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The Clinical Use of Brain SPECT Imaging in Neuropsychiatry

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ABSTRACT

This article reviews the literature on brain SPECT imaging in brain trauma, dementia, and temporal lobe epilepsy. Brain SPECT allows clinicians the ability to view cerebral areas of healthy, low, and excessive perfusion. This information can be correlated with what is known about the function or dysfunction of each area. SPECT has a number of advantages over other imaging techniques, including wider availability, lower cost, and high quality resolution with multi-headed cameras. There are a number of issues that compromise the effective use of SPECT, including low quality of some imaging cameras, and variability of image rendering and readings.

INTRODUCTION

Despite a vast literature on functional brain imaging in areas relevant to neuropsychiatry, the clinical utilization of SPECT, PET, QEEG, and fMRI remains limited. This article will review the literature on the usefulness, limitations, and controversies of using brain single photon emission computed tomography (SPECT) imaging in neuropsychiatric practice, especially as it applies to brain trauma, dementia, and temporal lobe epilepsy.

Brain SPECT imaging is a nuclear medicine study that uses isotopes bound to neuro-specific pharmaceuticals to evaluate regional cerebral blood flow (rCBF) and indirectly metabolic activity [(1)]. Currently in the U.S. there are three available radiopharmaceuticals, xenon gas, HMPAO (Ceretec) and ECD (Neurolite). Xenon can provide absolute quantification of rCBF but is cumbersome in clinical settings. HMPAO and ECD provide a moment-in-time image of relative rCBF, where each patient acts as his or her own control. Relative rCBF means that after the study is performed the processing computer takes the pixel with the greatest number of counts, makes it equivalent to 100 and then scales everything to it. The most intense pixel is usually found in the cerebellum on SPECT with HMPAO [(2)] and in the medial occipital lobe with ECD (3). The hallmark of a normal study is symmetrical perfusion [(4)].

A widely held misconception is that the clinical use of SPECT is restricted by limited resolution[(5)]. Early SPECT practice utilized single-headed cameras that produced low resolution images, especially in deep areas of the brain. However, sophisticated multi-headed gamma detectors with fan beam collimators have been available for the past decade. George reports that multi-head SPECT camera resolution is similar to PET at considerably less cost [(6)]. One of the significant problems with SPECT in clinical practice is the variability of the imaging gamma cameras and subsequent variability in the quality of the obtained images. Also, image renderings vary from clinic to clinic. Some clinics provide minuscule gray scale horizontal, coronal, and sagital SPECT slices on x-ray film. These images are difficult to interpret, even by experienced nuclear clinicians. Current manufacturers provide software for three-dimensional renderings that allow for more detailed and understandable images.

Another area of criticism of SPECT has been the issue of radiation exposure, especially in children. However, the average radiation exposure for one SPECT scan is 0.7rem (i.e., similar to a nuclear bone scan or brain CT) and is a safe procedure according to the guidelines established by the American Academy of Neurology [(7)]. The latter procedures are routinely ordered for many common medical conditions (i.e., bone fractures or head trauma), further suggesting that these levels of radiation exposure are generally acceptable in medical practice when indicated.

Another concern about SPECT imaging is the perceived lack of "normal" studies. In order to address this issue, the Society of Nuclear Medicine has established a large normative database at Yale University for clinician and researcher use (www.snm.org). The database currently has 236 "normal" adult studies. SPECT literature of the past 20 years has more than 43 studies that look at normative issues in over 2450 patients, including 150 children from birth on (see Table 1 for a sample of the some of the references[8-25]. These numbers do not include thousands of control subjects used in studies of specific neurological and psychiatric conditions. For example, Chiron et. al.[22] reported that at birth, cortical rCBFs were lower than those for adults; after birth they increased until 5 or 6 years of age to values 50%-85% higher than those for adults and thereafter decreased, reaching adult levels between 15 and 19 years. At the age of 3, however, they had the same relative blood flow patterns as adults. Mena et al. [23] report reference values for children age 6-15, as well as age related changes when comparing children to adults. Other common findings in normal studies suggest that women have generally higher perfusion than men and age, drug abuse, and smoking have a negative effect on rCBF. See Table 1 for a summary of some of the major studies on normal SPECT scans.

