

A FAMILY STUDY OF THE ASSOCIATION BETWEEN THE SEROTONIN TRANSPORTER GENE POLYMORPHISM AND ANXIETY AND DEPRESSION

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Background In 1996, Lesch et al. reported an association between the serotonin transporter gene polymorphism (5-HTTLPR) and anxiety-related personality traits. Approximately 25 studies trying to replicate this finding showed conflicting results. Non-replications may be due to low power to detect the small effect of 5-HTTLPR in studies with small sample sizes. We performed an association analysis in a large sample of siblings and their parents.

Methods In 466 families from the Netherlands Twin Register, 254 fathers, 305 mothers, 501 male and 744 female offspring were genotyped for 5-HTTLPR. These families were enriched for the absence or presence of high-scoring siblings on a composite score of neuroticism, anxiety and depression. The association was analysed between the ss, sl and ll variant of 5-HTTLPR and scores on self-report questionnaires of anxiety (STAI), depression (YASR) and neuroticism (ABV), measured on 5 occasions since 1991. Both within family association and total association were tested in QTDT.

Figure 1: Anxiety

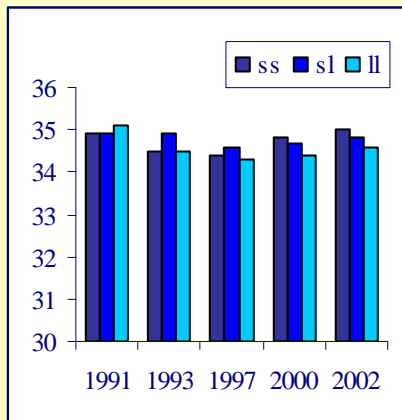


Figure 2: Depression

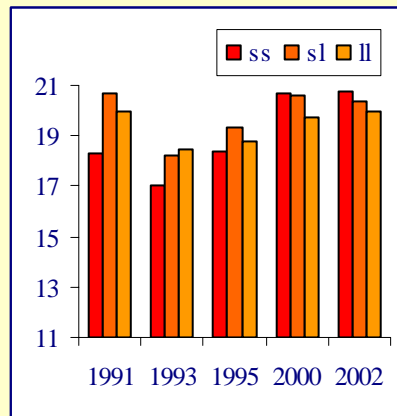


Figure 3: Neuroticism

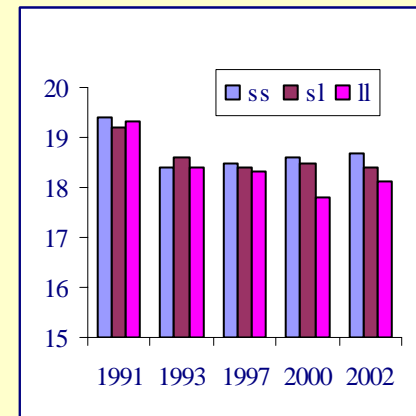
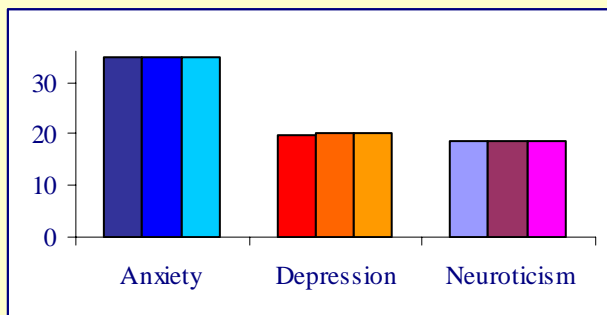


Figure 4: Mean Scores



Results Figure 1, 2 and 3 show the anxiety, depression and neuroticism scores in subjects with the ss, sl and ll genotype on the five different time points. Within family association was significant for anxiety, depression and neuroticism measured in 1991. Total association was significant for neuroticism measured in 2000 and 2002. Figure 4 shows the mean anxiety, depression and neuroticism scores over the five occasions for the subjects with the ss, sl and ll genotype. Neither the within family association tests nor the total association tests reached significance.

Conclusions These analyses clearly suggest **no association between 5-HTTLPR and anxiety-related traits**. They also show how associations can be found by coincidence. Had we chosen to report the results of the 1991 survey, we would have drawn the conclusion that there is a significant association between 5HTTLPR and anxiety-related traits. If measures at multiple occasions are available, mean scores should be analysed. This is illustrated by our results on neuroticism. Two out of the 5 total association tests were significant. However, the total association test with the mean score over the 5 occasions did not reach significance. The latter test had more power because of the high number of subjects and the reduction of measurement error.