

# Is *PLXNA2* a candidate gene for childhood and adult anxiety and depression?



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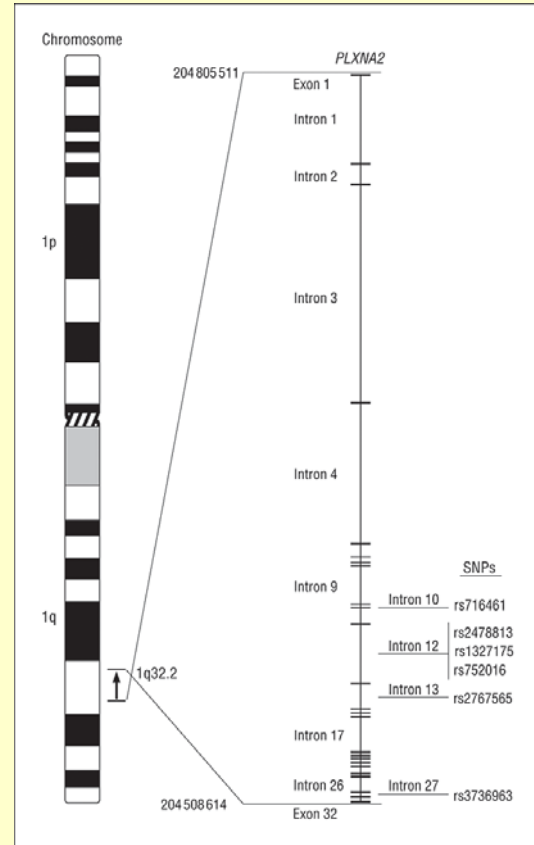
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**Background** Reduction in adult neurogenesis has been proposed as a mechanism for the onset of depression. Plexins participate in many cellular events that include axonal repulsion, axonal attraction, cell migration, axon pruning, and synaptic plasticity. *PLXNA2* has been implicated in psychiatric disorders. A recent study in Australian sib pairs reported that *PLXNA2* is a candidate for causal variation in anxiety and in other psychiatric disorders through its comorbidity with anxiety (Wray *et al. Arch Gen Psychiatry, 2007, 318-26*). We investigated the association between *PLXNA2* and anxiety and depression in adults and children.

**Methods** Adult subjects participated in longitudinal survey studies on neuroticism, anxiety and depression with self-report questionnaires up to five time points. Anxious depression was measured in young Dutch twins (ages 3-12 years) through maternal and paternal ratings. In total, 1809 adults and 838 young DZ twins were genotyped for six SNPs in *PLXNA2* (Figure 1). Using qTDT, the association between *PLXNA2* and the mean scores across the five occasions (adults) and the average maternal and paternal reports at each age was analyzed in the adults and the children.

**Results** In the adult sample, rs2478813 showed a dominant effect for neuroticism ( $p < 0.05$ ), but not for anxiety or depression (Table 1). In the children, rs2478813, showed a significant additive effect at age 10, but in the opposite direction. Rs752016 and rs2767565 showed a significant effect and a trend towards significance at age 10 and 12 respectively.

**Conclusions** We replicated the finding of Wray *et al* that *PLXNA2* is associated with anxiety related phenotypes. This association is not found before the age of 10. As this gene is involved in brain development, it might be of importance during adolescence, a period of large changes in the brain.



**Figure 1** (copied of Wray *et al.* (2007)). Location and gene structure of the gene encoding *PLXNA2* and position of genotyped SNP's.

Table 1: Anxiety, depression and neuroticism scores per genotype for rs2478533 in children and adults

	11	12	22
Anx /depression Age 10	1.4	2.4	2.8
Anx /depression Age 12	1.8	2.1	2.3
Neuroticism, adults	20.1	18.4	18.6