Access to this population of patients, in which an unusually large number of non-schizophrenic patients have been treated with long-term neuroleptic drugs, has given us an unusual opportunity to investigate the determinants of lack of awareness of TD. We have been able to demonstrate that the diagnosis of schizophrenia, particularly the 'defect' state, with cognitive deficit and negative symptoms, is associated with lack of awareness of TD.

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Cosegregation of Christmas Disease and Major Affective Disorder in a Pedigree

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Three males with factor-IX deficiency (Christmas disease) in one pedigree all had severe affective disorder. This apparent cosegregation, if true, would support the hypothesis that in some pedigrees, a gene for major affective disorder is located on the X chromosome.
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Major affective disorder/manic depression is known to have a strong genetic component (McGuffin, 1988). Many studies have suggested an X-linked mode of inheritance in a proportion of families (Risch *et al*, 1986). Linkage studies have given attention to the q27–q28 region of the X chromosome, which includes the genes for protan and deutan colour blindness, glucose-6-phosphate dehydrogenase, and factor IX. Some studies have found evidence for linkage between X-chromosome markers from this region and manic depression (Mendlewicz & Fleiss, 1974; Baron, 1977; Mendelwicz *et al*, 1979; Baron *et al*, 1987; Mendlewicz *et al*, 1987). Others (Gershon *et al*, 1979; Berrettini *et al*, 1990) have failed to replicate the finding of X linkage. There is strong evidence of linkage to colour blindness in one set of pedigrees (Baron *et al*, 1987) and less robust evidence of linkage to the factor-IX locus in another (Mendlewicz *et al*, 1987). Although physically close, there is considerable genetic distance between these two markers which flank the fragile-X site. Linkage to both markers in the same pedigree is, therefore, unlikely unless there are two separate genes for major affective disorder.

We report a family in which three males with factor-IX deficiency (Christmas disease) all had severe affective disorders. The association, if true, would support the proposal that, in some families, a gene for affective disorder is located at the

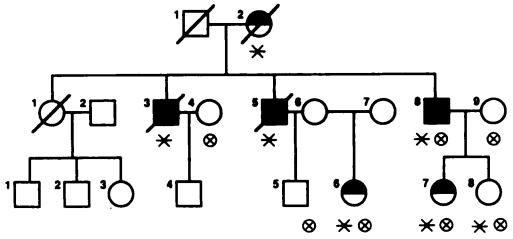

Fig. 1 The pedigree: □ males, ○ females; ■ severe affective disorder, ◒ mild affective disorder; * Christmas disease (males affected, female carriers); ⊗ individuals interviewed by authors.

subterminal region of the long arm of the X chromosome.

Case reports

The proband, II-8 in Fig. 1, has had a lifelong history of severe recurrent major depressive illness, requiring repeated admissions, and treatment with both antidepressant medication and electroconvulsive therapy (ECT). He has had at least two manic episodes, and meets Research Diagnostic Criteria for bipolar I disorder (Spitzer *et al*, 1978). He also has Christmas disease, confirmed on laboratory assay of factor IX.

The proband's brothers, II-3 and II-5, both affected with Christmas disease, had numerous admissions for severe depression, often with psychotic features. II-3 attempted suicide on at least three occasions before hanging himself at the age of 73. His sister, II-1, had no psychiatric history, and there is no known history of psychiatric illness in her children. The proband's mother, I-2, an obligate carrier for Christmas disease, had suffered from bleeding problems during tooth extractions and childbirth, and had lost the sight of both eyes in her 20s, following ocular trauma. She has been described as reclusive and difficult, although she never had psychiatric contact. She was an only child, and nothing is known about her parents. There is no history of psychiatric problems in her husband's family.

The proband had two daughters: III-7 has had a single major depressive episode in the setting of a divorce for which she received out-patient treatment; III-8 has no psychiatric history.

The proband's brother II-5 married twice. His son by his first marriage (III-5) had no psychiatric disorder, but his daughter by his second marriage (III-6) has had at least two depressive episodes for which she received treatment from her general practitioner.

Chromosome analysis of II-8, including high-resolution banding, revealed no obvious structural anomaly of his X chromosome. DNA samples extracted from white blood cells from II-8, II-9, III-6, III-7 and III-8 were digested with the restriction enzyme Taq I and probed with a factor-IX genomic probe (Giannelli *et al*, 1984). Normal polymorphic fragment sizes of 1.3 and 1.8 kb were observed along with a constant band of 5.3 kb, excluding the possibility of a deletion affecting the entire factor-IX gene.