Table 1
Examples of Brain SPECT Normative Studies

# normals	First author	Date of Study	Type	Age	Significant findings
159	SNM Yale	Past-present	HMPAO	Adult	Available for research www.snm.org
77	SNM Yale	Past-present	ECD	Adult	Available for research www.snm.org
187	Slosman	2001	Xe	Adult	Male-female differences and decline with age
48	Tanaka	2001	ECD	22-95	Intersubject variability small
6 -- 3 scans each	Jonsson	2000	HMPAO	Adult	Reproducibility was +/- 1.3%
53	Nakano	2000	ECD	18-87	rCBF decreases during normal aging
44	Wirestam	2000	HMPAO	Adult	fMRI and SPECT showed good agreement
26	Ernst	1999	HMPAO	Adult	fMRI and SPECT showed good agreement
13	Mena	1998	HMPAO	6-15	Normal values in children compared to adults
18	Goto	1998	HMPAO	20-81	Compare young and older scans
27	Krausz	1998	HMPAO	26-71	Aging associated with decreased rCBF
16	Schiepers	1997	ECD	Children	Safe agent for children because of favorable radiation dosimetry and stability
23 child 10 adults	Barthel	1997	ECD	4-15 27-56	Children have higher perfusion
9 -- 2 scans each	Deutsch	1997	HMPAO	Adult	Good within-subject 48-hour replicability, 2.8% variability
10HMPAO 10ECD 10PET	Koyama	1997	HMPAO/ECD	Adult	Highest areas of perfusion: HMPAO -- cerebellum/basal ganglia, ECD -- medial occipital lobe
52	Yang	1996	HMPAO	2-85	Negative correlation between CBF and advancing age
68	Catafau	1996	HMPAO	23-75	Symmetrical rCBF distribution can be assumed independent of age
26	Kobayashi	1996	I123	0-19	Age related rCBF changes; low early infancy, increased late infancy through early childhood, and decreased and constant after puberty
42	Chiron	1992	Xe	2 days to 19 yrs	Brain development related rCBF changes of corresponding brain regions
67	Yamashita	1988	Xe	Adult	rCBF decreased with advancing age, elderly smokers showed lower rCBF than elderly nonsmokers

POTENCIAL CLINICAL USE OF BRAIN SPECT IMAGING

According to the Society of Nuclear Medicine, the evaluation of suspected brain trauma, the evaluation of suspected dementia, the presurgical localization of epileptic foci, and the evaluation of cerebral vascular disease are acceptable indications for brain SPECT[26]. The Society of Nuclear Medicine has also published guidelines on the technical standards for performing and interpreting these studies [26].

BRAIN TRAUMA

There are 74 SPECT studies of brain trauma in the literature involving 1503 patients (see Table 2 for a summary of some of the studies 27-48). SPECT has the potential to aid in the diagnosis and treatment of brain trauma. It can help identify if trauma is present and which brain system or systems are affected. Common findings on SPECT in brain trauma include:

- decreased perfusion over sight of injury and/or opposite side (contra coup)
- decreased orbital prefrontal cortex perfusion
- decreased anterior temporal lobe perfusion (lies behind wing of sphenoid bone) and decreased posterior temporal lobe perfusion (contra coup injury within the body of the temporal lobe)
- decreased parietal lobe perfusion (at vertex of brain)
- decreased occipital lobe perfusion (hit directly or in contra coup fashion)
- focal increased perfusion over site of injury or in a contra coup area
- decreased posterior medial cerebellar perfusion
- findings often occur together - for example, decreased orbital prefrontal, decreased left and right anterior and posterior temporal lobes, decreased left and right parietal and occipital lobe perfusion. (27-28)

