



The Nutrition Society Winter Conference was held at the Royal Society, London on 7–8 December 2021

Editorial

Conference on ‘Obesity and the brain’

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The Winter Conference 2021 focused on the theme of obesity and the brain, with symposia on the consequences of obesity on brain function, developments in behavioural change interventions, neurobiology of appetite regulation and obesity treatment, and personalised medicine for obesity prevention and treatment. The first plenary lecture discussed sweetness perceptions and how non-nutritive sweeteners may lead to a mismatch between metabolic signals and reward systems in the brain, and the second plenary lecture presented novel approaches to the treatment of binge-eating disorders. This short report summarises the content of these scientific sessions.

Key words: Obesity: Appetite: Weight loss: Brain: Eating behaviour

The obesity pandemic is one of the greatest challenges in recent human history. The prevalence of obesity has been rising for the past 30 years and is estimated by the World Health Organisation to be the cause of at least 2.8 million deaths per year⁽¹⁾. It has long been appreciated that simply advising ‘eat less and move more’ is an ineffective weight management strategy, with the complexity of the interactions between biological, psychological, social and environmental factors governing regulation of energy balance being exemplified in the 2007 FORESIGHT Obesity Systems Map⁽²⁾. To make progress in prevention and treatment of obesity, it is necessary to understand it as a disease that is primarily a dysregulation of neuromolecular pathways, compounded by environmental factors that modify behaviour.

The 2021 Nutrition Society Winter conference was titled ‘Obesity and the brain’. In light of evidence that obesity increases the risk of severe coronavirus disease 2019 (COVID-19) illness, which in turn may result in persistent neurological problems (‘Long COVID’), the daily news backdrop of increasing rates of the new COVID-19 omicron variant during the run up to the conference firmly underlined the urgent need for new approaches to tackle obesity.

The programme was designed to assemble topics related to the role of the central nervous system in dysregulated eating behaviour, particularly the interface between the brain and environmental cues, food components, appetite hormones, gut microbial metabolites and psychological stimuli. There were four main symposia on the topics: ‘Obesity and brain function’, ‘Current challenges for behaviour change interventions’, ‘Neurochemistry of eating behaviour’ and ‘Personalised medicine for obesity prevention and management’. Two plenary talks discussed ‘Nutrient sensing and predictive neural coding’ and ‘New developments in treatment for emotional eating’. In addition, there was a sponsored symposium on ‘COVID-19-related beliefs and participation in a commercial weight loss programme during the pandemic’. This was the first winter conference to be held in a hybrid format and was attended by three hundred and thirty-six delegates representing eighteen countries from all over the world: one hundred and sixty-five attending in person at the Royal Society in London, and one hundred and seventy-one attending online. Sixty abstracts were presented: thirty in person as an oral or poster, and thirty as online poster presentations.

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Symposium 1: obesity and brain function

Following a warm welcome speech by Nutrition Society President, Professor Julie Lovegrove, the symposium was opened by Professor Louise Dye, University of Leeds, UK with her talk on 'The consequences of obesity for brain health'. Professor Dye cautioned that highly targeted, sensitive cognitive tests are needed to pick apart the subtleties of cognitive measures particularly when investigating the role of diet and energy balance. The role of oxidative and inflammatory stress in mediating the causal relationship between visceral fat and cognitive decline was outlined as well as the importance of reducing obesity in midlife to prevent the later development of dementia. Professor Dye concluded that more evidence and demonstration of mechanism of action was needed to form clear guidance for dietary guidelines specifically targeted at preventing cognitive decline and dementia.

Many studies suggest that dietary interventions may be protective for brain structure and function, although this has not been shown across the board. Dr Veronica Witte, Max Planck Institute, Germany, in her talk on 'Impact of obesity and diet on brain structure and function' presented data showing a large variability in individual trajectories of cognitive function with age and discussed some of the difficulties in trying to demonstrate dietary effects such as resveratrol supplementation on brain function while trying to control for other lifestyle factors. She presented deep learning modelling work carried out on a cross-sectional cohort to find determinants of brain age that could predict cognitive decline and that could be used to boost precision medicine, showing that an accelerated brain age was related to visceral adiposity. Dr Witte pointed out that more work was needed to be carried out on sex differences in adipose tissue biology and cognitive decline with age and made an appeal for improved harmonisation of protocols and data sharing in the investigation of diet, obesity and brain function.

