

PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Anorexia susceptibility gene variant

ArticleInfo		
ArticleID	:	4076
ArticleDOI	:	10.1186/gb-spotlight-20010504-01
ArticleCitationID	:	spotlight-20010504-01
ArticleSequenceNumber	:	147
ArticleCategory	:	Research news
ArticleFirstPage	:	1
ArticleLastPage	:	2
ArticleHistory	:	RegistrationDate : 2001-05-04 OnlineDate : 2001-05-04
ArticleCopyright	:	BioMed Central Ltd2001
ArticleGrants	:	
ArticleContext	:	130592211

Anorexia affects about 1% of teenage girls in the United States and in severe cases can be fatal. There is considerable debate as to the involvement of genetic factors in the predisposition to develop anorexia nervosa. It has been suggested that variants of the agouti-related protein (AGRP) - involved in controlling appetite - may be important in the development of anorexia nervosa in a subset of cases.

In the May issue of *Molecular Psychiatry*, Roger Adan and colleagues at the Utrecht University Medical Center, The Netherlands determined the sequence of the coding region of the human AGRP. A screen of the AGRP of 100 patients with anorexia nervosa revealed three single nucleotide polymorphisms (SNPs) and they further screened 45 additional patients and 244 controls for these polymorphisms.

The researchers found that two alleles were in complete linkage and were significantly enriched in 11% of anorexic patients, compared with only 4.5% of controls. In normal individuals AGRP reduces the activity of the melanocortin-4 receptor (MC4-r) resulting in an increased feeding signal. But, the variant form of AGRP results in diminished MC4-r activity and a subsequent reduction in the feeding signal. Adan *et al.* suggest that variations in the AGRP gene could therefore make an individual more susceptible to anorexia nervosa, although they stress that it is not the only gene that is involved in the disease. "It may contribute to explaining why a small proportion of people get eating disorders," comments Walter Kaye, a psychiatrist at the University of Pittsburgh "But it is not going to explain everybody."

They speculate that an antagonist of the MC4-r could be used as a pharmacological treatment for some patients suffering from anorexia nervosa.

References

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