

FEDERATION OF EUROPEAN NEUROSCIENCE SOCIETIES

10th FENS Forum of Neuroscience

2-6 July 2016 – Copenhagen, Denmark

<http://forum2016.fens.org/>

PRESS RELEASE

EMBARGOED UNTIL SUNDAY 3 JULY 17.15 CEST / 16.15 BST

**HOW THE GUT-BRAIN CONNECTION INFLUENCES OBESITY
AND EATING DISORDERS**

Many factors affect our eating behaviour. Whether we feel hungry or satiated is regulated by a complex interplay between gut and brain, involving food stimuli, as well as signals from hormones and neurotransmitters in our bodies. The brain regulates this information flow, increasing or decreasing one's appetite, ensuring the body can safely process food to provide and store energy. But in recent decades, obesity and related disorders have increased dramatically¹.

=====

Dr Beatrice Passani and her team at the University of Florence found a relationship between two brain systems known to influence eating behaviour, regulate food intake, and control appetite. Speaking to delegates today (3 July) at the FENS Forum of Neuroscience, Dr Passani described how a series of signals activate brain centres regulating appetite, inducing us to eat less.

Scientists know that consuming certain dietary fats induces release of oleoylethanolamide (OEA), a chemical in the small intestine, in turn stimulating production of oxytocin, inhibiting food intake. They also know that histamine in the brain, which regulates functions including wakefulness and memory consolidation, is also known to influence appetite, eating behaviour, and to regulate food intake. High histaminergic activity seems to suppress food intake, and low activity increases intake. Dr Passani and colleagues investigated whether OEA also involves the brain's histamine neurotransmitter system to induce satiety.

Her team measured food intake and behavioural indicators of satiety in mice with extremely low histamine levels. After 12 hours of food deprivation, followed by OEA injections, and re-exposure to food, a striking difference occurred: normal mice ate much less, as expected, but the low histamine mice ate eagerly. Essentially OEA was not effective, as the mice had reduced appetite suppression in response to OEA administration. When researchers induced histamine release in normal mice, they observed increased appetite suppression stimulated by OEA. The researchers also found that in the brain's cortex, OEA indirectly increased the amount of histamine released.

"We found that these two systems do talk to each other," said Dr Passani. The complex gut brain axis seems mediated by the histaminergic system. OEA induces histamine release to exert an appetite-suppressing effect. This indicates that the brain's histamine system controls several behaviours, including OEA as trigger and affecting appetite.

These findings suggest that normal appetite suppression depends on interactions between OEA secreted from the intestines with the brain's histamine system that seems to serve as a relay station, controlling eating behaviour.

Because histamine regulates functions such as wakefulness, appetite and memory consolidation, disruption of histamine may be associated with various brain disorders. Anti-histamines, including over-the-counter medications for allergies, are based on blocking histamine responses on histamine H1 receptors. Antipsychotic drugs for disorders such as schizophrenia, bind strongly to histamine H1 receptors in the brain, which seems to be the cause of unintended side effects such as obesity and sedation associated with antipsychotic treatment.

"These findings have implications in prevention of obesity, and in various disorders associated with antipsychotic treatments," she added. "We should take into account that these drugs may induce obesity and other unintended effects. She hopes that better understanding these drugs' effects might contribute to development of better medications to manage both cognitive and eating disorders.

=====

Knowing that obesity and eating disorders are closely connected with psychological and behavioural problems, and are often caused by chemical imbalances, **Professor Silvana Gaetani** and her colleagues at Sapienza University of Rome are examining how strengthening brain responsiveness to normal 'internal' cues might offer useful tools to combat overeating and obesity.

In all animals, including humans, energy intake and storage are controlled. As food is ingested, cues from smell and taste are integrated in the brain with signals from the body. These signals report the state of nutritional and energy load, such as the distension of stomach walls, the nutrient levels in the intestine, or fat and blood glucose levels. The brain organises and elaborates this information flow, decreasing the drive to eat, ensuring that the amount consumed in a single meal does not exceed what the body can safely handle.

Among these internal cues is oleoylethanolamide (OEA), a compound produced by the small intestine following the ingestion of oleic acid, which is particularly abundant in olive oil. High levels of OEA can reduce appetite, produce weight loss and lower blood cholesterol and triglyceride levels. It can also strengthen the memory of emotional events, possibly linking the high caloric and pleasurable effects of fat-rich food to the formation of a stable imprint in our brain, which, when excessive, might lead to food cravings and compulsive eating.

Professor Gaetani and colleagues in Italy and Switzerland have been investigating obesity and compulsive eating in rats. "We found that that not only does OEA control food intake in overweight animals exposed to a fat-enriched diet, but the compound is also able to control compulsive - or binge - eating driven both by stress and a high palatable diet," she said. They are investigating how this effect is linked to the modulation of brain circuits that respond to the pleasurable properties of food.

Professor Gaetani hopes that better understanding how OEA acts in such complex network might help in developing drug therapies and behavioural strategies that can redirect eating habits and energy metabolism toward a normal pattern.