Professor Amanda Killiaan, Radboud University, The Netherlands, presented some intriguing interim data in her talk on 'The BARICO Study: Impact of bariatric surgery on brain structure and function' showing marked improvements in cognitive function scores in a subset of a patient cohort who had undergone Roux en Y gastric bypass surgery for morbid obesity. Preliminary data from a small subset of patients who underwent MRI testing suggested that bariatric surgery can lead to improvements in cognitive function via improvements in vascular function possibly mediated by reductions in adipose tissue-related inflammation.

Plenary lecture 1: nutrient sensing and predictive neural coding

In an inspiring story of scientific serendipity, 'Nutrient sensing and predictive neural coding', Professor Dana Small, Yale University, USA, presented a fascinating sequence of experiments that showed how unexpected results can lead to important discoveries. By conducting

single-meal postprandial studies with beverages containing varying carbohydrate contents but matched for sweetness, her group showed that sweet taste can interfere with diet-induced thermogenesis responses when the sweetness is relatively mismatched to energy content using non-nutritive sweeteners. Metabolic signals arising from glucose metabolism can regulate central mechanisms of reinforcement involved in learned responses to the nutrient properties of foods that drive eating behaviour, but in addition sensory signals arising from sweetness perception can also regulate the thermogenic response to foods, which can cause 'prediction error signalling' if sweetness is stronger than that predicted by the energy content, sending the wrong message to the striatal dopamine system in the midbrain. Interestingly the gut-derived dopamine response was not vagally mediated in response to glucose, whereas it is in response to lipid in the gut. Finally, a human study showed that a small switch from low-fat, low-sugar foods to high-fat, high-sugar foods diminished activation of areas in the brain showing liking of low-fat foods and increased reactivity to food cues, indicating the importance of environmental exposure to unhealthy foods in shaping eating behaviours.

Symposium 2: current challenges for behaviour change interventions

Dr Helen Croker, World Cancer Research Fund International and University College London, UK, delivered a thought-provoking overview of 'Barriers to behaviour change in children' focusing on dietary behaviour change. Using a child-specific framework, Dr Croker considered the influences on eating behaviour: those centred on the child (e.g. food preferences, which are influenced by home environment as well as genetics); those centred on the food (e.g. energy density is associated with linking); community and demographic factors (e.g. parent income) and parents and family (e.g. parenting style, including parenting feeding style and the importance of avoiding coercive approaches). The important role of food advertising on energy consumption in children was briefly discussed, as well as parent views of challenges for dietary behaviour change.

According to Professor Falko Sniehotta, Heidelberg University, Germany and University of Newcastle, UK, in his talk on 'Maintaining weight loss: a behavioural science perspective', most weight loss attempts result in weight regain. However, he explained that there is strong evidence that weight regain can be reduced by long-term intervention. Drawing upon more than hundred behavioural theories, weight loss maintenance is more likely if individuals have a motive for not regaining weight and satisfaction with weight loss, if they can successfully self-regulate their eating behaviour and have strategies to overcome challenges, if they have greater psychological and physical resources, they have managed to form new habits that are automatic and not consciously controlled, and if they have a supportive environment and social support. However, *n*-of-1

randomised controlled trials, which randomly allocate repeated intervention(s) and control time periods and measure individuals over time⁽³⁾, suggest that all these elements of behavioural theory are not as equally important for everyone. Finally, he emphasised the role of emotional factors on weight regain and informed the audience that the NoHoW Trial⁽⁴⁾, which aims to determine the relative efficacy of intervening with/without behavioural and/or emotional regulation for effective weight management, will be reporting results in 2022.

Day 1 was fittingly concluded by the Cuthbertson Medal lecture on 'Total diet replacement: from bench to bedside' by Dr Nerys Astbury, University of Oxford, UK, who discussed her research on very low-energy diets using formula meal replacement products and the results of the DROPLET trial⁽⁵⁾, a pragmatic randomised controlled trial in patients with obesity showing greater weight loss and improvements in cardiometabolic risk markers at 12 months compared to usual care.

