Bipolar 1 disorder is not associated with the RGS4, PRODH, COMT and GRK3 genes

Diana Pinto Prata\textsuperscript{a,b}, Gerome Breen\textsuperscript{a,b}, Janet Munro\textsuperscript{b}, Maggie Sinclair\textsuperscript{c}, Sarah Osborne\textsuperscript{b}, Tao Li\textsuperscript{b}, Robert Kerwin\textsuperscript{b}, David St. Clair\textsuperscript{c} and David A. Collier\textsuperscript{a,b}

Although current psychiatric nosology separates bipolar disorder and schizophrenia into non-overlapping categories, there is growing evidence of a partial aetiological overlap between them from linkage, genetic epidemiology and molecular genetics studies. Thus, it is important to determine whether genes implicated in the aetiology of schizophrenia play a role in bipolar disorder, and vice versa. In this study we investigated a total of 15 single nucleotide polymorphisms (SNPs), and all possible haplotypes, of genes that have been previously implicated in schizophrenia or bipolar disorder - RGS4, PRODH, COMT and GRK3 - in a sample of 213 cases with bipolar affective disorder type 1 and 197 controls from Scotland. We analysed the polymorphisms allele-wise, genotype-wise and, for each gene, haplotype-wise but obtained no result that reached nominal significance ($p < 0.05$) for an association with the disease status. In conclusion, we could not find evidence of association between RGS4, PRODH, COMT and GRK3 genes and bipolar affective disorder 1 in the Scottish population. 

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Summary

We performed a candidate gene case–control association study between bipolar disorder and the RGS4, PRODH, COMT and GRK3 genes, which have previously been associated with schizophrenia and/or bipolar disorder (Li \textit{et al.}, 2000; Liu \textit{et al.}, 2002; Barrett \textit{et al.}, 2003; Chowdari \textit{et al.}, 2002). The sample consisted of 213 unrelated cases recruited through Scottish psychiatric hospitals and 197 controls, all white Scottish Caucasians. Patients met Diagnostic and Statistical Manual of Mental Disorder-IV criteria exclusively for bipolar I disorder, as defined by the OPCRIT program and based on case-note review and clinical interview with semistructured diagnostic questionnaires. Genotyping of 15 single nucleotide polymorphisms (SNPs) from the above genes was performed by KBiosciences (http://www.kbioscience.co.uk) using a competitive allele-specific polymerase chain reaction system (KASPar). In addition to interplate and intraplate duplicate testing, quality control criteria were: distinct genotype counts were 27, 93 and 70 in the controls and 36, 96 and 73 in the cases; for rs951436, 36, 101, 49 and 51, 99, 53; rs951439, 26, 95, 74 and 37, 94, 81 and rs2661319, 37, 96, 56 and 50, 99, 58. For PRODH, rs383964 counts were 38, 91, 65 and 39, 104, 69; rs372055, 8, 56, 132 and 8, 61, 140; rs450046, 2, 21, 171 and 1, 19, 192; rs385440, 2, 24, 169 and 1, 19, 191 and rs1808320, 2, 22, 170 and 1, 20, 186. For COMT, rs737865 was 19, 70, 99 and 17, 82, 100; rs4680 (val, met), 51(AA), 97, 45 and 45, 110, 54 and rs165599, 20, 91, 71 and 18, 100, 81. Finally, for GRK3, rs376895 showed 13, 79, 103 and 11, 90, 109; rs558934, 13, 82, 99 and 14, 95, 104 and rs5761116, 7, 48, 138 and 10, 62, 133. Haplotype estimation using GENECOUNTING 1.3 software (available at http://www.smd.qmu.ac.uk/itogen/idwts/software.html) (Zhao \textit{et al.}, 2002) also failed to reach significance for all genes. Therefore, our work does not support an involvement of RGS4, PRODH, COMT and GRK3 genes in the aetiology of bipolar affective disorder 1 in the Scottish population.

References