=====

Alterations in our gut microbiota - the trillions of bacteria and other microorganism living in our intestines - have recently been linked to changes in metabolism, brain function and behaviour.

Dr Harriet Schellekens and her colleagues at University College Cork in Ireland are investigating the mechanisms through which microbes in one's gut influence the regulation of appetite and food reward in the brain.

"It's now emerging that these microbiota can influence conditions such as stress, anxiety, depression, which all also significantly impact on food intake and, thus, may promote metabolic disturbances," she explained.

"Current anti-obesity drug treatments are often not effective and have shown severe side effects. A healthy microbiota is important in maintaining a healthy weight," said Dr Schellekens. So modulation of human gut microbiota has been suggested as a promising 'pharmaco-nutritional' strategy to manage obesity and related disorders.

Therefore, Dr Schellekens and her team investigated two key appetite receptors: the ghrelin receptor, and the serotonin receptor 2c. Both receptors play pivotal roles in the regulation of energy metabolism and appetite, and are also key in regulating food reward and hedonic eating behaviour which can override the feeling of fullness.

The researchers identified a direct interaction between these two receptors and their crosstalk in the regulation of appetite and food reward. They identified different bacterial strains and are now trying to uncover their potential as therapies to treat obesity.

Together, these research efforts clarify many aspects of appetite regulation, the brain, and the gut, and offer new possibilities to treatment of obesity and eating disorders.

END

Abstract Reference Passani: Brain histamine participates in the hypophagic and cognitive effects of oleoylethanolamide

Abstract Reference Gaetani: Oleoylethanolamide: A "fatty gut feeling" to combat obesity?

Abstract Reference Schellekens: Digesting receptor crosstalk in appetite regulation and food reward

Symposia S14: Gut-brain crosstalk in the regulation of feeding and eating disorders

Contact

FENS Press Office and all media enquiries:

Elaine Snell, Snell Communications Ltd, London UK (*English language*)

tel: +44 (0)20 7738 0424 (*before 1 July and after 10 July*); or mobile +44 (0)7973 953 794

email: Elaine@snell-communications.net

Metha Loumann, methamedia, Copenhagen, Denmark (*Danish language*)

tel: +45 60 82 04 03

email: ml@methamedia.dk

Further Reading - Passani:

Satiety factor oleoylethanolamide recruits the brain histaminergic system to inhibit food intake
Provensi G, Coccurello R, Leonardo Munari H, Giacobuzzo, Galeotti N, Nosi D, Gaetani S, Romano A, Moles A, Blandina P, and Passani MB *Biological Sciences - Neuroscience: PNAS* 2014 111 (31) 11527-11532; published ahead of print July 21, 2014, doi:10.1073/pnas.1322016111

Gaetani:

High dietary fat intake influences the activation of specific hindbrain and hypothalamic nuclei by the satiety factor oleoylethanolamide. Romano A, Karimian Azarib E, Tempesta B, Mansourib A, Micioni Di Bonaventura MV, Ramachandran D, Lutz TA, Bedse G, Langhans W and Gaetani S. *Physiology & Behavior* 2014 136:55-62.

Vagal afferents are not necessary for the satiety effect of the gut lipid messenger oleoylethanolamide (OEA) Karimian Azari AE, Ramachandran D, Weibel S, Arnold M, Romano A,

Gaetani S, Langhans W, and Mansouri A *American Journal of Physiology-Regulatory Integrative And Comparative Physiology* 2014 307(2):R167-78

The satiety factor oleylethanolamide recruits the brain histaminergic system to inhibit food intake, Provensi G, Munari L Umehara H, Coccurello R, Giacobuzzo G, Galeotti N, Nosi D, Gaetani S, Romano A, Moles A, Blandina P and Passani MB *Proceedings of The National Academy of Sciences of The United States of America*. 2014, 111(31):11527-32

Schellekens:

Ghrelin's Orexigenic Effect Is Modulated via a Serotonin 2C Receptor Interaction H. Schellekens, De Francesco PN, Kandil D, Theeuwes WF, Mccarthy T, Van Oeffelen WE, et al. *ACS Chem Neurosci*. 2015

Promiscuous dimerization of the growth hormone secretagogue receptor (GHS-R1a) attenuates ghrelin-mediated signaling. Schellekens H, Van Oeffelen WE, Dinan TG and Cryan JF. *Journal of Biological Chemistry*, 2013288, 181-91.

NOTES TO EDITORS

¹ The World Health Organization (WHO) in 2014 estimated that about 39% of the world's adult population are overweight; of these, about 13% are obese. Researchers in Italy and Ireland are investigating and uncovering influences between the gut and brain affecting on appetite regulation.

The 10th FENS Forum of Neuroscience, the largest basic neuroscience meeting in Europe, organised by FENS and hosted by the Danish Society for Neuroscience will attract an estimated 6,000 international delegates. FENS mission is to advance research and education in neuroscience within and outside Europe, to facilitate interaction and coordination between its members. FENS represents 43 national and single discipline neuroscience societies with about 24,000 member scientists from 33 European countries. <http://www.fens.org/>