Symposium 3: neurochemistry of eating behaviour

Following a sponsored breakfast symposium at the beginning of day 2 on 'COVID-19-related beliefs and participation in a commercial weight loss programme during the pandemic', symposium 3 brought us new perspectives on modulating central appetite pathways from both basic and clinical sciences. Professor Nicholas Dale's (University of Warwick, UK) presentation on 'Tastebuds in the brain' and 'Tanycytes – multipurpose nutrient sensors in the hypothalamus that can regulate feeding', certainly served up some meaty science to savour. Tanycytes are glial cells which line the wall of the third brain ventricle and interface with cerebrospinal fluid, as well as parenchyma including that of appetite neuronal networks in the hypothalamus, and blood vessels at the end of their processes. They can form a barrier and also transport substances such as leptin, and they can also form new tanycytes and new neurons via stem cell functionality. Professor Dale explained how tanycytes can sense sweet taste (including glucose and non-nutritive sweeteners) and amino acids by taste receptor signalling mechanisms equivalent to those found in the tongue, and that they can activate hypothalamic neuronal circuits in the arcuate nucleus that influence food intake, generally increasing feeding if activated optogenetically.

Building on this compelling research into the intricacies of appetite signalling in the brain, Professor Rachel Batterham, University College London, UK, discussed how this knowledge can be implemented to help people with obesity in her talk on 'A new era in gut-hormone based pharmacotherapy for obesity'. She started by emphasising that obesity is now recognised by many international medical organisations as a chronic progressive clinical condition and medical disease, which has the potential to improve the health of people with obesity by reducing weight stigma and creating more opportunities for treatment. Gut hormones and leptin act upon the hypothalamus, influencing orexigenic and anorexigenic neuronal circuits. However, we also eat because food is

pleasurable, and so hedonic neural pathways are also key to pharmacotherapy development. Previously, there have been significant problems with treating obesity with pharmacotherapy due to unfavourable risk–benefit outcomes, but there have since been significant advancements in understanding, including the role of gut hormones in the hypothalamus and reward regions of the brain. Professor Batterham explained that bariatric surgery is effective for long-term weight loss, not just by altering the anatomy of the gastrointestinal tract, but by modifying gut hormone secretion (e.g. a reduction in the hunger hormone ghrelin and an increase in satiety hormones GLP-1 and PYY), in addition to changes in food preferences, altered microbiome and improvements in leptin and insulin sensitivity. Liraglutide is a long-lasting GLP-1 analogue and causes an average of 7% weight loss, which represents a modest effect for individuals who are severely obese. Semaglutide is an even longer-lasting GLP-1 analogue taken as a once-weekly injection being trialled by the STEP programme of clinical trials leading to an average weight loss of 15% over 1 year in patients with an average BMI of 38 kg/m², with a third of patients achieving at least 20% weight loss^(6,7). Advances in science are yielding further potential therapies including cagrilintide, an amylin analogue, and many other gut hormone-based combination therapies that can target multiple areas of the brain to improve efficacy in weight loss.

Maternal obesity presents an important set of challenges, including an increased risk of gestational diabetes, pre-eclampsia, caesarean section, preterm birth, congenital abnormalities and complex delivery, plus an increased risk of obesity, CVD and type 2 diabetes in the child in later life through epigenetic mechanisms. 'Programming by maternal obesity – a pathway to poor cardio-metabolic health', was presented by Professor Susan Ozanne, University of Cambridge, UK, to explain the mechanisms that mediate maternal obesity-induced cardiovascular changes. Cardiac hypertrophy, systolic and diastolic dysfunction, hyperinsulinaemia and insulin resistance were observed in the offspring of obese dams who had been weaned onto a healthy diet and therefore were not themselves obese, indicating a programmed effect on cardiovascular function. Maternal insulin sensitivity, rather than total adipose tissue, seems to be most closely related to offspring insulin levels in the mouse model, presenting a potential therapeutic target for improving the cardiometabolic health of mothers and particularly their children by increasing insulin sensitivity during pregnancy, potentially via exercise interventions. Professor Ozanne concluded with the powerful message that pregnancy is a critical window of intervention when the metabolic consequences of obesity can be treated to improve the health of at least two generations.

