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Brain imaging with SPECT and PET

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Brain single photon emission computed tomography (SPECT) and positron emission tomography (PET) are well validated and relatively widely available modalities for the imaging of brain function or receptor densities. Although structural magnetic resonance imaging (MRI) and computed tomography (CT) provide exquisite anatomical detail, SPECT and PET provide complementary functional information. Frequently, brain pathology will manifest as functional changes before anatomical changes are detectable.

The imaging of cerebral metabolism indirectly via perfusion SPECT using Tc-99m hexamethylpropylene amine oxine (HMPAO) or ethylene cystinate dimer (ECD), or directly with PET using [F-18] fluorodeoxyglucose (FDG), is clinically well established. Perfusion SPECT is well tolerated by patients and widely available at relatively low cost. The performance of SPECT and how it reflects brain function are described elsewhere.[1] The imaging of neurotransmitter systems is increasingly being used clinically, with increasing numbers of radiopharmaceuticals becoming available commercially, e.g. [I-123] ioflupane to image striatal dopamine transporter (DAT) density. This article briefly discusses the most important clinical applications of brain SPECT and PET.

Dementias

In patients with dementia, anatomical imaging frequently shows little or no change. Characteristic patterns of functional involvement using SPECT and PET can, however, enable more accurate differentiation of these forms of dementia (Fig. 1). Early detection and accurate determination of the underlying cause of dementia provide information that is useful for patient management, and has prognostic implications.[2]

Alzheimer's dementia (AD) classically shows decreased function in the tempero-parietal regions bilaterally, although this may be unilateral during the early stages of the disease. Posterior cingulate gyrus and precuneus involvement are recognised as early hallmarks. As cases advance, the frontal cortex also becomes affected. Typically, the primary sensori-motor cortex, visual cortex, subcortical structures, e.g. the basal ganglia and thalami, and cerebellar lobes are spared. Currently, diagnosis of AD is based on clinical criteria, but there is a move towards complementing diagnostic criteria with molecular and neuro-imaging markers. Early detection of AD is likely to become increasingly important in genetically high-risk individuals.

Vascular dementias can result in lesions involving the cortex, subcortical structures or cerebellum. These types of dementias are normally asymmetric, and classically involve border-zone areas of cerebral arteries. Fronto-temporal dementias are characterised by frontal and/or temporal

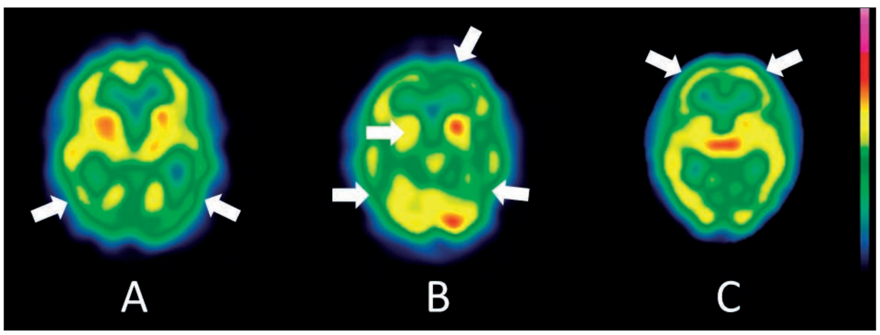

Fig. 1. Tc-99m HMPAO SPECT scans in 3 patients with dementia showing perfusion patterns suggestive of Alzheimer's disease, with bilateral temporo-parietal hypoperfusion (A), vascular dementia with multiple asymmetrical lesions affecting the anterior and posterior cortex and right striatum (B), and fronto-temporal dementia with frontal hypoperfusion (C).

