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Editorial Preface

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The introduction of neuroimaging techniques for the study of brain structure and function has revolutionised the endeavour to elucidate the pathology of psychiatric disorder, the Holy Grail in psychiatry (Krishnan, 1990). Emil Kraepelin discovered the two major mental disorders, dementia praecox and manic–depression, and conceived their aetiology in brain pathology. It was Alois Alzheimer, however, his most successful student, who discovered the neuropathology of Alzheimer's disease. Sigmund Freud, who started his inquiries in brain science, lost faith and shifted to the study of the mind. Brain science and mind 'science' rapidly became odd bed fellows and parted company. The breakdown in communication fostered a mistrust in both parties, aborting endeavours of reconciliation. The evidence for the neuropathology of the 'functional' psychoses has, however, been inconclusive. It was the advent of brain-imaging techniques that rejuvenated brain sciences and modern neurosciences. The introduction of neuroimaging techniques, such as the electroencephalogram (EEG) in the 1920s and the whole-brain blood-flow techniques (Berger, 1929; Kety & Schmidt, 1948), antedated the discovery of psychotropic drugs. Pneumoencephalography was also applied to study brain structure in schizophrenia (Storey, 1966). The true methodological leap, however, was the introduction of computerised methods to construct three-dimensional images from two-dimensional data, enabling the development of computerised tomography (CT), magnetic resonance imaging (MRI), positron-emission tomography (PET) and single-photon emission computerised tomography (SPECT).

The contents of this supplement are based on the proceedings of a symposium on this topic, complemented by reviews of other neuroimaging techniques to provide an up-to-date, state-of-the-art publication. Neuroimaging is a rapidly developing area in neurosciences, which we hope to have captured at a critical phase of development with an eye on the future.

Computerised tomography provided the means to visualise the live brain and to detect structural abnormalities; it has widespread applications in neurology, neurosurgery and psychiatry. In this supplement, Dr Burns reviews the CT technique in the differential diagnosis of dementia and examines the relationship between CT findings and the clinical picture of dementia of Alzheimer's type. He concludes that the main use of cranial CT techniques remains the exclusion of intracranial lesions, and while some CT findings correlate with the diagnosis of dementia, it is less useful in its differential diagnosis. Sophisticated techniques for scan analysis have shed light on the possible organic changes in depressive pseudodementia. Dr Burns concludes that the "CT scan is sleeping rather than dead".

The imaginative application of cranial CT to the study of schizophrenia (Johnstone *et al*, 1976) started a new era in the study of the biology of this disorder, resurrecting Kraepelin's concept of dementia praecox with the finding of CT brain abnormalities. Dr Lewis critically reviews the evidence 15 years on and examines the methodological problems in its application. Out of the 50 controlled studies in the world literature, he selects 21 studies that met stringent criteria for methodology for review. He concludes that there is relative enlargement of third and lateral ventricles and cortical sulci in some schizophrenic patients. These abnormalities appear to be long-standing, non-progressive and similar to the changes seen in neurodevelopmental disorders. He raises the important issue of the epidemiology of risk factors that determine these structural abnormalities as determined by the studies on control populations. As for the future, Dr Lewis suggests that although the baton has now passed to MRI, the CT technique will be used in conjunction with functional imaging techniques, such as PET and SPECT, "allowing us not just to see the machine, but its ghost as well".

Dr Besson, in a large review, provides a lucid exposition of the principles and the theory of MRI and its application in the study of neuropsychiatric disorders. This is illuminated by case studies in which the clinical characteristics are examined in relation to neuropathological, neurofunctional and therapeutic outcome in conditions such as Korsakoff's and Wilson's disease. He also introduces the concept of multimodality imaging of integrated anatomical–functional imaging with case studies of SPECT superimposed on MRI in Alzheimer's disease and superimposed PET on MRI in a case study of psychotic depression. The advantages of MRI over CT scan are exemplified in its ability to quantify images and

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identify regions of focal pathology through altered relaxation times. Finally, Dr Besson enriches his contribution by providing a multimodel approach to understand the MRI changes in the case of alcoholic brain disease.