Table 2
Examples of Brain SPECT Studies in Brain Trauma

# Patients	First Author	Study Date	Type	Age	Significant findings
24	Baulieu	2001	ECD	Adult	Valuable in predicting behavior after TBI
21	Hoffman	2001	HMPAO/MRI	Adult	Lesions common after minor TBI (77%)
16	Stepien	1999	HMPAO	Adult	Useful in early and late TBI consequences
5	Laatsch	1999	HMPAO Bef/aft rehab	Adult	rCBF changes related to neuropsychological test improvement
32	Abu-Judeh	1999	HMPAO	11-61	(1) Sensitive for mild TBI rCBF changes; (2) changes can occur without loss of consciousness; (3) more sensitive than CT; and (4) changes may explain symptoms in the absence of other imaging abnormalities.
228	Abdel-Dayem	1998	HMPAO/ECD	11-88	41 with mild TBI without LOC had normal CT, 28 had abnormal SPECT
6 – 2 times	Otte	1997	ECD and PET	Adult	Whiplash group showed decreased rCBF in parieto-occipital regions
20	Emanuelson	1997	SPECT/CT	Children	CT and SPECT similar in patients with severe injury, SPECT more sensitive in mild TBI
35	Gilkey	1997	Xe	Adult	Reduced rCBF with post traumatic headache
43	Kant	1997	HMPAO/MRI/CT	Adult	SPECT more sensitive than CT or MRI in mild TBI
136	Jacobs	1996	HMPAO -- prospective	Adult	SPECT at 12 months postinjury is a reliable predictor for clinical outcome.
28	Goshen	1996	HMPAO/CT/ MRI	Children	SPECT useful evaluating pediatric post-TBI
53	Sakas	1995	HMPAO	Adult	Focal zones of hyperemia were present in 38% of patients
14	Varney	1995	HMPAO/ normal CT	Adult	Significant anterior mesial temporal and orbitalfrontal hypoperfusion.
10	Bavetta	1994	HMPAO prospective	Adult	SPECT yields useful prognostic data
67	Jacobs	1994	HMPAO	Adult	(1) Correlated with severity of trauma; (2) negative initial SPECT is reliable predictor of favorable outcome; (3) a positive initial SPECT needs a follow-up scan
29	Ichise	1994	HMPAO	Adult	In chronic TBI SPECT is a more sensitive study than CT or MRI

20	Nedd	1993	HMPAO	Adult	SPECT more sensitive than CT or MRI in mild to moderate TBI.
36	Oder	1992	HMPAO	Adult	Highest correlation was between frontal flow and disinhibitive behavior
15	Roper	1991	HMPAO	Adult	SPECT can detect focal disturbances of rCBF not seen on CT

SPECT can aid in understanding patient symptomotology and assist clinicians in developing targeted treatment strategies [29-30]. For example, decreased prefrontal cortex perfusion is often associated with executive dysfunction and may be helped with psychostimulants [31], whereas decreased temporal lobe perfusion is often associated with irritability and mood instability and may be helped with anticonvulsant medication [32].

Literature indicates that SPECT can help evaluate perfusion abnormalities not only in cases evaluating blunt brain trauma, but also in cases of post-concussive syndrome and whiplash [33-36]. Several authors report extensive and prolonged perfusion abnormalities on SPECT after a patient has experienced relatively minor brain trauma [37-40]. Minor brain injuries that leave brain tissues grossly intact have left some patients with severe functional deficits. Brain injured patients with normal EEG, CT, and/or MRI scans often complain of headaches, memory loss, concentration difficulties, dizziness, perceptual sensitivities, and emotional lability. Such patients may be labeled as malingering, when there are significant functional abnormalities present. Several researchers have investigated the differences between functional and structural imaging techniques with patients who have sustained various degrees of head trauma.

Emanuelson et. al. [40] demonstrated differences between SPECT and structural imaging through the evaluation of 20 brain injured patients who complained of problematic post head injury symptoms (i.e., headache, dizziness, etc). Although CT and SPECT revealed similar levels of abnormality in severely brain injured patients, significant CT and SPECT differences were found in mildly injured patients. SPECT detected more affected areas of the brain than CT. Similar findings have been reported in comparisons between SPECT and EEG, CT and MRI [41-45].

Researchers have also compared the differences between functional imaging and structural imaging in relation to clinical outcome and prognosis. Jacobs et. al. [29] used SPECT to prospectively evaluate 67 mildly to moderately brain injured patients. Each patient had a clinical evaluation and a SPECT scan within four weeks of the initial injury and three months after the first scan. Of the 33 patients who showed no significant abnormalities on their initial SPECT scan, 97% of the patients resolved their clinical symptoms within three months. By contrast, of the 34 patients who had abnormalities on their first SPECT scan, 59% of the patients continued to experience significant clinical symptoms. The positive predictive value of an abnormal initial scan was only 20/34 (59%), but if the second scan 12 months later was also abnormal the sensitivity for the repeat SPECT was 19/20 (95%). These authors suggest that negative initial SPECT studies can be a reliable predictor of a favorable clinical outcome. In another study Jacobs et al.[46] evaluated the predictive capacity of HMPAO SPECT for clinical outcome during a follow-up period of 12 months after mild head injury. They prospectively evaluated 136 patients with mild head injury who underwent initial SPECT imaging within 4 weeks after the trauma and re-evaluated patients at 2.9-3.3 months, 5.7-6.3 months, and 11.9-12.6 months postinjury. All patients with an abnormal SPECT underwent a repeat study at the subsequent time of evaluation. Patients with a previously normal SPECT scan did not undergo a repeat study. Clinical reassessments were performed as long as the earlier study had been positive or until patients were completely asymptomatic. During all follow-up evaluations, SPECT had a high sensitivity and negative predictive value, increasing from 91% and 89%, respectively, at 3 months to 100% at 6 months and at 12 months. At 12 months postinjury, the authors observed considerable improvement in the specificity and positive predictive value of SPECT (85% and 83%, respectively).