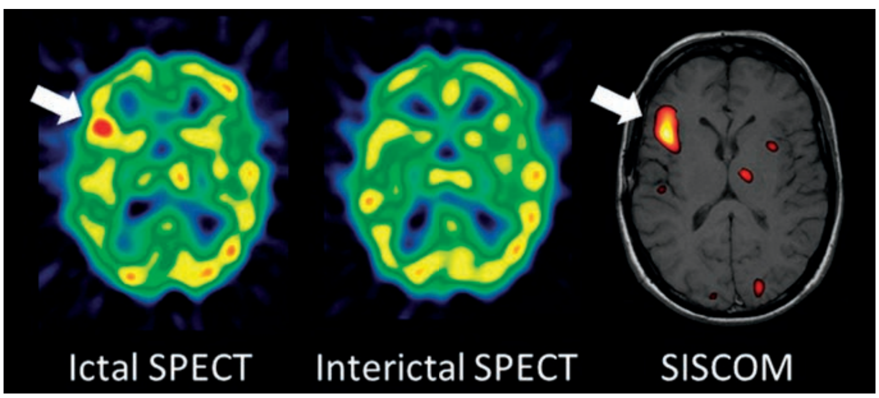

Fig. 2. Scans in a patient with refractory focal epilepsy with an epileptogenic focus, showing increased perfusion on ictal SPECT localised to the posterior aspect of the right frontal lobe on SISCOM.

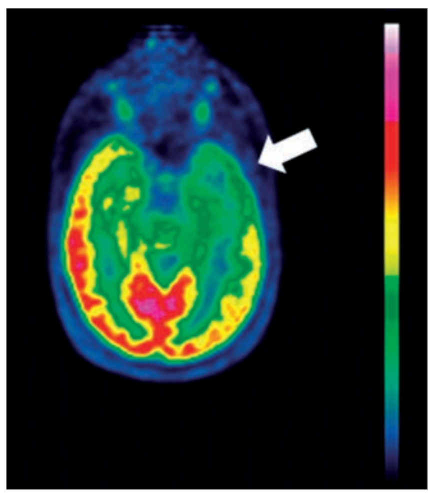

Fig. 3. An FDG-PET study in a patient with an epileptogenic focus in the left temporal lobe. The scan shows widespread hypometabolism in this lobe, more extensive than that in the epileptogenic focus alone.

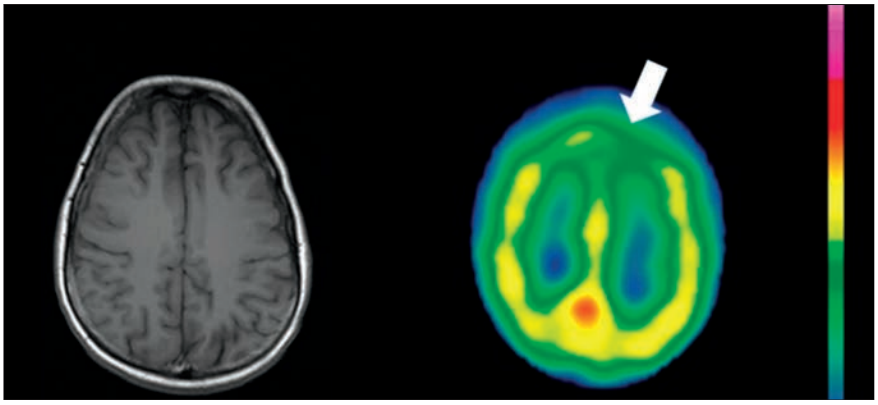

Fig. 4. Scans in a patient with a head injury sustained in a motor vehicle accident 4 years previously, who subsequently developed altered personality, cognitive fallout, and depression. The MRI scan (left) is normal, while SPECT shows anterior frontal hypoperfusion consistent with mTBI.

