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Proceedings of the summer meeting of the British Neuropsychiatric Association, Cambridge, 18-20 July 1993

The topics of the meeting were **obsessive compulsive disorders and developmental neuropsychiatry** and, for the first time in the short history of the Association, a whole session was devoted to presentation of scientific papers from the members.

Dr P White (London) dealt with **objective attention deficit in the postviral fatigue syndrome**. A follow-up study was presented of 250 general practice attenders, most of whom had Epstein-Barr virus infections. When seen six months later, about half had a discrete fatigue syndrome with subjective cognitive impairment. In some of these patients fatigue was unrelated to the presence of anxiety or depression. Fatigued patients performed significantly worse than the rest on a paced, auditory, serial addition task, suggesting the presence of attentional deficits. Lesser degrees of impairment were also observed in those with significant psychiatric symptoms. The differences between groups disappeared, however, when differences in IQ were taken into account.

The genetics of the narcoleptic syndrome were discussed by Dr M Dahlitz (London), including the association of the HLA DR2 DQ1 with the narcoleptic syndrome. This association is restricted to the DR2 subtype DR15, and DQ1 subtype DQ6. Cloning and sequencing studies on the HLA DR-DQ region have failed to demonstrate any specific mutations in subjects with narcolepsy. On the other hand, there is no HLA association in the narcoleptic syndrome with daytime sleepiness and sleep paralysis without cataplexy. This syndrome should be considered as a separate disorder. Recent evidence suggests that different genetic associations may be present in different ethnic groups with this syndrome.

In a twin study of 15 monozygotic pairs reported by Dr Dahlitz, only one pair was concordant for narcolepsy and both twins were found to be HLA DR2 DQ1 negative.

Dr A McKay (Cambridge) addressed **neuropsychological impairment in manic-depressive psychosis**. The findings were presented of memory testing in 45 patients meeting DSM-III-R criteria for major depression or bipolar disorder, who were in remission and had no unrelated brain pathology. Intact memory was reported in those who had recovered from an acute episode of depression regardless of age. But significant impairment was present in four out of 10 patients with a severe, chronic illness who had spent long periods in hospital. In addition to memory impairment, these four patients also had executive (frontal) deficits, and in two there was evidence of more widespread cognitive impairment. These findings suggest that enduring neuropsychological deficits may occur in a subgroup of patients with chronic affective illness.

Psychiatric sequelae of surgical treatments for epilepsy were dealt with by Dr H Ring (London), who presented the preliminary findings from a prospective follow-up study of patients undergoing temporal lobectomy for epilepsy at the National Hospital. Of the 36 patients seen six weeks after surgery, six had symptoms of depression, eight of anxiety, five were dysthymic and one had a schizophrenic psychosis. Two-thirds were free from seizures and, in the rest, fit frequency had been significantly reduced. Postoperative psychiatric complications were more common in those who had previous psychiatric problems, but psychiatric morbidity was unrelated to the postoperative control of epilepsy. This study highlights the importance of close pre- and postoperative monitoring.

Dr J Moriarty (London) described **functional imaging in Gilles de la Tourette syndrome, using HMPAO-SPECT** in 50 patients and 20 normal controls. Perfusion, using the visual cortex as a control region, was calculated in 14 regions of interest throughout the brain. Hypoperfusion was observed in the left caudate, anterior cingulate, and dorsolateral prefrontal cortex in the patients compared with the controls. Patients on medication had higher perfusion rates in the affected areas. Correlations between perfusion and clinical symptoms were not significant except for a link between hypoperfusion in the dorsolateral prefrontal cortex and high depression ratings.

Evidence for autosomal dominant gene transmission in Gilles de la Tourette syndrome was presented by Dr V Eapen (London), who presented the results of the segregation analysis of the families of 40 patients with the syndrome. Her findings are in keeping with the presence of an autosomal dominant gene with high penetrance. Depending on the classification systems used, the penetrance ranged from 0·882 to 1·00 for males and from 0·452 to 0·582 for females. Her data suggest that obsessive compulsive behaviour is an integral part of the syndrome and that isolated tics in other family members are best considered as phenotype copies.

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Unexpected focal brain lesions in schizophrenics and their relationship to abnormal involuntary movements were described by Dr S Cooper (Belfast). Unsuspected brain lesions were found in the CT scan of 12 of 79 schizophrenics with abnormal involuntary movements (15%). This rate was similar to that (12%) found in patients with carcinoma who were scanned to exclude brain secondaries. Schizophrenics with tardive dyskinesia had more marked sulcal widening, especially frontal, than schizophrenics without involuntary movements.

A review of cerebral biopsies for the diagnosis of dementia was presented by Dr D Bonner (London) who discussed the diagnostic yield of a series of 25 brain biopsies performed at the National Hospital for Neurology and Neurosurgery over the past 12 years in patients with dementia. A definite diagnosis was possible in 14 cases (Alzheimer's disease in six, progressive multifocal leucoencephalopathy in two, sarcoidosis in two, and one case each of toxoplasmosis, Creutzfeldt-Jakob's disease, cortical Lewy body disease and infarct). Non-diagnostic abnormalities were present in four and the rest were normal. Postoperative morbidity was low, one patient developed seizures and pre-existing dysphasia deteriorated in another. Patients with focal changes on imaging and abnormal CSF were more likely to have diagnostic biopsies and this should be kept in mind when selecting patients. Treatable causes of dementia were present in three patients.