Symposium 4: personalised medicine for obesity prevention and management

The last symposium of the conference focused on uncovering the potential for individually targeted approaches to body weight regulation. Dr Carlos Celis-Morales,

University of Glasgow, UK, gave an overview of the Food4Me proof-of-principle study in his talk on 'Personalised nutrition for obesity prevention and management – does it work?'. Dr Celis-Morales described the study design and primary research questions of the Europe-wide Food4Me online intervention study conducted in about 1600 individuals in seven countries⁽⁸⁾. The take-home message was that personalised advice had modest effects on reductions in body weight and waist circumference but there was no added value to provision of genotypic or phenotypic-based advice, and no evidence to suggest that response to personalised advice differs by FTO genotype. However, Dr Celis-Morales concluded that it is important to investigate personalised advice over longer periods and to compare digital/remote interventions v. face-to-face interventions in their efficacy in improving health via personalised advice.

Dr Henrik Munch Roager, University of Copenhagen, Denmark, completed the symposium by evaluating the evidence that inter-individual differences in gut microbiome compositions could be an additional determinant of weight gain and weight loss in his talk on 'How diet–microbial interactions and microbial metabolites may influence weight loss'. The concept of enterotypes has allowed nutritional science to link specific genera of gut bacteria to long-term dietary patterns, including linking weight loss responses to dietary interventions such as the new Nordic diet. Dr Munch Roager presented evidence that weight loss is more marked following a high-fibre intervention in individuals with a high *Prevotella*: *Bacteroides* ratio at baseline, and then he went on to discuss potential mechanisms based on differences in ability to metabolise food and extract energy. Microbial metabolites such as secondary bile acids may regulate energy expenditure in adipose tissue, and SCFAs stimulate production of gut hormones GLP-1 and PYY that affect appetite regulation. He concluded that more research on personal microbiome responses to foods in terms of energy harvesting should be a priority, and that more work is needed to test the hypothesis that enterotypes may help to predict weight loss responses to fibre-rich diets.

Plenary lecture 2: novel approaches to emotional eating

The conference concluded with a plenary talk on new developments in the management of eating disorders with a focus on emotional eating by Professor Janet Treasure, King's College London, UK. Her presentation began with an explanation of the link between binge-eating disorders and other psychiatric disorders, such as attention-deficit/hyperactivity disorder and emotional disorders. There are also certain cognitive traits that are commonly observed in binge-eating disorders, such as decreased flexibility and planning, and reinforcement sensitivity, including a greater sensitivity to punishment and reward, and tendency to act impulsively when experiencing negative emotions. Links with weight stigma and a culture of commodification of food and beauty were briefly touched upon. The second part of the lecture was an interesting overview of novel ways to

target emotional eating in treatment of binge eating, particularly important in light of 50% recovery rates after cognitive behavioural therapy as recommended by evidence-based guidelines. An example being the trials of virtual reality exposure experiences where patients can experience scenarios by responding to the therapist as an avatar that the patient has designed themselves in order to regain control and autonomy have yielded emerging evidence that this might be effective in reducing binge-eating behaviours. Finally, Professor Treasure discussed the development and testing of a new app called FOOD-T for treatment of binge eating by training the brain to inhibit attention and action towards highly palatable foods, shown to be effective in some aspects and with the potential for delivery at a scale.

Conclusions

The topic of 'Obesity and the brain' is a vast area of research and the conference brought together a representative selection of some of the latest advances in understanding the neurobiology, psychology, neuropharmacology and psychiatry of body weight regulation and novel approaches to obesity management. One of the key take-home messages was that we, as a society, need to work on achieving a shift away from relying solely on individual will-power towards treating obesity as a clinical disease that needs professional support alongside wider social and environmental changes to decelerate the current growth in its prevalence, and to reduce the burden of obesity-related ill health.

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