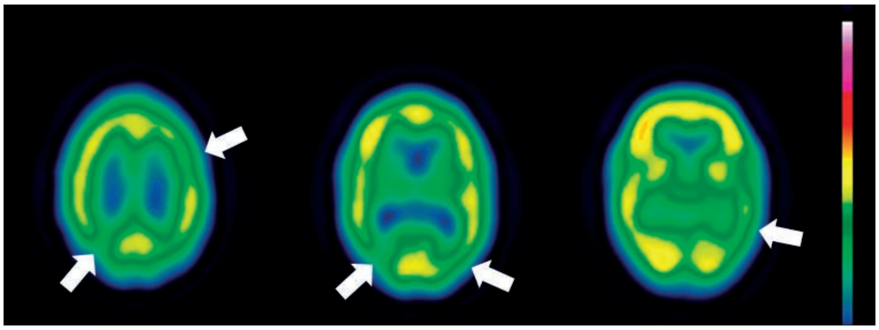

Fig. 5. A patient with SLE presented with clinical features suggestive of neurolupus. SPECT shows multiple areas of hypoperfusion in the left frontal and bilateral parietal cortex consistent with neuropsychiatric SLE.

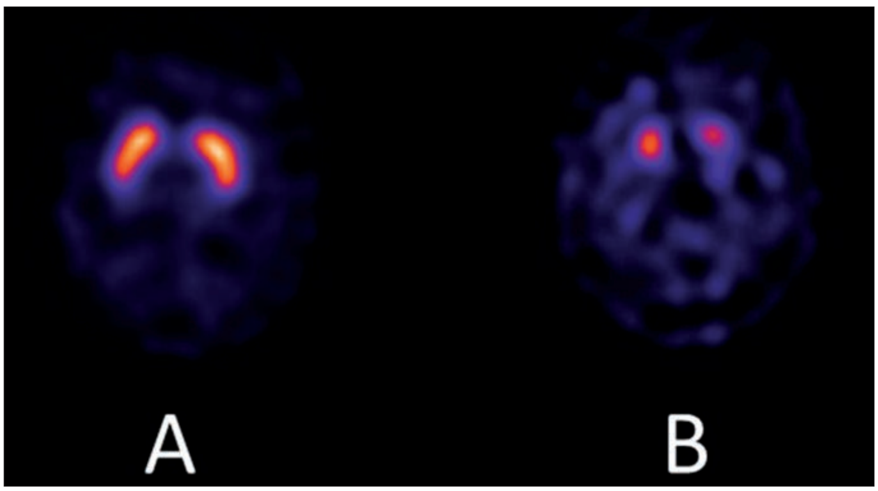

Fig. 6. Scans of two patients with parkinsonism. In one case, DAT SPECT shows normal striatal DAT density, virtually ruling out Parkinson's disease or other causes of presynaptic dopaminergic neuron degeneration (A). The second scan shows a patient with Parkinson's disease with marked loss of striatal uptake, particularly in the putamen, and a high level of background activity (B).

cortex hypometabolism, with relative sparing of the parietal cortices and precuneus. Lewy body dementia (LBD) can be distinguished from AD based on occipital hypometabolism, and/or abnormal striatal DAT binding.[3]

Epilepsy

Patients with refractory focal epilepsy, who are candidates for surgical resection of the epileptogenic focus, frequently benefit from SPECT and/or PET imaging.[4] The planning of surgery in epileptic patients requires close collaboration between the disciplines of neurology, neurosurgery, radiology, and nuclear medicine. MRI is essential in the management of these patients, although not all epileptogenic foci can be accurately localised using this modality and, conversely, not all anatomical foci are the cause of a patient's seizures.

The ability of perfusion brain SPECT to capture a snapshot of brain perfusion in a relatively short time frame enables ictal SPECT to localise epileptogenic foci. Injection of a radiopharmaceutical as soon as possible after seizure onset demonstrates a focal area of increased activity at the site of the epileptogenic area. In comparison, an interictal scan (obtained between seizures) shows no abnormalities or even an area of decreased activity at this site. The detection of the epileptogenic focus is further enhanced using Subtraction Ictal SPECT Co-registered with MRI (SISCOM), which requires subtraction of the interictal SPECT from the ictal SPECT, and superimposing the images onto anatomical MRI for accurate anatomical localisation of the lesion (Fig. 2).

