

## Proceedings of the joint summer meeting of the British Neuropsychiatric Association and the British Association for Psychopharmacology, Cambridge, 15-17 July 1995

The topics of the meeting were *the neuropsychiatry of movement disorders and neuroimaging, psychiatry, and psychopharmacology*. The second day was held jointly with the British Association for Psychopharmacology.

The first day the BNPA met at Robinson College and the session on *the neuropsychiatry of movement disorders* was opened by Professor D Brooks (London) with a lecture on **cerebral dysfunction in movement disorders: PET studies**. Based on his own research at the Hammersmith Hospital he reviewed the functional brain anatomy of the various components of movement as identified in PET studies. With appropriate PET paradigms it has been possible to identify "decision making areas" which show increases in regional cerebral blood flow. The dorsolateral prefrontal regions, anterior supplementary motor area (SMA), and parietal areas 40 and 7 are part of this circuit. Within this circuit, "preparedness" did not require the activation of prefrontal areas, but increased regional cerebral blood flow was found in the SMA, cingulate, basal ganglia, and motor cortex. Using similar paradigms "imagined movements" were shown to increase regional cerebral blood flow in the "decision making circuits" and basal ganglia, but not in the cerebellum.

By comparison with normal patterns of movement, PET studies have highlighted abnormalities present in various movement disorders. In Parkinson's disease abnormalities could be detected in SMA and dorsolateral prefrontal areas using imaginary and finger sequences of movement, which were reversed by apomorphine. Activation of the SMA, dorsal prefrontal, and primary motor areas is seen following pallidectomy, confirming that in Parkinson's disease the pallidal output has an inhibitory effect on the cortex.

In genetically determined dystonia, there is overactivity in the SMA, dorsal prefrontal areas, and striatum together with a reduction of regional cerebral blood flow in the motor cortex and parietal areas. In writer's cramp the overactivity disappears with injection of botulinum toxin, but the underactivity of the motor area remains. This pattern seems to be pathognomonic of genetically determined dystonia and differs from that found in dystonia after lesions of the globus pallidus, when there is no underactivity of the motor cortex. In Huntington's disease the pattern of activation is similar to that of genetically determined dystonia, but no overactivity occurs in the striatum.

Professor A Harding (London) considered **ethical problems in neurogenetics: the model of Huntington's disease**. The application of molecular genetics to clinical practice has led to improvements in diagnosis and genetic counselling, but it has also encountered some unexpected ethical difficulties. There are three types of genetic tests: diagnostic, predictive, and prenatal. For diagnostic testing the possibility of a genetic disease should be discussed in advance and informed consent obtained. In the case of positive results, it is essential to take into account the needs of relatives for information and genetic advice, as there are implications for the whole family. Most experience for predictive tests comes from Huntington's disease, but can be applied to other autosomal dominant late onset disorders. International guidelines, which take into account the views of lay Huntington's disease organisations, have been published in an attempt to deal with relevant ethical issues. The implications of a positive result need to be discussed during pretest counselling in relation to post-test emotional reactions, life insurance, employment, lifestyle, and effects on partners and family members. The decision to take a predictive test should be the sole choice of the person concerned and it is generally thought that testing should not be performed on subjects under age.

Other ethical problems which have arisen in presymptomatic testing for Huntington's disease and other diseases include refusal by key relatives to give blood samples, testing monozygotic twins, and requests for tests from subjects with a 25% risk (who have an affected grandparent), which could provide unwanted information for their parent at risk. It is generally held that the applicant's right to be tested should take priority, but this issue needs full consideration.

Prenatal tests can assess whether or not the fetus carries the relevant mutation, but not the severity of the disease. This can make the decision to terminate pregnancy difficult. DNA is ideally analysed from chorionic villus samples obtained at 8-10 weeks gestation and results are thus available in time for a first trimester abortion. Testing is potentially harmful to the pregnancy and is therefore inappropriate unless the couple are committed to terminating high risk pregnancies. The continuation of a high risk pregnancy also raises the possibility of the child having an unsolicited presymptomatic test.

Dr T Robbins (Cambridge) discussed **frontal cognitive impairment in Parkinson's disease**. Cognitive impairment in Parkinson's disease affects executive function and although deficits conform to the "frontal lobe" pattern, significant differences can be found compared with patients with frontal lobe lesions. Neurochemical abnormalities affecting corticofrontal-striatal loops and involving 5-HT, cholinergic, and dopaminergic systems are responsible for these deficits. Dr Robbins' strategy involves using tasks validated in patients with frontal lobe lesions and contrasting the performance of patients with Parkinson's disease on these tasks with their performance on non-frontal tasks such as pattern recognition. Using a set shifting task patients with early Parkinson's disease show significant impairment which improves with dopaminergic drugs. There are differences in the way that patients with Parkinson's disease and those with frontal lobe lesions performed these tasks. Thus whereas perseveration is common in those with frontal lobe lesions, patients with Parkinson's disease exhibit "learnt irrelevance" (a reluctance to go back to previously irrelevant stimuli). Patients with Parkinson's disease also perform poorly on planning tasks, exhibiting inaccuracy and slowness. This impairment is related to dopaminergic deficits and responds to medication initially. Impairment of spatial, verbal, and visual working memory can also be seen in Parkinson's disease, but by contrast with patients with frontal lobe lesions, patients with Parkinson's disease are able to use strategy. They are also impaired on tasks in which temporal lobe input is required, and a different chemical substrate (cholinergic) may account for these deficits.

