PW01-232 - **CONNECTIVITY GENES IN COMORBID ALCOHOLISM AND BIPOLAR DISORDER**

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Introduction: Bipolar disorder (BPD) and alcoholism are strongly comorbid and both have significant genetic influences but no consistent genetic vulnerability has been found. We aimed to find bipolar-alcoholism vulnerability genes.

Method: A genome-wide association study (GWAS) of 510 patients with bipolar disorder (BPD), of whom 143 met Research Diagnostic Criteria (RDC) alcoholism diagnoses, and 506 ancestrally matched supernormal controls. We genotyped 372K genetic markers on an Affymetrix 500K-array. Chi-square analysis of allelic association using PLINK, and permutation testing for gene-wise association of genes previously associated with alcoholism-related phenotypes using COMBASSOC, were performed.

Results: No marker met genomewide significance. Gene-wise analyses of markers clustering near genes already implicated in alcoholism, but which were not associated in non-alcoholic BPD, were: Cadherin-11 (CDH11, $p = 6 \times 10^{-4}$), Exportin 7 (XPO7), neuromedin-U receptor 2 (NMUR2), collagen type XI-alpha 2 (COL11A2) and Semaphorin-5A (SEMA5A).

Discussion: These genes replicated prior genetic reports implicating “connectivity” (adhesion, migration and neuronal signalling) genes in addictions and comorbid BPD. Connectivity genes regulate neuronal connections during development and play roles in later neuroadaptive and mnemonic processes. These processes may influence addiction vulnerability, as seen clinically in denial, cognitive impairment, and repetitive substance misuse and relapse behaviour. We propose that we have identified genes i) increasing susceptibility to alcoholism that could be unmasked or released by the presence of bipolar affective disorder; ii) and genes increasing susceptibility to affective disorder that also predispose to secondary alcoholism. We were **limited** by small sample size. Larger **future** studies are needed.

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