Fatty food cravings genetically programmed

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(Medical Xpress) -- In a new study published in *Neuropsychopharmacology*, Dr. Alasdair MacKenzie has found a genetic switch that regulates thirst and appetite and is believed to be the reason many people from Western countries are more prone to high fat diets and alcohol consumption that those in Asian countries.

Researchers believe this switch was turned on during the Ice Age when it was necessary for Europeans to consume high fat diets and higher alcohol content in order to survive the conditions. The complications seen from fat and alcohol were not a problem back then because the average life expectancy was between 30 and 40 years.

The switch is located in an area of the brain called the hypothalamus and regulates appetite and thirst and controls the galanin gene. According to the researchers, the stronger the switch is turned on, the more likely a person is to crave and consume higher fat content foods. The weaker version of this switch was only found in 16 percent of Europeans compared to 30 percent of Asians studied.

Galanin is also produced in the amygdala and controls anxiety and fear. The researchers found that this switch is also active in the amygdala and could play a role on the emotional state of an individual and depression.

Researchers hope that the discovery of this switch and how it affects food cravings could lead to future treatments in obesity and weight control. Because of the connection to emotional states, this switch could also play a role in future depression treatments.

More information: Differential Activity by Polymorphic Variants of a Remote Enhancer that Supports Galanin Expression in the Hypothalamus and Amygdala: Implications for Obesity, Depression and Alcoholism; Scott Davidson, Marissa Lear, Lynne Shanley, Benjamin Hing, Amanda Baizan-Edge, Annika Herwig, John P Quinn, Gerome Breen, Peter McGuffin, Andrew Starkey, Perry Barrett and Alasdair MacKenzie; *Neuropsychopharmacology* , (29 June 2011) doi:10.1038/npp.2011.93

Abstract

The expression of the galanin gene (GAL) in the paraventricular nucleus (PVN) and in the amygdala of higher vertebrates suggests the requirement for highly conserved, but unidentified, regulatory sequences that are critical to allow the galanin gene to control alcohol and fat intake and modulate mood. We used comparative genomics to identify a highly conserved sequence that lay 42 kb 5′ of the human GAL transcriptional start site that we called GAL5.1. GAL5.1 activated promoter activity in neurones of the PVN, arcuate nucleus and amygdala that also expressed the galanin peptide. Analysis in neuroblastoma cells demonstrated that GAL5.1 acted as an enhancer of promoter activity after PKC activation. GAL5.1 contained two polymorphisms; rs2513280(C/G) and rs2513281(A/G), that occurred in two allelic combinations (GG or CA) where the dominant GG alelle occurred in 70-83 % of the human population. Intriguingly, both SNPs were found to be in LD (R2 of 0.687) with another SNP (rs2156464) previously associated with major depressive disorder (MDD). Recreation of these alleles in reporter constructs and subsequent magnetofection into primary rat hypothalamic neurones showed that the CA allele was 40 % less active than the GG allele. This is consistent with the hypothesis that the weaker allele may affect food and alcohol preference. The linkage of the SNPs analysed in this study with a SNP previously associated with MDD together with the functioning of GAL5.1 as a PVN and amygdala specific enhancer represent a significant advance in our ability to understand alcoholism,

obesity and major depressive disorder.

Press release