Guest-editorial

Applications of SPECT in cognitive neuroscience, neurology and psychiatry

Single photon emission computed tomography has two common acronyms – SPECT and SPET. This is inconvenient when performing literature searches and should be resolved. A search for 1999 captured 105 SPET references and 1285 SPECT references so popular opinion is with this option which has been used consistently in the articles in this issue. SPET [or "S"PET as it is sometimes called] is a deliberate preference in some cases to emphasise the strong association with PET. It is, of course, appropriate to compare and contrast such similar technologies and the paper by Montaldi and Mayes has highlighted the strengths and weaknesses of PET, SPECT and fMRI for mapping neuroactivation patterns. As fMRI operates at a lower energy band within the electromagnetic spectrum than the emission tomography techniques and does not have the potential to produce ionisation in tissue it is a theoretically safer method and will always be the method of choice for the study of activation if suitable paradigms can work effectively within the high field environment of a magnetic resonance scanner. The risks associated with PET and SPECT are, however, based on conservative extrapolation of known effects at higher exposure levels, are tightly regulated, and are small, being comparable to many every day activities (for a more complete description see Patterson and Wyper [1]). The problem from the scientific perspective is that as long as there is a theoretical risk, PET and SPECT exposure has to be regulated and so the number of repeat conditions is constrained, whereas fMRI measurements can be repeated and are limited more by cost and fatigue. Even with this limitation, however, SPECT and PET can be used very successfully to investigate activation. Of these two techniques, PET, with ^{15}O water CBF measurement, has better signal to noise ratio although the gap is narrowing and current work being undertaken by the NeuroPhysics Corporation offers the prospect of neuro-SPECT with reconstructed transaxial resolution of 4.8 mm at 30 kc/s/uCi/ml or 2.9 mm at 11 kc/s/uCi/ml. The main difference for activation work is that ^{15}O water PET has faster washout and paradigms with up to 12 different or repeat conditions can be used, whereas SPECT, with the trapped $^{99\mathrm{m}}$Tc labelled compounds HMPAO or ECD, is ideal for capturing activations which can be sustained for around 60 seconds and which are difficult to capture with real time imaging in PET or fMRI. Each technique has its place.

Where emission tomography comes into its own is in the direct measurement of synaptic function by use of tracers with high selectivity and affinity for specific synaptic binding sites. With PET, ^{18}F [$T_{1/2} = 110$ mins] is the most commonly used radioisotope whereas with SPECT most studies to date have used the 159 Kev gamma emitter ^{123}I [$T_{1/2} = 13.2$ hrs]. Fluorine chemistry is reckoned to be more straightforward than iodine chemistry and the challenges presented to radio-chemists by SPECT are therefore somewhat greater, but as highlighted in papers in this issue by Acton and Mozley and by Shaw et al., there are a growing number of clinically useful SPECT ligands available. Most of these have to be synthesised in a local radiopharmacy and so studies are restricted to the larger University based centres of excellence, but the recent achievement by Nycomed-Amersham in obtaining a European product licence for the dopamine transporter ligand FP-CIT [DaTSCAN®] indicates a desire by companies to bring the unique power of emission tomography for imaging synaptic function to the marketplace. SPECT rather than PET, being available in all specialist hospitals and with the capacity for delayed imaging several hours after tracer administration to allow for non-selective washout, may well be the imaging modality of choice for this work.

This issue of Behavioural Neurology highlights both the routine and the research roles of SPECT but most emphasis is on pushing forwards the frontiers rather than appraising clinical practice. The paper by Duncan demonstrates the ability of the trapping mechanism of the routine SPECT perfusion tracers to capture the lo-

Behavioural Neurology 12 (2000) 1–2
ISSN 0953-4180 / $8.00

cation of seizure activity. This is a critical investigation prior to surgery for intractable epilepsy. There are two papers on imaging specific neurochemical systems, perhaps not surprisingly focusing on the neurotransmitter pathway which has received most attention from PET and SPECT investigators, the dopamine system. Acton and Mozley describe studies in patients with Parkinsonian symptoms showing the role of SPECT in both the diagnosis of movement disorders and in the objective monitoring of neuroprotective therapies. They introduce one of the few ^{99m}Tc labelled compounds being developed for neurotransmitter studies [^{99m}Tc-TRODAT-1]. Technetium labelling offers the potential for more cost effective imaging, a critical factor if these techniques are to survive health economic appraisal. Shaw et al. show how the development of new SPECT tracers has led to an improved understanding of the action of anti-psychotic drugs in schizophrenia. New tracers may well hold the key to the changing role of SPECT, both in research and in clinical practice, but the technical complexity and development costs involved in developing these should not be underestimated.

Several papers in this issue demonstrate how the power of basic perfusion SPECT can be enhanced by robust image analysis. The development by Friston et al. [2] of statistical parametric mapping (SPM) and its subsequent modification for use with SPECT has been pivotal in the development of SPECT as a technique to study the association between regional perfusion and clinical function. Both Ashton et al. and Ebmeier re-analysed old data using SPM and uncovered latent information, the former finding that perfusion in the cingulate is associated with negative symptoms in a group of neuroleptic naive schizophrenic patients and the latter finding that morning regression slopes were steeper than evening regression slopes when comparing posterior cingulate perfusion with depression rating in patients with major depression. Tooth et al. investigated cognitive deficits after surgery for aneurysmal subarachnoid haemorrhage [SAH] and, using SPM, found a large common area of subcortical hypoperfusion in the patient group compared to controls. Studies like this, linking SPECT and cognitive testing, could play an increasing role in the comparison of SAH treatments. The paper by Stamatakis et al. focuses on the application of SPM in head injury. It is shown that, although care is needed in the application of SPM, the technique can add robustness to the classification of individual lesions and can also be used for group analyses despite gross abnormalities in individual scans. The other paper on SPM, by Barnes et al., explores the use of SPM to help in the classification of abnormalities in scans of patients with dementia. Use of SPM for individual scan classification is fraught with problems, not least in the establishment of an appropriate control data set, but they were able to demonstrate that the method works from a technical perspective and produces SPM patterns consistent with scan appearance. They found, however, that at present there is no evidence to support the routine use of SPM for classification. The main problem appears to be in interpreting rather than identifying equivocal perfusion patterns. More longitudinal studies with histology are required to compare imaging patterns with proven pathology.

The clinical areas covered in this special issue on SPECT include epilepsy, movement disorders, dementia, stroke, schizophrenia, depression and head injury. In the first three of these SPECT has an established routine role in clinical practice. In all other areas where the investigation of brain function is critical SPECT has contributed in research studies. Time will tell to what extent today's research evolves into routine practice. The papers selected for this issue have been chosen to be representative of developments in these clinical areas. They are of value in their own right and, importantly, point to other neuroimaging work in each particular specialist field.

References

[1] Patterson, J. and Wyper, D.J., Basics of SPECT; in: *SPECT Imaging of the Brain*, Duncan, ed., Kluwer Academic Publisher, 1997, pp. 1–42.

[2] Friston, K.J., Frith, C.D., Liddle, P.F. and Frackowiak, R.S.J., Comparing functional (PET) images. The assessment of significant change, *Journal of Cerebral Blood Flow and Metabolism* **11** (1991), 690–699.

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