Dr E Bullmore (London) described **fractal ways of looking at the brain**. Fractal dimension (FD) is a non-integer value that corresponds with the perceived structural complexity of an object. FD can be measured in EEG using fast, computerised methods allowing large quantities of data to be presented in a compact form. The FD of the EEG signal is between 1·3 and 1·85. Slow waves have a lower FD. Dr Bullmore presented the fractal analysis of 50 intracerebrally recorded seizures in nine patients. Ictal onset was accompanied by a rapid increase in FD, and fractal analysis could be used to quantify the intensity and duration, and the extent of generalisation of the seizure. It was also possible to diagnose the anatomical location of the focus, sometimes more accurately than by traditional inspection of EEG.

In the session on **obsessive compulsive disorders**, Dr P McGuire (London) reported a PET study in four untreated patients using an activation paradigm that exposed them to "contaminants" capable of provoking increasing degrees of anxiety and compulsive behaviour. The activation patterns of the two responses were similar, but anxiety was more highly correlated, with increased blood flow in the hippocampus, insula, and cingulate gyrus, whereas the closer associations for compulsive behaviour were with increased blood flow in the orbitofrontal cortex, globus pallidus, and thalamus. Decreased blood flow in the right frontal eye fields and inferior parietal lobule, a region controlling the direction of attention, was common to both anxiety and compulsive behaviour paradigms.

Dr M Robertson (London) discussed **obsessional disorder in Gilles de la Tourette syndrome (GTS)**. In her series of 90 patients from the National Hospital for Neurology and Neurosurgery, obsessive compulsive behaviour was present in a third and was often accompanied by coprolalia, echolalia and compulsion to touch. The frequency and severity of obsessional symptoms were greater in depressed patients. Obsessional symptoms in Gilles de la Tourette syndrome were similar to those of primary obsessive compulsive behaviour but, in the latter, fear of contamination and compulsive cleaning were more common and usually preceded by an external stimulus, whereas in Tourette syndrome, preoccupation with symmetry, touching and counting, and thoughts of violence and self harm without external precipitants were more frequent.

Dr J Bird (Bristol) reviewed the results of **psychosurgery for obsessive compulsive disorder**. He discussed the outcome of multifocal leucocoagulation in a series of 138 patients with intractable disease or anxiety disorders followed up for intervals ranging from two to 20 years. The operation was performed using electrodes implanted in the orbital and paracingular regions. Adverse effects were significant in 4% (seizures and personality deterioration). Results were comparable for patients with obsessive compulsive disorder and anxiety and, in both groups, about half of the patients were symptom free at follow up and another 30% significantly improved. There was also a trend for improvement in IQ scores at follow up. Relapses had occurred in 20% of patients. Dr Bird pointed out that the number of these operations had decreased from 70 in 1981 to the current rate of 25 per year because of better pharmacological and behavioural treatments, but the outcome of this series is nevertheless impressive.

The session on **developmental neuropsychiatry** contained two presentations dealing with autism. Dr A LeCouter (London) discussed the **genetics of autism** with reference to the Institute of Psychiatry twin and family studies. Looking for the expression of a broad phenotype, 60% of monozygotic twins were concordant for autism, whereas there was no concordance for dizygotic twins. In the family study, which looked at the relatives of 99 autistic probands and 36 controls with Down's syndrome, there was an increased loading for autism, pervasive social disorder, and cognitive abnormalities in the families of autistic probands, but not in the control group. Evidence from these two studies suggest that autism may be the most heritable of psychiatric conditions and that a multiple gene model, with each gene having a small effect, fits the available data best.

Dr S Baron-Cohen (London) talked about

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the "**theory of mind**" as the central deficit in autism. This is the ability to attribute mental states to self and others, and to make sense of people's behaviour in terms of mental states (beliefs, desires, intentions). Studies tapping into the theory of mind have analysed the use of language, and pretend play and deception, and considerable knowledge has accrued as to how and when awareness of mental states develops. Preliminary imaging studies in normals suggest that orbitofrontal regions are involved in these tasks. Studies in autistics suggest that deficits in gaze monitoring, attention and executive functions may be present and central to the abnormal development of the theory of mind.

Dr G Jackson (London) reported **new developments in the study of childhood epilepsy** and in particular the contribution of MRI and magnetic resonance proton spectroscopy (MRS). Hippocampal abnormalities are clearly detectable with MRI and T2-weighted maps can show a focal decrease in signal corresponding to loss of neurons in the affected side. The quantity of N-acetyl-aspartate, a neuronal marker, can be ascertained by MRS, usually as a ratio to choline plus creatine. This ratio is low in the affected medial temporal structures of children with temporal lobe epilepsy compared with controls in the Great Ormond Street series. The combination of structural MRI and MRS has improved localization of epileptic foci and progress is likely to continue with the use of functional MRI imaging.