Focal interictal hypometabolism on FDG-PET has also been shown to correlate with seizure foci (Fig. 3). Hypometabolic areas on PET often extend well beyond the true epileptogenic zone. PET can therefore not be used to refine surgical borders, but is useful for guiding intracranial electrode placement.

Mild traumatic brain injury

Mild traumatic brain injury (mTBI) typically involves loss of consciousness, loss of memory, alteration in mental state, or focal neurological deficit. Commonly, it is associated with headache, impaired thought processes, memory problems, attention deficit, mood swings and frustration. Abnormalities are more frequently found in mTBI patients when SPECT is performed than with MRI and CT scans.[5] Hypoperfusion in the frontal and parietal lobes is common (Fig. 4), although the basal ganglia, as well as the occipital, parietal and cerebellar areas, can also be affected. SPECT has a high sensitivity and negative predictive value for mTBI, and a normal study is predictive of good recovery.[5] However, given its limited specificity, SPECT alone is not enough to diagnose mTBI.

Neurolupus

Brain SPECT and PET have a well-established role in facilitating the diagnosis of neuropsychiatric involvement in systemic lupus erythematosus (SLE). Varied and often subtle clinical manifestations make this a challenging diagnosis. Anatomical MRI is frequently normal or does not provide an explanation for the signs and symptoms, in which case SPECT or PET imaging is appropriate.[6] These typically reveal a pattern of multifocal perfusion deficits, and are useful, objective tools to assist clinicians in selected cases (Fig. 5). These modalities have a good sensitivity, but a modest specificity.

Parkinsonism

The clinical evaluation of patients with parkinsonism can be extremely challenging, even in expert hands. The distinction between Parkinson's disease (PD), other parkinsonian syndromes such as multiple system atrophy, progressive supranuclear palsy, corticobasal degeneration and LBD, and other conditions such as essential tremor, has important implications for treatment and prognosis.

SPECT and PET imaging of DAT, dopamine receptors, brain glucose metabolism, and myocardial autonomic function are increasingly used to assist with these difficult distinctions.[3] Most of these modalities are already available in South Africa. DAT imaging reveals reduced presynaptic neuronal degeneration in PD and other parkinsonian syndromes, even when clinical features are subtle, while conditions such as essential tremor have normal striatal DAT density (Fig. 6).

Conclusion

In this brief overview the main indications for brain SPECT and PET are discussed. These imaging modalities are available in most major centres in South Africa and are frequently required for the optimal management of a diverse group of neuropsychiatric conditions.

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The use of nuclear medicine in childhood

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This article briefly discusses some of the more common nuclear medicine investigations available for use in the paediatric population.

Thyroid scintigraphy

In neonates with hypothyroidism detected on neonatal screening and confirmed by subsequent testing, a radionuclide thyroid scan should be performed as soon as possible. It must be undertaken in all nuclear medicine departments as a matter of urgency. Any delay in treatment should be avoided. Thyroid replacement therapy can interfere with the uptake of Tc-99m pertechnetate and therefore should be started as soon as the scan is completed.

The radionuclide thyroid scan provides information on the probable cause of the hypothyroidism. The absence of Tc-99m pertechnetate uptake in the expected position or in an ectopic site usually confirms agenesis. In thyroid glands with an abnormal embryological descent the volume of thyroid tissue is usually smaller than normal, with poor function (Fig. 1). Increased pertechnetate uptake is rarely seen in the gland, in keeping with dyshormonogenesis, which has a higher hereditary incidence.[1]

Renography

Hydronephrosis is the most commonly detected renal congenital abnormality. The majority of children with hydronephrosis detected antenatally will not need surgical intervention.[2,3] The role of renography in children with moderate and severe hydronephrosis is to assist to identify children who need surgical intervention.