Discussion

The apparent cosegregation reported here may have arisen by chance. Alternatively, it may be due to linkage between Christmas disease and a locus for major affective disorder. The small size of the pedigree results in a positive but not 'significant' lod score between the Christmas disease and a putative affective disorder locus (lod score of 0.903 at $\Theta = 0$, gene frequencies set at 0.002 for Christmas disease and 0.01 for affective disorder, penetrance of heterozygotes for affective disorder set at 0.80).

Assuming true linkage, the gene is likely to be codominant, producing the complete affective disorder phenotype in the males, with more minor disturbance (individuals I-2, III-6 and III-7), or none at all, in the females. In the case of III-7, this occurred in the context of stress (her divorce). Alternatively, because we know that I-2 had bleeding problems, it is possible that non-random X inactivation could have caused preferential expression of the genes for both Christmas disease and affective disorder.

A further explanation for the apparent cosegregation is genetic association within this pedigree, due to a single mutation, such as a large deletion causing both disorders. The results of the chromosome analysis on II-8 and of the DNA studies make this less likely. Our studies, however, do not rule out the possibility of a deletion affecting some of the F9 locus or its associated regulatory regions. In order to investigate this possibility further we intend to use other DNA markers close to the F9 locus. We have also isolated high-molecular-weight DNA from all available members of the pedigree to carry out an analysis using pulsed-field gel electrophoresis.

Because of its structure, the reported pedigree does not support factor-IX linkage over and above X linkage in general. The literature, however, supports factor-IX linkage less than other nearby markers, such as colour blindness. It may be possible to detect a recombination between markers near the factor-VIII locus (telomeric to factor XI and nearer the locus for colour blindness) and the putative locus for affective disorder in this pedigree and thus lend some support to the claim of Mendelwicz *et al* (1987).

In conclusion, despite the lack of statistical power in this pedigree, we feel that it lends support to the X-linked hypothesis for the transmission of affective disorder in a proportion of families.

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Anorexia Nervosa in a Patient with XY Gonadal Dysgenesis

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This is the first report of a case of anorexia nervosa in a woman with XY gonadal dysgenesis. Anorexia nervosa is a potential complication of gonadal dysgenesis, stemming not only from the disorder itself but from its investigation and treatment.

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We report the first case of XY gonadal dysgenesis and anorexia nervosa. There have been 27 case reports of coincident anorexia nervosa and gonadal dysgenesis; the majority of these cases have had XO chromosomes, although mosaic XO/XX chromosomes have been reported.

Case report

At 17 years, the patient was investigated for primary amenorrhoea. She was below normal weight for her height, felt self-conscious about her 'boyish' figure, and had received, anonymously, a letter calling her a 'freak'. Although the amenorrhoea was initially suspected to be weight-related, on investigation a diagnosis of gonadal dysgenesis with XY chromosomes was made.

The patient was given oestrogen therapy which resulted in significant breast development and weight gain to a maximum of 66 kg at 20 years. She was teased and became preoccupied with her weight and concerned about her prominent 'masculine' jaw, high hips, and big feet. The patient was never told directly that she had a Y chromosome but discovered this on reading her own notes at 18 years while in hospital for the removal of her streak ovaries.

These events coincided with the break-up of her parents' marriage, work stress and, later, sexual harassment by a male flatmate. What began as minor dieting had, by 21 years, become anorexia nervosa. She was 41 kg and, although her weight fluctuated, rising to 47 kg at the time of her only, but short-lived, sexual relationship at 23 years, she lost weight and at the time of presentation she again weighed 41 kg (height 1.74 m; body mass index (BMI) 13.6). She fulfilled the DSM-III-R criteria for anorexia nervosa (American Psychiatric Association, 1987) and had a phobia of normal body weight. She severely restricted her diet, avoiding carbohydrates, and exercised vigorously to maintain her low weight.

During a period of in-patient treatment she was able to discuss in psychotherapy her fears of sexuality. She dreaded appearing masculine and was unsure of her feminine identity. The patient felt that she should have been allowed to discuss these feelings earlier, at the time of the initial diagnosis.

Discussion

To the authors' knowledge this is the first reported case of concurrent XY gonadal dysgenesis and