The more subtle problems of **clumsy children** and the need to assess their disability in the community were addressed by Professor E Ross (London). These children (perhaps as many as 5% of the population) fail to acquire skills requiring fluent coordination of movement and their deficits cannot be explained as a result of mental retardation or neurological disease. Dyslexia and attention deficits may be present in severe cases. The aetiology and outcome of the syndrome are poorly understood. Professor Ross made a plea for using simple screening methods in the community to detect those in need of specialised educational help.

Professor I Goodyear (Cambridge) talked about **hormonal aspects of depression in childhood**. The incidence of depression in childhood increases significantly from the age of eight when symptoms start to resemble those in adults. In children depression often appears in conjunction with other diagnoses. In those with prominent anxiety symptoms, Professor Goodyear's data suggest that elevated basal cortisol levels may be an important marker. In the case of those with major depression and obsessive compulsive disorder, low morning levels of 19 C-steroids were found in about a third. These two abnormalities appear to be unrelated. It remains to be determined whether the abnormal cortisol regulation represents a vulnerability factor for depression, for further relapses or whether it impedes recovery.

Professor P Graham (London) presented the evidence for **food intolerance in hyperactivity** that has emerged from double-blind trials carried out at the Institute of Child Health. Hyperactive children were put on a highly restrictive diet for two to three weeks to see if this resulted in behavioural improvement. If this were the case, individual foods were introduced at the rate of one per week until the child was on a normal diet. If behaviour deterioration resulted after the introduction of a particular food, it was withdrawn and a double-blind exposure to the "active" food performed. Striking differences were found in this way between "active" foods and placebos. Professor Graham emphasised that dietary treatment is expensive in professional time, that it is only helpful in a few children and that it should be seen as an improvement rather than a cure. Enzymatic, toxic, and metabolic mechanisms have been postulated to explain these effects, but no conclusive evidence is yet available.

Dr A Holland (Cambridge) discussed the **Prader Willi syndrome (PWS) as an example of genetic obesity**. The disease is characterised by hypotonia at birth, a typical facial appearance, immature gonadal development, short stature, and severe obesity. Half of those with the syndrome have a deletion of the proximal part of the long arm of chromosome 15 (q11–13). A similar chromosome abnormality is present in Angelman's syndrome which is clinically different from Prader Willi syndrome. Genomic imprinting has been implicated in both. If the deletion occurs on the paternal chromosome, Prader Willi syndrome results, whereas Angelman's syndrome occurs with deletion on the maternal chromosome.

Patients with Prader Willi syndrome exhibit overeating from the age of two. Dr Holland's study performed at the Institute of Psychiatry, suggests that these patients have a deficit in the satiety cascade needing blood sugars in the diabetic range before satiety occurs. This represents a failure of insulin release. Early rebound hunger was also a feature, but the postabsorption mechanisms, mediated by cholecystokinin, appear to be normal.

Dr A Thompson (London) presented the results of a **neurological follow-up study of patients with phenylketonuria**. Neurological deficits—for example, quadriparesis, dystonia, ataxia, and tremor—neuropsychological impairment, and subtle behavioural disturbances have been described in adult patients and these deficits appear to be related to the frequency of exposure to high levels of phenylalanine. Dr Thompson's study included 34 patients (25 diagnosed at birth and nine late in life) with a wide spectrum of dietary control. Neurological abnormalities were present in all of those with a late diagnosis and in 10 of the 25 diagnosed at birth. MRI revealed white matter periventricular abnormalities in all patients. The severity of abnormalities diagnosed by MRI was closely linked to the duration of exposure

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to high levels of phenylalanine and to the blood levels at the time of the study. On the other hand, the MRI changes were not closely related to the severity of neurological disability or deterioration in IQ. These results suggest that tight dietary control is necessary for as long as possible, although it is uncertain whether neurological damage can be prevented in all cases.

The video case presentations included the following: Dr E Feldman (Nottingham): **atypical depression with a frontal tumour**; Dr B Scheepers (Bristol): **manual bowel evacuation during sleep—a sleep arousal phenomenon?**; Dr K O'Driscoll (Prestwich): **a family with basilar migraine**; Dr S Chua (Cambridge): **tardive dystonia responding to clozepine and clonazepam**; Ms J McGrath (Oxford): **two cases of psychological reaction to neurological disorder**; Dr D Kingham (Bristol): **a neuropsychiatric obsessional** and Dr A House (Leeds): **movement disorder and thinking**.

The retirement of Professor Alwyn Lishman as Chairman of the Association was announced at the Annual General Meeting. At the request of the membership he was elected Honorary President of the Association. Dr Maria Ron, Reader in Neuropsychiatry at the Institute of Neurology (London) was elected Chairman. Dr E Reynolds came to the end of his term in the committee and Professor D Neary, Professor of Neurology (Manchester) and Dr B Toone, Consultant Psychiatrist at the Maudsley and Kings College Hospitals (London) were elected to the two vacancies in the committee. It was also agreed to create an annual prize (£500) for original research or an essay in a topic relevant to neuropsychiatry. Details will be announced later.

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