Discovery of anti-appetite molecule released by fibre could help tackle obesity

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(Medical Xpress)—New research has helped unpick a long-standing mystery about how dietary fibre supresses appetite. In a study led by Imperial College London and the Medical Research Council (MRC), an international team of researchers identified an anti-appetite molecule called acetate that is naturally released when we digest fibre in the gut. Once released, the acetate is transported to the brain where it produces a signal to tell us to stop eating.

The research, published in *Nature Communications*, confirms the natural benefits of increasing the amount of fibre in our diets to control over-eating and could also help develop methods to reduce appetite. The study found that acetate reduces appetite when directly applied into the bloodstream, the colon or the brain.

Dietary fibre is found in most plants and vegetables but tends to be at low levels in processed food. When fibre is digested by bacteria in our colon, it ferments and releases large amounts of acetate as a waste product. The study tracked the pathway of acetate from the colon to the brain and identified some of the mechanisms that enable it to influence appetite.

lead author of the study Professor Gary Frost, from the Department of Medicine at Imperial College London, said:

"The average diet in Europe today contains about 15g of fibre per day. In stone-age times we ate about 100g per day, but now we favour low-

fibre ready-made meals over vegetables, pulses and other sources of fibre. Unfortunately our digestive system has not yet evolved to deal with this modern diet and this mismatch contributes to the current obesity epidemic. Our research has shown that the release of acetate is central to how fibre supresses our appetite and this could help scientists to tackle overeating."

The study analysed the effects of a form of dietary fibre called inulin which comes from chicory and sugar beets and is also added to cereal bars. Using a mouse model, researchers demonstrated that mice fed on a high-fat diet with added inulin ate less and gained less weight than mice fed on a high-fat diet with no inulin. Further analysis showed that the mice fed on a diet containing inulin had a high level of acetate in their guts.

Using positron emission tomography (PET) scans, the researchers tracked the acetate through the body from the colon to the liver and the heart and showed that it eventually ended up in the hypothalamus region of the brain, which controls hunger.

In collaboration with Consejo Superior de Investigaciones Científicas (CSIC) in Madrid, the researchers investigated the effects of acetate in the hypothalamus using a cutting-edge scanning technique called High Resolution Magic Angle Spinning.

Professor Sebastian Cerdán from CSIC said:

"This complements the PET scans and allows us to follow the metabolism of acetate in the hypothalamus. From this we could clearly see that the acetate accumulates in the hypothalamus after fibre has been digested. The acetate then triggers a series of chemical events in the hypothalamus leading to the firing of pro-opiomelanocortin neurons, which are known to supress appetite."

This is the first demonstration that acetate released from dietary fibre can affect the appetite response in the brain. The research also showed that when acetate was injected into the bloodstream, the colon or the brain it reduced the amount of food eaten by mice.

Co-author on the study Professor Jimmy Bell, from the MRC Clinical Sciences Centre, said:

"It's exciting that we have started to really understand what lies behind fibre's natural ability to supress our appetite and identified acetate as essential to the process. In the context of the growing rates of obesity in western countries, the findings of the research could inform potential methods to prevent weight gain."

Professor Gary Frost added:

"The major challenge is to develop an approach that will deliver the amount of acetate needed to supress appetite but in a form that is acceptable and safe for humans. Acetate is only active for a short amount of time in the body so if we focussed on a purely acetate-based product we would need to find a way to drip-feed it and mimic its slow release in the gut.

"Another option is to focus on the fibre and manipulate it so that it produces more acetate than normal and less fibre is needed to have the same effect, providing a more palatable and comfortable option than massively increasing the amount of fibre in our diet. Developing these approaches will be difficult but it's a good challenge to have and we're looking forward to researching possible ways of using acetate to address health issues around weight gain."

Professor David Lomas, Chair of the MRC's Population and Systems Medicine Board, added:

"It's becoming increasingly clear that the interaction between the gut and the brain plays a key role in controlling how much food we eat. Being able to influence this relationship, for example using acetate to suppress appetite, may in future lead to new, non-surgical treatments for obesity."

More information: "The short-chain fatty acid acetate reduces appetite via a central homeostatic mechanism." Gary Frost, et al. *Nature Communications* 5, Article number: 3611 DOI: 10.1038/ncomms4611. Received 16 July 2013 Accepted 11 March 2014 Published 29 April 2014

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