

FOCUS ON RESEARCH

A GENETIC LINKAGE STUDY TO DETECT QUALITATIVE TRAIT LOCI FOR UNIPOLAR DEPRESSION ASSOCIATED WITH OEDEMA IN THREE LARGE PEDIGREES

Researchers

Professor Douglas Blackwood, Dr Matthew Dunnigan, Dr Walter Muir, Professor David Porteous, Dr Val Murray, Dr Anthony Pelosi, Dr. Peter Visscher

Aim

Depression is often a chronic illness associated with considerable morbidity and high rates of death by suicide. The lifetime prevalence is between 6% and 10%, with twice as many women affected as men. It is also well established that some types of depression are strongly heritable and family studies offer a powerful means to investigate the role of genes contributing to the disorder. We have performed a genetic linkage study in families as a first step towards identifying genes that could play a part in depression in young adults. Linkage analysis is a method for identifying the position on a chromosome where candidate genes implicated in depression, might be located. In the laboratory several hundred DNA "markers" are applied to DNA samples from individuals belonging to families affected by a disorder. The pattern of markers in relatives with the disorder is compared with the pattern found in relatives who are well and differences in the patterns act as signposts to the location on chromosomes of genes that could play some part in the disorder. Once linkage has been established at a particular region further studies are initiated to discover the identity and function of the genes lying within that region.

Project Outline/Methodology

Members of four families took part in this study. The families were chosen because in each there were several family members with a sub type of depression thought to be highly heritable where depression is accompanied by distressing and unexplained symptoms of swelling in the hands, face and legs. Relatives were interviewed by a doctor who rated symptoms of depression and recorded symptoms of unexplained swelling. A blood sample was obtained and DNA extracted and used in a genome-wide analysis for linkage.

Key Results

66 members of four families were interviewed by an trained psychiatrist and by a physician experienced in the diagnosis and management of the condition "unexplained swelling symptoms". 28 individuals

reported a lifetime history of two or more episodes of major depressive disorder and of these 22 also described symptoms of swelling. 13 subjects described swelling with no depression. In one family depression and swelling was associated with diabetes and the possibility of common causation is being followed up. A linkage study using 425 genetic markers identified three chromosomal locations with suggestive evidence for linkage. The most promising of these was a region on chromosome 14. These and a further seven loci showing some linkage evidence are being systematically examined for genes that could play some part in depression.

Conclusions

Linkage analysis has identified several chromosomal regions that could harbour genes contributing to the disorder and linkage at these loci is being examined in detail.

What does this study add to the field?

This is the first detailed clinical assessment of families multiply affected with depression accompanied by unexplained swelling symptoms, an important sub group of heritable depressive illness. The discovery of possible linkage regions in these families is a step towards identifying causative genetic factors in depression.

Implications for Practice or Policy

Gene discovery is likely to be the first step towards identifying the biological basis of depression and hopefully will eventually point the way towards rational treatment strategies, drug target discovery and perhaps even preventative measures.

Where to next?

Future strategies for further genetic studies will depend on the outcome of the detailed linkage studies now being performed and could include the direct analysis of candidate genes identified at the chromosomal regions identified through linkage.

Further details from:

Professor Douglas Blackwood, The Royal Edinburgh Hospital, Edinburgh, EH10 5HF (d.blackwood@ed.ac.uk)

