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Press release

Anorexia/bulimia: a bacterial protein implicated

Eating disorders (ED) such as anorexia nervosa, bulimia, and binge eating disorder affect approximately 5-10% of the general population, but the biological mechanisms involved are unknown. Researchers at Inserm Unit 1073, "Nutrition, inflammation and dysfunction of the gut-brain axis" (Inserm/University of Rouen) have demonstrated the involvement of a protein produced by some intestinal bacteria that may be the source of these disorders. Antibodies produced by the body against this protein also react with the main satiety hormone, which is similar in structure. According to the researchers, it may ultimately be possible to correct this mechanism that causes variations in food intake.

These results are published in the journal *Translational Psychiatry*, in the online issue of 7 October 2014.

See video on the discovery: http://youtu.be/f6UgdQXK7Jw

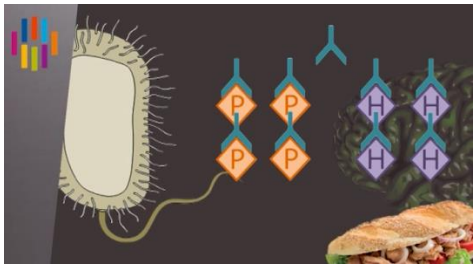
Anorexia nervosa, bulimia and binge eating disorder are all eating disorders (ED). If the less well defined and atypical forms are included, ED affect 15-20% of the population, particularly adolescents and young adults. Despite various psychiatric, genetic and neurobiological studies, the molecular mechanism responsible for these disorders remains mysterious. The common characteristic of the different forms of ED is **dysregulation of food intake**, which is decreased or increased, depending on the situation.

Sergueï Fetissov's team in Inserm Joint Research Unit 1073, "Nutrition, inflammation and dysfunction of the gut-brain axis" (Inserm/University of Rouen), led by Pierre Déchelotte, studies the relationships between the gut and the brain that might explain this dysregulation.

The mimic of the satiety hormone

In this new study, the researchers have identified **a protein that happens to be a mimic of the satiety hormone (melanotropin)**. This protein (ClpB) is produced by certain bacteria, such as *Escherichia coli*, which are naturally present in the intestinal flora. Where this protein is present, antibodies are produced against it by the body. These will also bind to the satiety

hormone because of its structural homology to ClpB, and thereby modify the satietogenic effect of the hormone. **The sensation of satiety is reached (anorexia) or not reached (bulimia or overeating).** Moreover, the bacterial protein itself seems to have anorexigenic properties.



Variations in food intake in the presence of the bacterial protein

To obtain these results, the researchers modified the composition of the intestinal flora of mice to study their immunological and behavioural response. Food intake and level of antibodies against melanotropin in the 1st group of mice, which were given mutant *E. coli* bacteria (not producing ClpB) did not change. In contrast, antibody level and food intake did vary in the 2nd group of animals, which received *E. coli* producing ClpB protein.

The likely involvement of this bacterial protein in disordered eating behaviour in humans was established by **analysing data from 60 patients.**

The standardised scale "Eating Disorders Inventory-2" was used to diagnose these patients and evaluate of the severity of their disorders, based on a questionnaire regarding their behaviour and emotions (wish to lose weight, bulimia, maturity fears, etc.). **Plasma levels of antibodies to ClpB and melanotropin were higher in these patients.** Furthermore, their immunological response determined the development of eating disorders in the direction of anorexia or bulimia.

These data thus confirm the involvement of the bacterial protein in the regulation of appetite, and open up new perspectives for the diagnosis and specific treatment of eating disorders.

Correcting the action of the protein mimicking the satiety hormone

*"We are presently working to **develop a blood test** based on detection of the bacterial protein ClpB. If we are successful in this, we will be able to establish specific and individualised treatments for eating disorders," say Pierre Déchelotte and Sergueï Fetissov, authors of this study.*

At the same time, the researchers are using mice to study how to correct the action of the bacterial protein in order to prevent the dysregulation of food intake that it generates. *"According to our initial observations, it would indeed be possible to **neutralise this bacterial protein using specific antibodies, without affecting the satiety hormone,"*** they conclude.

Sources

Bacterial ClpB heat-shock protein, an antigen-mimetic of the anorexigenic peptide α-MSH, at the origin of eating disorders
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This study was carried out in collaboration with other teams and platforms of the Institute for Research and Innovation in Biomedicine (IRIB) Normandy Rouen, and with the University of Tartu (Estonia). It extends other work published by the research team in 2013, which demonstrated molecular mechanisms for increasing the appetite by immunoglobulins that protect the hunger hormone (ghrelin) in obese people.

These works were the object of two demands of patents deposited by Inserm Transfert.

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