Dr Cunningham Owens (Edinburgh) discussed **movement disorders in schizophrenia**. He emphasised that although recognition of abnormal movements in schizophrenic patients can be difficult, they had been described, including tardive dyskinesia, by Kraepelin and Bleuler long before the neuroleptic era. He referred to his previous survey of long stay patients at Shenley Hospital where a subgroup of patients had never been exposed to neuroleptics. Abnormal movements were found to be related to poverty of speech, flat affect, and cognitive impairment. Although abnormal movements were more severe in medicated patients, they were qualitatively similar in those who had never received drugs. Patients in this subgroup were older and had been ill for longer. Although similar movement disorders have been seen in normal elderly subjects, their presence was twice as common in schizophrenic patients who had never had medication, in whom they were detected in 45% of cases.

The following short papers were presented:

**Poor motivation after brain injury: evidence implicating dopamine dysfunction and impaired sensitivity to reward** Dr J Powell (London): **Joint winner of the 1994 BNPA prize.**

Poor motivation, passivity, and slowness to initiate activity are common after severe head injury. Damage to central dopaminergic circuitry, which underlies the ability to respond to reward, may be the cause of these deficits. In her own study Dr Powell observed the presence of these deficits and their apparent lack of correlation with affective disturbance. She also presented evidence from single case studies to support the finding that bromocriptine, a dopamine D2 postsynaptic receptor agonist, produces striking improvements in motivation, responsiveness to reward, and cognitive performance.

**Computerised brain MRI segmentation and the partial volume effect** Dr E Bullmore (London): **joint winner of the 1994 BNPA prize.**

Due to finite spatial resolution of MRI and the complexity of brain anatomical interfaces, some pixels represent a mixture of several tissue types. Outright assignment of such "bipartial" or "tripartial" volume pixels to one class or the other is often difficult and unreliable. Dr Bullmore described a system of tissue classification of multiecho MRIs, which uses a polychotomous logistic model for discriminant analysis combined with a Bayes allocation rule incorporating prior probabilities, and spatial connectivity tests to assign pixels to one of four possible classes: grey matter, white matter, CSF, or unclassified. The system compares well with existing ones and has a higher between rater reliability.

**Willed movement in schizophrenia: a PET study** Dr S Spence (London).

Dr Spence discussed the findings of his PET study of schizophrenic patients with delusions of passivity. He used an activation paradigm comparing externally paced and freely selected movement with rest. Statistical parametric mapping showed bilateral parietal and medial prefrontal overactivity, more pronounced in the right hemisphere in schizophrenic patients than in controls. These data suggest that the motor system is dysfunctional in schizophrenic patients with delusions of passivity.

**Subcortical abnormality in Gilles de la Tourette's syndrome: an MRI study** Dr J Moriarty (London).

Dr Moriarty described a volumetric MRI study of adults with Gilles de la Tourette's syndrome compared with healthy volunteers. Subtle changes were present in the patient group including a greater cross sectional corpus callosum area and a lack of normal asymmetry in the volume of the caudate nucleus. This study did not, however, find structural abnormalities in the anterior striatal and anterior medial temporal areas to correlate with the reduced perfusion described in functional imaging studies.

**Association between hippocampal NAA and psychosis: 1H MRS study of schizophrenia and epilepsy** Dr M Maier (London).

Dr Maier presented his work using in vivo proton magnetic resonance spectroscopy to investigate hippocampal abnormalities in

patients with temporal lobe epilepsy with and without associated schizophrenia-like psychosis. These patients were compared with a group of patients with schizophrenia and with healthy volunteers. A group effect was present for left hippocampal N-acetyl-aspartate and choline, with these metabolites being progressively more depleted in schizophrenic, non-psychotic epileptic, and psychotic epileptic patients. The depletion of N-acetyl-aspartate, considered to be a neuronal marker, in the psychosis of epilepsy suggests that the greater the damage in the left hippocampus the greater the chance of psychotic symptoms.

**A cognitive process approach to memory impairment in schizophrenia** Mr D Nathaniel-James (London). Mr Nathaniel-James presented the results of his study of 25 patients with chronic schizophrenia and matched healthy volunteers using a cognitive process approach to memory impairment. The hallmark of the patients' performance was the presence of significant impairment of immediate memory with comparatively spared long delay memory. Deficits of memory were present irrespective of the encoding strategies used and were unrelated to chronicity. Memory disturbances were correlated with poor performance in tests of executive function. He suggested that the memory deficits in schizophrenia resemble those found in patients with subcortical disease or frontal lobe lesions.

**Frontal lobe disturbances in patients with multiple sclerosis** Dr J Foong (London).

The relation between cognitive impairment and MRI lesion load in patients with multiple

sclerosis has been difficult to demonstrate. In her study Dr Foong used automated tests of working memory and strategic planning (from the CANTAB battery) in a group of 40 patients with definite multiple sclerosis and matched controls. Using these specific frontal lobe tests, it was possible to show impairment in spatial working memory and strategic planning in these patients and to show a correlation between the severity of impairment and the MRI frontal lesion load as measured using automated methods.

Dr N Hindley (Oxford) presented a **case of possible cyclical Cushing's disease**.

Abstracts of the presentations of the *joint symposium of the BNPA and the British Association for Psychopharmacology* have already been published in the *Journal of Psychopharmacology* 1995;9 (3)(suppl) abstracts 1-4. **The 1995 BNPA prize** was shared between Mr D Nathaniel-James for his essay **A cognitive process approach to the study of memory impairment in schizophrenia** and Dr P Talbot for his essay **The inter-relationship between classical motor neurone disease and frontal lobe dementia**.

The next meeting of the BNPA will be a joint meeting with the British Neuropsychological Society and will take place on 19 January 1996 at the London Zoo, Regent's Park. The topic will be *disorders of reasoning and perception*.

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