Medical genetics: advances in brief

Association of tuberous sclerosis of temporal lobes with autism and atypical autism

Bolton PF, Griffiths PD. *Lancet* 1996;349:392-5.

Commentary. Developmental abnormalities in autism

Lainhart JE. *Lancet* 1996;349:373-4.

Children with tuberous sclerosis are known to have a greater chance of developing autism or atypical autism than children with a similar degree of intellectual impairment from other causes. Bolton and Griffiths set out to test the hypothesis that the site of cortical tubers in this condition is related to the development of autism. Nineteen patients with tuberous sclerosis were examined for their level of intellectual function as well as evidence of psychopathology before the brain scan results were known. Scanning was either by magnetic resonance imaging or computed tomography. Scans were unavailable on one of the patients. The radiology was assessed by an expert without knowledge of the clinical findings in the subjects. Nine of the group met the criteria for autism or atypical autism and eight of these had epilepsy. There was a higher chance of mental handicap in the children who were diagnosed with autism. Tubers were seen in all but two of the subjects, most commonly in the frontal lobes, then parietal, occipital, and temporal lobes. Magnetic resonance imaging detected more tubers than computed tomography. Tuber number was higher in those with more intellectual impairment and was associated with a diagnosis of autism. There was a strong association between the probability of developing autism and the possession of tubers located in the temporal lobes. Eight of the nine patients with autism had tubers in this site; none of those without autism had temporal lobe tubers. This association was independent of intelligence. The authors discuss the role of the temporal lobe in the aetiology of autism, discussing whether early interference with the normal processing of information about facial expression could lead on to the development of autism. The importance of these findings in the understanding of autism in patients without tuberous sclerosis is also explored and neuroanatomical changes documented in other studies

are discussed. Practically, these findings may help in predicting prognosis in infants with tuberous sclerosis based on findings from radiological investigations.

ANGELA BARNICOAT

Familial intracranial aneurysms

Ronkainen A, Hernesniemi J, Puranen M, *et al.* *Lancet* 1996;349:380-4.

The familial aggregation of intracranial aneurysms is well known but has been difficult to investigate because of the invasive nature of screening tests. These authors set out to estimate the prevalence of intracranial aneurysms in symptom free first degree relatives of affected patients, and to find out if familial aggregation of cases could be accounted for by pedigrees with adult polycystic renal disease. Records of 1445 patients with cerebrovascular malformations were used to identify 1150 with intracranial aneurysms. Telephone enquiry and further records were studied to identify relatives who were also affected and symptomatic. Magnetic resonance angiography was offered to 698 asymptomatic first degree relatives over 30 years of age, with digital subtraction angiography considered where abnormalities were detected. Ultrasonography was used to screen for renal disease. A total of 438 relatives were screened of whom 36 were shown to have intracranial aneurysms. The incidence in first degree relatives of patients is 8.7%. No new pedigrees with polycystic renal disease were identified by the screening. The authors point out that it is not possible to know how many screened people were given false negative results in this investigation. One relative with a normal screening result has subsequently had a subarachnoid haemorrhage. Despite this problem the study has suggested a two to fourfold increase in risk to first degree relatives. A further concern is the high cost of magnetic resonance angiography and its lack of universal availability. Detection of asymptomatic aneurysms would allow surgery to be carried out much more safely than in the acute presentation of a ruptured aneurysm. Seven percent of families with familial intracranial aneurysms were affected with polycystic renal disease. The authors suggest that there is a distinct condition of familial intracranial aneurysms and highlight the

need for further studies to document the best genetic model for this condition.

ANGELA BARNICOAT

Incidence of insulin-dependent diabetes mellitus among Sardinia-heritage children born in Lazio region, Italy

Muntoni Sa, Fonte MT, Stoduto S, *et al.* *Lancet* 1997;349:160-2.

The interaction between genetic and environmental factors in the aetiology of diabetes continues to puzzle. Muntoni and colleagues have studied the incidence of insulin dependent diabetes in children born in the Lazio region of Italy (which has a low incidence of diabetes of 6.5 per million) who are of Sardinian ancestry (which has a high incidence of 30.2). The Sardinian emigration took place from 1950 to 1980, and those living in Lazio are said to be representative of the general Italian population. Children born of one or two parents of Sardinian ancestry born in Lazio were identified from census data. Two independent methods were used to identify diabetic children and the same 17 children were identified with both methods; three had two Sardinian parents and seven each had a Sardinian mother or father. There did not seem to be high exposure to Sardinian environmental factors, as none returned to the island frequently or used special foods from Sardinia. The children of two Sardinian parents have an incidence of diabetes similar to Sardinians living on Sardinia (but because of small numbers the figure has wide confidence limits). The children who had one Sardinian parent have an incidence of diabetes half that of Sardinians but double that of those living in Lazio. Drawing conclusions from the data is still puzzling. The results suggest a strong genetic influence in the aetiology of insulin dependent diabetes. Sardinians are apparently a homogeneous population who might carry certain genes at high frequency. However, the retention of the high risk after migration appears to be at odds with some earlier studies in other locations. Furthermore incidence of diabetes on Sardinia has increased steeply over the past 25 years or so and it seems unlikely that this change is genetically mediated. The possibility of environmental factors which are unidentified but which have been taken with migrants is not yet excluded. The authors emphasise the contribution of both genetic and environmental factors to diabetes.

ANGELA BARNICOAT