RGS2 ggenetic variation: association analysis with panic disorder and dimensional as well as intermediate phenotypes of anxiety

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Accumulating evidence from mouse models points to the G protein-coupled receptor RGS2 (regulator of G-protein signaling 2) as a promising candidate gene for anxiety in humans. Recently, RGS2 polymorphisms were found to be associated with various anxiety disorders, e.g., rs4606 with panic disorder (PD), but other findings have been negative or inconsistent concerning the respective risk allele. To further examine the role of RGS2 polymorphisms in the pathogenesis of PD, we genotyped rs4606 and five additional RGS2 tag single nucleotide polymorphisms (SNPs; rs16834831, rs10801153, rs16829458, rs1342809, rs1890397) in two independent PD samples, comprising 531 matched case/control pairs. The functional SNP rs4606 was nominally associated with PD when both samples were combined. The upstream SNP rs10801153 displayed a Bonferroni-resistant significant association with PD in the second and the combined sample (P = 0.006 and P = 0.017). We furthermore investigated the effect of rs10801153 on dimensional anxiety traits, a behavioral avoidance test (BAT), and an index for emotional processing in the respective subsets of the total sample. In line with categorical results, homozygous risk (G) allele carriers displayed higher scores on the Agoraphobic Cognitions Questionnaire (ACQ; P = 0.015) and showed significantly more defensive behavior during fear provoking situations (P = 0.001). Furthermore, significant effects on brain activation in response to angry (P = 0.013), happy (P = 0.042) and neutral faces (P = 0.032) were detected. Taken together, these findings provide further evidence for the potential role of RGS2 as a candidate gene for PD.
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