The renogram investigates renal function. Tc-99m MAG3 is the preferred radiopharmaceutical. The four main aspects of renal function evaluated on a renogram are renal blood flow, renal function, transit of urine from the renal cortex to the renal pelvis, and flow of urine from the kidneys to the bladder. The only parameter reproducible in the same patient on different days is the differential renal function (DRF), comparing the function of one kidney with that of the other.

The current working definition of renal obstruction is any impairment of renal outflow that, left untreated, would lead to a loss of renal function or would prevent the normal maturation of renal function.[4] Using renographic criteria, obstruction can only be diagnosed if the patient has a decrease in DRF of more that 10% on the affected side on serial studies. A decrease of more than 5% in DRF should be considered as

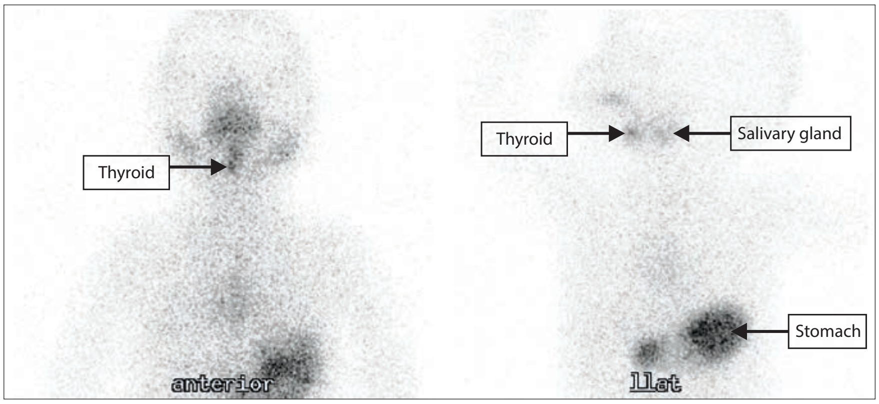

Fig. 1. An example of a poorly functioning lingual thyroid.

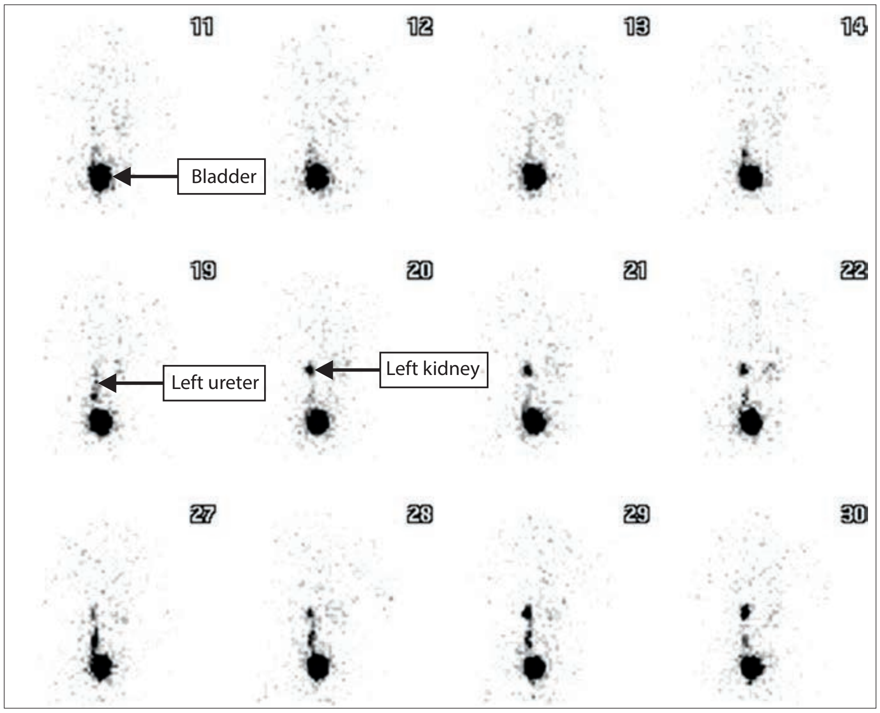

Fig. 2. Posterior images of an indirect cystogram showing reflux of a large volume into the left kidney.

a warning sign and the interval of follow-up studies, e.g. renal ultrasound and renograms, should be shortened. Cases of bilateral hydronephrosis are more complicated and are not discussed in full in this article.