Results from functional brain imaging studies have also been associated with neuropsychological testing results. Ichise et. al. [47] suggest that SPECT may present additional objective evidence for some neuropsychological impairments that testing alone may not provide. SPECT can also demonstrate improvements in brain function as a result of cognitive rehabilitation training (CRT). Laatsch et al.[48] studied 5 patients who had acquired brain injury and initially demonstrated neuropsychological deficits and various degrees of hypoperfusion on SPECT. Following CRT, all clients were able to return to productive employment or schooling. Examination of the neuropsychological testing results revealed significant improvement in performance following CRT which were generally maintained after treatment. SPECT data revealed that, in a majority of cases, significant increases in relative cerebral blood flow redistribution was also seen. It is necessary to replicate these findings in larger groups of patients.

One of the most controversial issues in brain trauma is the issue of brain damage in the absence of

loss of consciousness. Abu-Judeh et al. [37] present SPECT findings in 32 patients who suffered mild traumatic brain injury without loss of consciousness and normal CT scans. The most common complaints were headaches in 26 patients (81%), memory deficits in 15 (47%), dizziness in 13 (41%) and sleep disorders in eight (25%). The results show that 19 (59%) had abnormal SPECT studies.

SPECT can assist in the diagnosis, prognosis, and treatment of patients who have sustained brain trauma. It is conceivable that SPECT may also uncover brain trauma in clinically confusing or complex cases because patients often fail to report or forget about significant brain injuries. One limitation of the use of SPECT in brain trauma is that often there is no prior SPECT study available for comparison. Therefore, it is often not possible to date the trauma. Remote trauma from childhood may appear similar to recent trauma. If a trauma pattern is evident on a scan it is not possible to say when it occurred.

DEMENTIA

There are 83 studies on brain SPECT imaging and dementia in the literature involving over 4500 patients (see Table 3 for a summary of some of the studies 50-86).

