IN THE NEWS

Antidepressant scare

"Scientists find Prozac 'link' to brain tumours" was the headline in the *Independent* newspaper on 26 March as it reported the results of work by John Gordon (Birmingham University, UK) and colleagues. Unsurprisingly, the suggestion that patients taking certain antidepressants might be at increased risk of some types of cancer caused something of a scare — and both pharmaceutical companies and scientists were at pains to point out that there is absolutely no evidence for such a link.

The root of the story was the finding, published in *Blood*, that serotonin could enter lymphoma cells *in vitro* and cause them to die. Selective serotonin-reuptake inhibitors (SSRIs) interfered with the uptake of serotonin into the cells, and thus prevented their deaths. This led to the idea that patients taking SSRIs, such as Prozac, might be at increased risk of brain tumours.

Several media sources carried stories the next day refuting the suggestion that Prozac and other SSRIs used as antidepressants could increase the risk of brain tumours — for example, *BBC News Online* (27 March) carried a quote from Gordon saying, "I have looked at a number of large-scale studies looking specifically at these drugs in relation to cancer, and there is nothing to suggest that they increase cancer risk." Gordon urged patients to continue taking their drugs, amid fears that patients suffering from severe depression could, in extreme cases, commit suicide if they suddenly stopped taking antidepressants.

Rachel Jones

PSYCHIATRIC DISORDERS

Work in progress

Despite the media attention that potential environmental causes of autistic disorder have received, the evidence for an involvement of specific environmental factors is far from robust. By contrast, there is strong evidence for a genetic aetiology of autism, and the genetic mechanisms that underlie this disorder are gradually being unravelled. In a recent issue of *Molecular Psychiatry*, the latest advances in identifying the genes responsible for autism are reported in four papers, each focusing on a different chromosomal location.

Current genetic models predict that most cases of autistic disorder are multifactorial, involving several — at least two and possibly more than ten — susceptibility genes that interact to produce the phenotype. Several genome screens have indicated that chromosome 7q contains an autism susceptibility locus, but specific susceptibility genes within this region remain to be identified. As part of a continuing study of the 7q locus, Bonora *et al.* examined four adjacent genes within 7q32 — *PEG1/MEST*, *COPG2*, *CPA1* and *CPA5* — in patients with autism who were selected from families in which linkage to chromosome 7q had been detected. They screened these genes for genetic variation, and examined variants with potential functional significance for an association with autism. However, no sequence variants were found that could be related to autistic disorder. Because *PEG1* and *COPG2* are 'imprinted' genes (the maternal or paternal copy of the gene is selectively expressed), Bonora *et al.* looked for imprinting mutations that might be involved in autism. They found no imprinting abnormalities in the lymphocytes of autistic patients. So, it seems unlikely that these genes have an important role in the aetiology of autism — a finding that could help to shape future studies of candidate genes that map to the 7q locus.

Positive genetic findings were made in three further studies of autism. Serotonin has been implicated in the pathophysiology of autistic disorder, and the serotonin transporter gene (*SLC6A4*, localized to chromosome 17q) has therefore been a primary candidate in the search for autism susceptibility genes. Although *SLC6A4* has been examined in several previous studies, no clear involvement in autism has been established. Kim *et al.* carried out a comprehensive screen of *SLC6A4* for polymorphisms in autistic individuals, and identified new variants that might be linked to this disorder.

Jamain and co-workers focused on the gene for glutamate receptor 6 (*GLUR6/GRIK2*), which is localized to chromosome 6q21 — a candidate region. The authors found a significant linkage and association of *GLUR6* with autism; they argue that alterations in GLUR6 function could contribute to a range of symptoms, including cognitive, motor and motivational impairments.

In the last study, Buxbaum *et al.* turned their attention to a marker, 155CA-2, within the $GABA_A$ receptor β3 subunit gene (*GABRB3*), which is localized to 15q11–13 — a region that has been strongly implicated in autism. The 155CA-2 marker has been associated with autism in one previous study, but not in others. Buxbaum and colleagues found evidence for an association between 155CA-2 and autism, adding weight to the idea that genetic variants within *GABRB3* might be involved in autistic disorder.

Autism is a complex condition, and genetic models will ultimately need to account for its range of symptoms, its phenotypic heterogeneity, and the fact that more males than females are affected. Although studies of candidate genes are still in their infancy, many investigations are now underway. Pinning down the genetic mechanisms of autistic disorder represents a considerable challenge, but the studies presented here give us reason to believe that we are moving, little by little, towards this target.

Rebecca Craven

References and links

ORIGINAL RESEARCH PAPER Kim, S.-J. *et al.* Transmission disequilibrium mapping at the serotonin transporter gene (*SLC6A4*) region in autistic disorder. *Mol. Psychiatry* **7**, 278–288 (2002) | Bonora, E. *et al.* Mutation screening and imprinting analysis of four candidate genes for autism in the 7q32 region. *Mol. Psychiatry* **7**, 289–301 (2002) | Jamain, S. *et al.* Linkage and association of the glutamate receptor 6 gene with autism. *Mol. Psychiatry* **7**, 302–310 (2002) | Buxbaum, J. D. *et al.* Association between a *GABRB3* polymorphism and autism. *Mol. Psychiatry* **7**, 311–316 (2002)

FURTHER READING Folstein, S. E. & Rosen-Sheidley, B. Genetics of autism: complex aetiology for a heterogeneous disorder. *Nature Rev. Genet.* **2**, 943–955 (2001)