Genetic association studies into anorexia nervosa

M.C.T. Slof-Op 't Landt[1,2,3], I. Meulenbelt[2], E.F. van Furth[1], M. Bartels[3], D.I. Boomsma[3], & P.E. Slagboom[2]

[1] Center for Eating Disorders Ursula, Leidschendam, The Netherlands
[2] Leiden University Medical Centre, Molecular Epidemiology Section, Leiden, The Netherlands
[3] Department of Biological Psychology, VU University, Amsterdam, The Netherlands

Introduction

We investigated the contribution of the genetic variation within serotonin receptor 1D (HTR1D), brain-derived neurotrophic factor (BDNF) and stathmin (STMN1) to eating disorders, and specifically to anorexia nervosa.

In previous studies genetic variation within HTR1D and BDNF was associated with anorexia nervosa. Stathmin 1 (STMN1) is a new candidate gene, due to its location at the site of a positive linkage signal in a genome wide scan for anorexia nervosa (1p33-36), and its role in the regulation of fear in rats.

Participants

- 287 female eating disorder patients (107 AN), age range (16-61 years)
- 770 female twins (one per family) from the Netherlands Twin Registry, age range (13-61 years)

Measures

In the patient population eating disorder diagnoses were made by semi-structured interview.

Genotyping

Five single nucleotide polymorphisms (SNPs) were selected from previous studies (HTR1D: n=4; BDNF: n=1). In addition, 10 tag SNPs were selected to detect the majority of the genetic variation within the BDNF (n=7), and STMN1 (n=3) genes. The SNPs were measured using Sequenom.

Analyses

Case-control association analyses were performed for eating disorders and anorexia nervosa, using logistic regression analyses in SPSS. Haplotype-based analyses were performed in Haploview.

Results

In table 1 minor allele frequencies (MAF) and p-values per SNP are presented for the control, eating disorder and anorexia nervosa population. Nominal p-values not adjusted for multiple testing are shown.

BDNF: Four SNPs were significantly associated with anorexia nervosa. Haplotype analyses showed that the four associated alleles represent one particular haplotype. This haplotype was significantly associated to anorexia nervosa (OR=1.37, p=0.03).

STMN1: One SNP was significantly associated with eating disorders (OR=1.24, p=0.05).

Table 1. MAF and p-values for control, ED and AN populations

	Control	ED patients		AN patients	
	MAF	MAF	p	MAF	p
BDNF					
Rs6265	0.19	0.22	0.19	0.20	0.70
SNP 1	0.32	0.28	**0.05**	0.25	**0.02**
SNP 2	0.27	0.24	0.16	0.19	**0.02**
SNP 3	0.45	0.47	0.40	0.52	**0.05**
SNP 4	0.11	0.09	0.12	0.09	0.22
SNP 5	0.19	0.18	0.41	0.17	0.34
SNP 6	0.16	0.15	0.75	0.11	**0.05**
SNP 7	0.47	0.48	0.73	0.49	0.61
STMN1					
SNP 8	0.35	0.31	0.14	0.33	0.63
SNP 9	0.43	0.44	0.61	0.41	0.61
SNP 10	0.25	0.29	**0.05**	0.27	0.48
HTR1D					
Rs605367	0.32	0.32	0.77	0.33	0.95
Rs6300	0.09	0.08	0.52	0.08	0.81
Rs676643	0.16	0.15	0.68	0.14	0.55
Rs674386	0.30	0.28	0.47	0.29	0.65

Discussion

Significant associations to anorexia nervosa and/or eating disorders were shown for four SNPs within BDNF and one within STMN1. The four BDNF SNPs formed one haplotype. Carriers of this haplotype were at higher risk to develop anorexia nervosa. Carriers of the minor allele of STMN1 SNP 10 had a higher risk to develop an eating disorder.

The next step is to seek replication for this study.

E-mail: r.optlandt@centrumeetstoornissen.nl

Centrum Eetstoornissen Ursula