Genome Wide Association analysis for Borderline Personality Disorder Characteristics

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Sample
- 1261 unrelated Dutch adults from the Netherlands Twin Registry.
- Mean age 45.8 (SD = 14.2), 65% women.

Phenotype
-BPD features were assessed with the PAI-BOR quantitative scale *(Morey LC, Psychological Assessment Resources, 1991).*
- Square root transformation.

Genotyping & Quality Control
- Perlegen 600k SNP chip.
- Software PLINK.
- Genome build 35.
- Duplicate and Mendelian errors < 2 per SNP.
- MAF > 0.01.
- Missing genotypes < 0.05 in SNPs and individuals.
- HWE > 0.00001.
- Genomic control inflation factor = 1.0.
- 431886 SNPs remain.

Genome-wide association tests
- Quantitative linear test for associaton.
- Sex and age included as covariates.

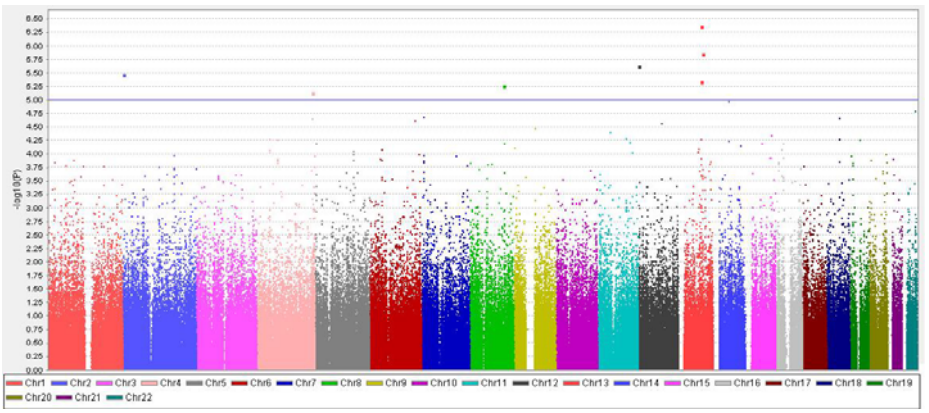
Aim 1
Test for association in genes that were identified in earlier genome wide association studies of Bipolar Disorder.

GENE	Chromosome	N SNPs	N P<0.05	Best SNP	Best SNP P
RFTN1	3	63	2	rs12492816	0.01654
EGFR	7	62	1	rs12538371	0.02091
GRM3	7	21	3	rs6955917	0.01781
ATP6V1G1	9	3	0	rs2274595	0.4068
DFNB31	9	28	4	rs730646	0.004917
TSPAN8	12	6	0	rs1705237	0.07427
CACNA1C	12	122	12	rs2238056	0.02331
TMEM132E	17	16	0	rs10445388	0.2228
MYO5B	18	92	5	rs1617706	0.007687
CDH7	18	11	3	rs17783381	0.008033

Aim 2
Test for association in the identified linkage region 9p24.1 at marker D9S286 +/- 1 mb *(MA Distel et al., Psychiatric Genetics, In press) .*

Best SNP in this region is rs10733549 with p 0.00067. This is in the PTPRD gene, which has 268 SNPs typed and 15 SNPs with P < 0.05. The linkage peak is 30 mb away from DFNB31 and ATP6V1G1.

Aim 3 Identify new genetic variants.



Chromosome	SNP	BP Location	P	GENE
2	rs17495118	2682917	0.0000035	MYT1L / TSSC1*
4	rs1106051	184664506	0.0000074	CLDN22 / CDKN2AIP*
8	rs17476727	111176730	0.0000054	KCNV1*
12	rs10849328	582880	0.0000024	NINJ2
13	rs9573671	75327312	0.0000047	LMO7
13	rs1323573	75397003	0.0000004	LMO7*
13	rs4146682	79600066	0.0000014	SPRY2*

* Gene closest to SNP, no known genes at SNP location.

LMO7 has 51 typed SNPs, 20 have P < 0.05. NINJ2 has 26 typed SNPs, 6 have P < 0.05.

Conclusions
- CACNA1C, CDH7, MYO5B, GRM3 and DFNB31 show indication of replication.

- Linkage to region 9p24.1 may be related to the candidate genes PTPRD, DFNB31 and ATP6V1G1.

- The LMO7 gene on chromosome 13 shows suggestive evidence of association, as well as the NINJ2 gene on chromosome 2. The other SNPs are not located in currently known genes.

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