Table 3
Examples of Brain SPECT Studies in Dementia

# Patients/ normals	Author	Date of Study	Type	Significant Study Findings
24/12	Cappa	2001	HMPAO	Combination of neuropsychological tests and SPECT is useful in separating FTD from AD
23DLB 50AD 20NL	Lobotesis	2001	HMPAO	Temporoparietal hypoperfusion is common to both AD and DLB. Occipital hypoperfusion more frequently seen in DLB.
70 Dementia autopsy 71NL	Jagust	2001	HMPAO	SPECT can provide useful information indicating presence of AD in addition to clinical information obtained
116AD 23NLS	Tsolaki	2001	HMPAO	Decreased parietal and temporal perfusion in AD. SPECT and neuropsychological test correlation on MMSE and CAMCOG
12	Staff	2000	HMPAO Donepezil	Overall increase rCBF, especially in frontal area
30	Ashford	2000	ECD	rCBF corresponds closely to distribution of AD pathology described in autopsy studies.
40	Charpentier	2000	HMPAO	AD and FTD are differentiated by SPECT
16FLD 52AD 19subcort dem 28NLS	Sjogren	2000	HMPAO	anterior-to-posterior rCBF-SPECT ratio separated FTD group from the other dementia groups
18	Shih	1999	ECD 3Ddisplays	3D displays helpful to assess severity and progression of AD-related hypoperfusion and is potentially more reliable than the MMSE.
14DLB 14AD 14NL	Ishii	1999	HMPAO	Decreased occipital perfusion and well preserved medial temporal perfusion help distinguish DLB from AD.
69	Claus	1999	SPECT	Left temporal rCBF predicts decline in language function and survival in patients with early probable Alzheimer's disease
34/12	Arbizu	1999	HMPAO	SPECT and neuropsychological tests can distinguish controls from AD and mild to moderate grades of dementia
20	Benoit	1999	ECD	Highest correlation for MMSE was left temporoparietal area
36	McKelvey	1999	HMPAO	SPECT abnormalities assessed by visual inspection do not correlate with severity of impairment in AD
116DA 20nls	Muller	1999	HMPAO	MMSE and delayed recall test differentiated significantly between patients and controls, SPECT yielded no further differentiation
363 pro-spective	Talbot	1998	HMPAO	SPECT most useful in distinguishing AD from VD and FTD, least useful in differentiating AD from DLB
60/16	Blanco	1998	SPECT	Parietotemporal location of defective perfusion is of diagnostic value.
136	Johnson	1998	HMPAO	Useful as one aspect of the preclinical prediction of AD
34/12	Arbizu	1997	HMPAO	Temporo-parietal cortex most value in discriminating between AD and controls
261 Xe 162 HMP	Bonte	1997	Xe/HMPAO	Biopsy 54 – Sensitivity 86%, specificity, 73%; positive predictive value, 92%; and negative predictive value, 57%.
302	Hanyu	1997	I123	Sensitivity for AD was 86.3%, and specificity was 91.2%
200/119 autopsy	Jobst	1997	HMPAO/CT	SPECT alone had 89% sensitivity, 80% specificity, and 83% accuracy; and the combination of SPECT and CT was 80% sensitive, 93% specific, and 88% accurate.
19AD 21FLD	Pickut	1997	HMPAO	SPECT helpful in discriminating FLD from AD. Bifrontal

				hypoperfusion found most powerful predictor of clinical classification
27 autopsy	Read	1995	HMPAO	SPECT predicted diagnosis 92.6%, compared with clinical diagnosis 74.1%. Distinct patterns with dementia caused by AD, FTD, and Jakob-Creutzfeldt Disease
29	Wolfe	1995	I123	Temporal rCBF ratio predicted rate of decline of specific memory measures
7/7/7	Alexander	1995	SPECT	Support use of rCBF in distinguishing FLD from AD and severe depression.
71 autopsy confirmed	Jobst	1994	HMPAO	Combination of SPECT, CT and clinical criteria yielded diagnostic sensitivity of 90% and a specificity of 97%.
8AD 8FLD 8NL	Starkstein	1994	HMPAO	Specificity of changes in rCBF in diagnosis of different types of dementia
16	Engle	1993	HMPAO	Correlations were demonstrated between cerebral blood flow in the posterior brain regions and performance on tests of language, memory, attention, figure copying, judgment, and similarities.
5	Miller	1993	HMPAO	This study suggests that the right hemisphere may be primary for the control of social conduct.
29AD/78nl	Johnson	1993	HMPAO	Sensitivity 91% and specificity 86% accurately distinguishes AD patients from elderly controls
34/11	Battistin	1990	HMPAO	A positive correlation found between magnitude of the parietal deficits and severity of dementia

MCI = mild cognitive impairment
AD = Alzheimer's Disease
DLB = Dementia Lewy Boldy Type
FLD = Frontal-temporal dementia
MID = Multi-infarct dementia
VD = Vascular dementia

To date, autopsy reports have been the "gold standard for an Alzheimer's Disease (AD) diagnosis." However, research suggests that SPECT can be helpful when evaluating patients who are experiencing cognitive decline[50]. Functional brain imaging patterns have been associated with Alzheimer's Disease (AD; parietal and temporal lobe deficits), Frontal Lobe Dementia (FLD; frontal and temporal lobe deficits), Multi-infarct Dementia (MID; a vascular pattern of decreased activity in multiple areas), and pseudodementia (PSD; a pattern associated with depression; decreased left prefrontal cortex activity and increased thalamo-limbic activity) [51-53]. Patients diagnosed with different dementia disorders can present with similar symptomotology (i.e., social withdrawal and behavioral disinhibition) [54]. Because treatments for the different disorders vary differential diagnosis is important. Research suggests that SPECT, in combination with clinical history and other diagnostic tests can be helpful for this purpose [55].