In cases of a decrease in renal function most of the function will recover with prompt surgical intervention.[3]

It is tempting to interpret the drainage as shown on renogram curves, but this is not reproducible. If drainage is normal, the patient is unlikely to develop obstructive uropathy. There are numerous causes for poor drainage on a renogram; using this as a criterion for interpreting obstruction may lead to unnecessary surgical intervention with associated complications.

Indirect cystography

This is a relatively non-invasive way of detecting vesico-ureteric reflux (VUR) in children who are potty trained. On a renogram, most of the activity clears from the kidneys and is found in the bladder at the end of the study. Therefore, without inserting a catheter, there is contrast medium in the bladder. The child then simply voids in front of the camera and the presence or absence of significant reflux can be confirmed (Fig. 2).

An advantage is that the renogram provides information on renal function and the presence of renal scars, in addition to being a non-invasive way of detecting reflux.

Investigating urinary tract infection (UTI)

In recent years, there has been a move towards decreasing the number of investigations in children with UTI.[5] When faced with a child with UTI, those with a normal urinary tract are investigated far more conservatively than those with abnormalities of the kidneys, ureters or bladder. However, further imaging may be indicated in children with recurrent or atypical UTI.

Milk scans

In children with possible gastro-oesophageal reflux disease, milk scans are an elegant physiological way of investigating the problem. This is a four-part study.

Part one: While sitting on the mother's lap in front of the camera, the child drinks a small amount of his usual feed with a small amount of tasteless radiopharmaceutical added to it. The transit of activity through the oesophagus is then evaluated.

Parts two and three: Once the child has completed the entire feed, he is placed supine on the camera and an image is recorded to establish whether there was aspiration during swallowing. This is followed immediately by a reflux search conducted for 30 minutes - 1 hour, depending on the institutional protocol. Using this method of investigation, reflux disease can be evaluated according to the frequency, volume, height and duration of refluxes.

Part four: Images are recorded at the end of the reflux study and again 2 hours after the feed as a screening test to assess gastric emptying and to check for aspiration that could have occurred owing to reflux.

Meckel's scans

Meckel's diverticuli that contain gastric mucosa lead to repeated gastrointestinal bleeds. These bleeds usually present early in life.[6] Tc-99m pertechnetate is taken up by normal gastric mucosa. The patient is injected with pertechnetate and dynamic images are recorded, usually for about an hour. If there is functional gastric mucosa in a Meckel's diverticulum, uptake is seen in the diverticulum at approximately the same time as the stomach mucosa is visualised.

This scan will not detect diverticuli that do not contain functioning gastric mucosa.

Bone scans

In children older than 6 weeks, bone scans are extremely useful in determining the site(s) of osteomyelitis and septic arthritis.

Liver scans

Children with prolonged neonatal hepatitis should be investigated urgently, as the outcome of a Kasai procedure for biliary atresia is poorer in older babies.[7] In patients with jaundice, the radiopharmaceutical of choice is Tc-99m mebrofenin. If activity is seen passing from the biliary tree into the gut, biliary atresia can be ruled out. However, the absence of excretion does not confirm the diagnosis of biliary atresia but prompts further, more invasive, investigations.

Fever of unknown origin

The combination of information on areas of increased metabolic activity with anatomical localisation makes F-18 FDG-PET/CT an excellent tool for investigating fever of unknown origin.

Conclusion

This is a very short, selective summary of how nuclear medicine can contribute to the field of child health. Studies specific to more specialised areas, such as oncology of paediatrics, have not been addressed in this article.

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