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Poster presentation

An analysis of allele sharing in a region of linkage with bipolar affective disorder

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Introduction

Previously, we described the significant linkage of bipolar affective disorder (BPAD) with a 14 cM region of chromosome 4p15-16 in a single large Scottish pedigree (F22). A number of independent groups have subsequently provided additional evidence for linkage to this region. It is likely that a founder mutation is responsible for these linkage signals and would be co-inherited with a region of flanking sequence.

Methods:

We describe a strategy for identifying regions of excess allele sharing between hypothesised mutation carrying chromosomes when compared to control chromosomes of the linked families. This involved identifying and genotyping ~200 SNPs within genes from the linked region. A modified nested permutation analysis is used to assess significance of shared haplotypes.

Results:

Comparison of the linked haplotypes in the four families identified two ~4 Mb sub-regions of interest in the F22 candidate region. Analysis of allele sharing highlighted a ~200 kb region within one of the ~4 Mb candidate regions with significantly higher sharing than seen in control chromosomes.

Conclusions:

Following up multiple linkage analysis results with allele & haplotype sharing analysis has allowed us to progress from a large linkage region to small regions of allele sharing. These results overlap with the association study ongoing in this region. Comprehensive functional analysis of the genes in these regions is now feasible and underway.