Numerous authors have reported bilateral decreases of activity in the parietal and temporal lobes of AD patients (56-58). Bonte et. al. [59] performed xenon SPECT studies in 261 patients and HMPAO SPECT in 162 patients with possible dementia and compared them to SPECT images of an elderly healthy control group. In each patient without AD, further classification of disease was attempted. Histopathologic correlation was available in 54 patients (with autopsy in 51, with biopsy in three). The results of the study showed SPECT diagnoses were true-positive in 37, true-negative in eight, false-positive in three, and false-negative in six patients. Sensitivity was 86%; specificity, 73%; and the positive predictive, 92%. The authors concluded that SPECT may assist in the early and late diagnoses of AD and in the differential-diagnosis of the dementias when there is a complicated or confusing clinical picture.

In a prospective study of more than 200 cases of dementia and 119 controls [60], annual HMPAO SPECT studies, annual medial temporal lobe CT scans, and the presence of the apolipoprotein E4 (Apo E4) genotyping were used to evaluate the diagnostic potential of functional and structural neuroimaging in the differential diagnosis of dementia compared to clinical diagnoses. Autopsy histology is known for 118, of whom 80 had AD, 24 had other "non-AD" dementias, and 14 controls with no cognitive deficit. All clinical diagnoses were made according to National Institute of Neurological and Communicable Disease and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) and the DSM-III-R criteria, and all histopathological diagnoses according to the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) criteria. The diagnostic accuracy of CT alone was 85% sensitive, 78% specific, and 80% accurate; SPECT alone was 89% sensitive, 80% specific, and 83% accurate; and the combination of the two was 80% sensitive, 93% specific, and 88% accurate. The Apo E4 genotype was 74% sensitive but yielded 40% false positives in the histologically confirmed series. The diagnostic accuracy afforded by the method of CT and SPECT is better than that of any established clinical criteria and reveals that the combination of MTL atrophy and parietotemporal hypoperfusion is common in AD, much less common in other dementias, and rare in normal controls. The authors conclude that SPECT can significantly enhance diagnosis.

Julin et. al. [61] compared 28 patients diagnosed with AD to eight patients diagnosed with FLD. The researchers used SPECT, MRI, and EEG to measure a number of different factors, including cerebral blood flow, brain atrophy, white matter changes, and neurophysiologic changes. The FLD patients in this study had significantly lower blood flow in the frontal lobes and significantly higher blood flow in the parietal lobes than did AD patients. Other authors report similar findings between FLD and AD patients [62-63]. SPECT literature also reports differences in temporal-parietal brain functions in AD patients when compared to epilepsy, MID, Parkinson's disease, and other dementia disorders [64-66].

Jagust et al. [67] measured radioactivity densities in multiple brain regions of 50 patients to evaluate the predictive utility of rCBF measurements for AD. Although the presence of AD was confirmed by overall temporal-parietal perfusion similar to previous studies, right parietal lobe hypoperfusion was additionally a significant predictor of longer survival. Even considering such variability in the literature, some authors suggest that brain SPECT patterns have predicted cognitive decline in AD more reliably than demographic and course variables (i.e., age, prior dementia duration, and initial severity) [68-69].

Engel et al. [70] suggest that SPECT and neuropsychological testing have correlates that are clinically relevant. Correlations were demonstrated between cerebral blood flow in the posterior brain regions and performance on tests of language, memory, attention, figure copying, judgment, and similarities. Alzheimer's disease patients exhibited more language impairment than multi-infarct dementia patients. In the authors' opinion, SPECT promises to provide diagnostic information and data relevant to interpretation of neuropsychological deficits.

Apathy is a pervasive noncognitive neuropsychiatric disturbance in Alzheimer disease, which causes significant caregiver distress. Craig et al. [71] studied the relationship between rCBF and the presence and severity of the personality disturbance, apathy, in 31 individuals with Alzheimer disease. The presence of apathy was associated with more severe prefrontal and anterior temporal dysfunction. These regional cerebral perfusion relationships with apathy were independent of cognitive decline except in the dorsolateral prefrontal cortex. These results demonstrate the association of apathetic syndromes with prefrontal and anterior temporal regional brain dysfunction and are consistent with similar findings previously reported in other disorders.

