25 kg/m^2 or over in 2009 was a significant mediator of the total effect of SSB intake in 2005 on T2DM risk in 2013 (natural indirect effect 1.10, 95%CI (1.07, 1.13) and mediated 15.9% of the total relationship.

Conclusion: The consumption of SSBs increased the risk of T2DM incidence in women but not in males. Obesity mediated a proportion of this relationship but most of the effect appeared to act through other mechanisms.

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Invited talk: Lipid metabolism and the complications of diabetes

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Diabetes is a disorder of lipid as well as glucose metabolism. The lack of insulin signalling, caused by either insulin deficiency in type 1 diabetes or insulin resistance in type 2 diabetes, disrupts lipid metabolism in part through effects on the process of de novo lipogenesis. This process requires the activity of fatty acid synthase (FAS), a multifunctional enzyme that synthesises the saturated fatty acid palmitate from malonyl-CoA, acetyl-CoA, and NAPDH. Studies over the past decade have demonstrated that FAS has complex tissue-specific effects that are relevant to the complications of diabetes. In liver, FAS participates in the generation of an endogenous phospholipid ligand for PPARalpha, a transcription factor that promotes fatty acid oxidation and is the target of fibrate drugs used in clinical practice. In the hypothalamus, FAS controls feeding behaviours. At the vascular endothelium and at the intestinal epithelium, FAS is required for normal homeostasis by promoting the palmitoylation of endothelial nitric oxide synthase (eNOS) and mucin 2, respectively. In cardiac muscle and skeletal muscle, FAS alters calcium metabolism through effects on the membrane environment. In macrophages, FAS promotes inflammation and atherosclerosis. In adipose tissue, FAS regulates the conversion of beige adipocytes in part by generating ether lipid ligands for PPARgamma, a transcription factor required for adipogenesis. Pharmacological inhibitors of FAS have been demonstrated to treat diabetes in animal models. However, potentially detrimental effects of FAS inhibition in certain tissues limit this approach. Available evidence suggests that FAS channels lipids to specific intracellular sites, raising that possibility that modulating this process could treat diabetes complications such as retinopathy, vascular disease, and other disorders related to chronic inflammation.

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Invited talk: Protein kinase Ce in adipose tissue — Not merely an effector but a regulator of lipid intermediates?

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Obesity and lipid oversupply have been linked with defective insulin action in liver and muscle for some time. As lipid-activated kinases, isoforms of the protein kinase C (PKC) family are strong candidates for mediating the inhibitory effects of lipid intermediates. More specifically, PKCε is widely believed to play a direct role in liver insulin resistance through inhibition of proximal insulin signalling. Our laboratory has extensively investigated the effects of global and tissue-specific PKCε ablation on in mice. This has revealed previously unsuspected roles for the kinase in the regulation of lipid metabolism and glucose homeostasis.

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Invited talk: Ectopic lipids and defective glucose metabolism: Cause or association?

Clinton Bruce

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Accumulation of lipids in non-adipose tissues, particularly liver and skeletal muscle, is associated with the development of insulin resistance.

However, it is not entirely clear whether ectopic lipid accumulation plays a causal role in the development of insulin resistance or whether this is simply an associative relationship. We have conducted a number of studies to explore this relationship. Firstly, to further understand the role of muscle lipids in mediating insulin action, we generated a muscle-specific knockout of a key enzyme in phospholipid synthesis, CTP:phosphoethanolamine cytidylyltransferase (ECT), which resulted in marked (2—3-fold) increases in both diacylglycerol and triacylglycerol content in muscle. Despite this increase in lipid content, whole body and skeletal muscle insulin sensitivity, as determined by euglycemic hyperinsulinemic clamp, was not altered. These findings demonstrate that lipid accumulation in muscle is not always associated with insulin resistance. To examine the role of hepatic lipids, we performed a study where chronically (8 wk) high-fat, high-sucrose fed (HFSD) mice were switched back to a standard chow diet for 7 days. Upon the switch, energy intake was reduced, resulting in reductions of fat mass and hepatic diacylglycerol and triacylglycerol content. However, these parameters were still elevated compared to chow-fed mice, thus representing an intermediate phenotype. Nonetheless, glucose intolerance and hyperinsulinemia were completely normalised in mice that underwent the 7 day diet switch. This indicates that lipotoxicity per se does not necessarily maintain the glucose intolerant and insulin resistant state in HFSD fed mice. Rather, it appears that persistent over nourishment is likely to be the major factor responsible for causing defects in glucose metabolism. Together, these findings dissociate tissue lipid accumulation from the development of insulin resistance and glucose intolerance.

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Invited talk: Do factors secreted from the fatty liver cause diabetes?

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Obesity is a risk factor for the development of secondary complications including dyslipidemia, non-alcoholic fatty liver disease, cardiovascular disease and type 2 diabetes. An accumulation of lipid in the liver, which is clinically known as hepatic steatosis, is a pathologic abnormality that is common in obese and type 2 diabetes patients. Hepatic steatosis occurs when fatty acid supply outweighs fatty acid demand and occurs in a time-course that usually precedes the induction insulin resistance and type 2 diabetes. In this presentation, we describe how 'omics' approaches are used to delineate the hepatocyte protein and lipid secretome in health and obesity. Further, we report on the pre-clinical validation of several liver secreted factors that cause insulin resistance and disturbances in systemic metabolic homeostasis.

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Invited talk: Diabetes surgery — Has the time arrived?

John Dixon

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Bariatric-metabolic (BM) surgery as a treatment for type 2 diabetes (T2DM) has progressed rapidly. There is now high quality evidence of efficacy, safety, reduced morbidity and mortality, and very favourable health economic profile. Yet surgery is rarely performed as a treatment for Type 2 diabetes and has been slow to enter the treatment algorithms of managing diabetes. The International Diabetes Federation has provided a position statement, and the NHMRC and NICE have included BM surgery in their algorithms for managing weight in patients with obesity and T2DM.

An international consensus conference was convened in collaboration with leading diabetes organisations to develop guidelines to inform clinicians and policy makers about benefits and limitations of metabolic surgery for T2DM. The evidence collected, the process used to reach consensus, and the level of international acceptance will be presented.

Key points of consensus:

Given its role in metabolic regulation, the gastrointestinal tract constitutes a meaningful target to manage T2DM.

There is now sufficient clinical and mechanistic evidence to support inclusion of metabolic surgery among anti-diabetes interventions for people with T2DM and obesity.

Metabolic surgery should be recommended to treat T2DM in patients with Class III obesity (BMI $\geq 40\,kg/m^2$) and in those with Class II obesity (BMI 35.0—39.9 kg/m^2) when hyperglycaemia is inadequately controlled by lifestyle and optimal medical therapy. Surgery should be considered for patients with T2DM and BMI 30.0—34.9 kg/m^2 if hyperglycaemia is inadequately controlled despite