



Meet the Scientist

Dr John Menzies, University of Edinburgh, UK



Dr. John Menzies is a postdoc in Gareth Leng's lab at the University of Edinburgh. In collaboration with Mike Shipston (Edinburgh) and Roger Adan (Utrecht), the group focuses on understanding the brain's energy-regulation and reward pathways and their influence on palatable food intake.

Tell us a bit about yourself and your lab?

I am a research scientist in the Centre for Integrative Physiology at the University of Edinburgh. We are interested in the brain regions underlying food choice, the anticipation of palatable food and termination of feeding. Our main aim is to further understand the brain pathways that control our innate preference for palatable foods.

What is it about your research that particularly interests you?

Until recently the influence of pleasure and reward in eating has been underappreciated. However, it is becoming clear that much of our eating behaviour is driven by pleasure and reward rather than by energy requirements. Modification of these brain reward pathways may be a route to improving health. The key to successful modulation of feeding behaviour likely lies in the signalling between the gut and the brain. The gut produces many peptide hormones that act in the brain and mimicking these may lead eventually to medicines that can suppress our desire to overeat.



John and his colleagues took their research to the public in Edinburgh last November at a "Science Live" event at the National Museum of Scotland

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Why is eating so rewarding?

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What is the problem that this research is addressing?

Once we have accumulated fat stores, we do not need extra energy and should not overeat. However, the prevalence of obesity is high and rising worldwide. This must reflect a strong drive to eat despite the physiological systems that signal to our brain how much fat we already have. In addition to these homeostatic signals, it appears that the rewarding properties of palatable foods are extremely influential in determining how much we eat. Certain foods are preferred over others and our desire for these rewarding foods can easily overcome the physiological mechanisms that normally signal that we are 'full up'. This would be fine if palatable foods were nutritionally balanced but unfortunately the foods we find enjoyable tend to be high in sugar, fat, salt and calories. The outcome is almost inevitable - reward (or pleasure)-driven feeding encourages overeating, weight gain and obesity. It is becoming clear that modifying food intake therapeutically by targeting these homeostatic pathways may be futile in most cases of human obesity. Instead, it may be more valuable to understand and exploit brain pathways that are linked with hedonic (pleasure-driven) food intake.

What is already known?

Over fifty years ago it was shown that stimulation of regions of the brain associated with motivation, reward and pleasure caused animals to spend long periods continually self-

stimulating. They did so at the expense of grooming, drinking, engaging in sexual behaviour or caring for their offspring, even enduring aversive stimuli to access the lever. It is clear that activation of this hedonic (pleasure) pathway can have profound and powerful effects on behaviour. A complex neural network radiating from these reward regions to many other parts of the brain has subsequently been shown to be active during the anticipation and consummation of pleasurable behaviours, including palatable food intake. The interconnected neural pathways activated by stimuli predicting food reward and by the psychological enjoyment associated with hedonic eating are becoming increasingly better characterised. Specific changes in these pathways have been noted in obese humans and in rodent models of obesity, indicating that this system may be a tractable target for anti-obesity therapy.

What research are you undertaking in Full4Health?

Gut-derived peptides like ghrelin (a stomach-derived hunger signal) and leptin (a fat cell-derived signal of energy stores) continually signal homeostatic information to the brain. These peptides also have a hedonic function, they can modify the pleasure and reward associated with food. However, little is known about which populations of reward-related neurones are peptide-sensitive, what neural circuits they form and how these networks evoke, inhibit or modify behaviours. We use optogenetic technology to control neuronal activity and, therefore, animals' behaviour. This is achieved by equipping neurons with a light-activated on/off-switch. By shining light on neurons with an in-dwelling light source we can study the neuronal networks that evoke complex feeding behaviour in living animals.

What do you hope will be the major outcomes?

Using an optogenetic approach in a rat model of hedonic food consumption we will determine how specific neural populations influence food anticipation, the motivation to commence eating, food choice and satiety. By activating or inhibiting these homeostatic and reward pathways we will obtain a greater understanding of the interconnectedness of these pathways and potential targets of therapeutic intervention