The contribution by Dr Lock and colleagues follows, on psychiatry in the new magnetic resonance era, introducing the integrated magnetic resonance examination capable of acquiring anatomical, pathological and biochemical information in integrated clinical studies. Magnetic resonance spectroscopy (MRS) is depicted as the only technique in clinical medicine that provides non-invasive access to living chemistry. The advantages and disadvantages of this integrated examination are outlined, including the "human-machine" limitations and factors which affect the reproducibility of data. State-of-the-art clinical and animal studies are reviewed where developments relevant to psychiatry may be feasible and preliminary research findings are presented to illustrate relevant points. Dr Lock contends that this integrated MRI examination provides a non-invasive "biopsy", recognising the potential of this technique for "fishing in uncharted waters". The MRS technique, however, is compromised by its low sensitivity compared with other functional imaging techniques such as PET and SPECT.

Continuing with the MRI–MRS theme, Dr Waddington and colleagues provide a review and study of MRI–MRS in schizophrenia. The advantages of MRI over CT are highlighted: high resolution, good tissue contrast, multiplanar facility, and the lack of ionising and hazardous radiation. These advantages allow longitudinal prospective studies of first-episode patients, to examine the evolution of the disorder in relation to the structural and functional abnormalities. The precision of the technology has highlighted problems of methodology such as the subtle relationship between morphological changes and educational attainment and the extent of the normal range of these structural measures. The critical review of the quantitative and qualitative findings in schizophrenic populations is complemented by the results of MRI and MRS studies undertaken by Dr Waddington and colleagues: the MRI study showed a significant rate of morphological abnormalities in schizophrenic patients and phosphorus-31 MRS showed no spectral differences in the temporoparietal regions, except for evidence for increased intracellular pH, probably indicating localised tissue injury in this region.

The second section of this supplement is concerned with functional neuroimaging techniques. Dr Geaney and myself critically review the use and utility of SPECT in the diagnosis of dementia. SPECT, the most recently introduced neuroimaging technique, is a generally available and inexpensive method of measuring cerebral blood flow with evident usefulness in the management of dementia. The development of technitium-99m-labelled pharmaceuticals such as HMPAO to measure cerebral blood flow was a major advance in SPECT technology. SPECT studies using $^{99}Tc^{m}$-HMPAO to investigate dementia are critically reviewed: the technique is a useful aid in the diagnosis of subtypes and the validity and significance of this requires full evaluation of outcome in follow-up studies to post-mortem of patients investigated by SPECT. Geaney *et al* (1990) have shown that patients with Alzheimer's disease had reduced rCBF in the posteroparietotemporal region compared with controls as determined by $^{99}Tc^{m}$-HMPAO and SPECT. Central cholinergic stimulation with physostigmine produced a focal increase in regional cerebral blood flow in the posteroparietotemporal region in patients with Alzheimer's disease, but not in controls.

The study by Dr Upadhyaya and colleagues, however, casts doubt on the utility of SPECT in the management of dementia, with the finding that a discernible proportion of elderly patients with depressive illness show perfusion defects. These results may have important implications for the management and prognosis of depression in old age.

Positron-emission tomography (PET), the most powerful tool available for the measurement of brain function, is dealt with by Dr Bench and colleagues from the MRC Cyclotron Unit in Hammersmith Hospital in a large review describing its basic principles and application to the study of brain metabolism in neuropsychiatric disorders. A major focus of the review is on the development of resting-state metabolism studies by the application of specific activation paradigms and refined methods of data analysis. Studies have consistently shown regional abnormalities in the major psychoses as well as abnormalities specific to panic and obsessive–compulsive disorders traditionally thought to have a psychological aetiology. They conclude that future PET programmes will couple metabolic measures with activation paradigms of specific functional systems and studies using tracers for neuroreceptors will attempt to provide a parallel neurochemical basis for the metabolic profiles. These techniques will lead to major advances in elucidating the pathophysiology of psychiatric disorders as well as the delineation of clinical subgroups.

The application of cognitive brain potentials in psychiatry is reviewed by Drs Blackwood and Muir. The event-related potentials are selected from

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the on-going EEG activity by averaging epochs of EEG following repeated sensory or cognitive stimuli in their temporal relationship to the stimulus depicting sensory and cognitive components of perception. This technique furthers the understanding of the neuropsychology and the neurophysiology of psychiatric disorders and aids in their diagnosis. Studies of P300 responses suggest their utility in distinguishing subtypes of dementia, schizophrenia and depression.

The application of neuroimaging techniques in the study of psychiatric disorders has provided one of the most dramatic developments in biological psychiatry. There is little doubt that integrated, structural–functional techniques will lead to major advances in the understanding of the biology of psychiatric disorders, refining their classification and guiding management.

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