The majority of the literature indicates that SPECT can assist in the differential diagnosis of dementia disorders when used in conjunction with clinical examination and neuropsychological testing. However, there are several negative studies in the literature that suggest that the predictive value of SPECT is not high enough to be used on a routine clinical basis [72-73]. In addition, there are other pathological processes that can give produce patterns consistent with AD and FLD patterns, most notably brain injury that affects the prefrontal cortex pole and anterior temporal lobes (like FLD) or a brain injury that affects the temporal and parietal lobes. As with any test it is important that SPECT be used and interpreted within a clinical context.

TEMPORAL LOBE EPILEPSY

There are 72 studies on brain SPECT imaging and temporal lobe epilepsy (TLE) in the literature involving over 2100 patients (see Table 4 for a summary of some of the studies 96-107).

Table 4
Examples of Brain SPECT Studies in Epilepsy

# Patients	First Author	Study Date	Type	Age range	Significant findings
117	Hwang	2001	PET/SPECT/MRI	Adult	PET or ictal SPECT are complementary, most helpful in cases of negative MRI findings
65	Lawson	2000	HMPAO	Children	Ictal SPECT without MRI findings is useful for surgical localization
13	Avery	2000	HMPAO	Adult	Ictal SPECT more accurate than EEG/MRI
30	Sarikaya	1999	HMPAO	Children	SPECT parameters may be used for correlating with clinical parameters
118	Won	1999	PET/SPECT/MRI/Video EEG	Adult	MRI, PET, and ictal SPECT correctly identified lesion in 72%, 85%, and 73% of patients
75	Oliveira	1999	ECD	Adult	Ictal SPECT easily achieved and accurately localize epileptogenic zone in temporal and extratemporal epilepsies. Ictal SPECT more sensitive and specific than interictal SPECT
46 papers, meta-	Devous	1998	multiple	all	SPECT localization in patients with temporal lobe seizures were 0.44

analysis					(interictal), 0.75 (postictal) and 0.97 (ictal). False-positive rates low relative to diagnostic evaluation (7.4% for interictal and 1.5% for postictal studies)
59	O'Brien	1998	HMPAO	Children	Provides specific localizing information in a high proportion of these patients
20	Guillon	1998	HMPAO	Adult	Interictal SPECT correlated with EEG irritative zone.
14	Menzel	1996	ECD	Children	Interictal SPECT showed hypoperfusion areas in 80%. Ictal rCBF SPECT informative in all
45	Matsuda	1996	HMPAO	Adult	Interictal SPECT gives useful information about epileptic focus and antiepileptic drugs
20	Rodrigues	1996	HMPAO	Adult	Focal hypoperfusion in 93%, ictal hyperperfusion in all
30	Ho	1996	HMPAO	Adult	Ictal SPECT helpful for subclassification of TLE, clinical features relatively unhelpful
21	Alper	1995	HMPAO	Children	Pathology on SPECT, CT, and EEG were 67%, 38%, and 52%, respectively. SPECT showed congruent, or more extensive, lesions in 8 patient with CT lesions. Six of 13 with normal CT, had abnormal SPECT.
55	Otsubo	1995	HMPAO	Children	Interictal/postictal SPECT can lead to greater accuracy in localizing epileptic foci
28	Duncan	1993	HMPAO	Adult	Ictal/postictal SPECT reliable for presurgical localization of complex partial seizures
79	Uvebrant	1991	HMPAO	Children	SPECT relevant information in 79% of cases, MRI 49% and CT 36%
34	Shen	1990	HMPAO	Adult	Intericta/ictal SPECT easily obtained and provides reliable information in presurgical evaluation of intractable epilepsy

Temporal Lobe Epilepsy (TLE) is one of the most frequently encountered chronic epileptic disorders and has been associated with numerous psychiatric symptoms, such as depressed mood, anergia, irritability, euphoric mood, atypical pain, insomnia, fear, and anxiety [88]. The medial aspects of the temporal lobes are frequently involved in TLE and they are difficult to evaluate with routine EEG studies and therefore may be missed. Ictal SPECT and, to a lesser degree, interictal and peri-ictal SPECT have been used to accurately identify seizure foci. SPECT findings in epilepsy most often reveal focal decreased perfusion in the interictal phase and focal increased perfusion in the ictal phase of a seizure [89-94]. In a review of 30 studies, Devous et al. [89] found that SPECT localization in patients with temporal lobe seizures were 0.44 (interictal), 0.75 (postictal) and 0.97 (ictal). False-positive rates were low.

Shen et. al. [94]utilized brain SPECT imaging to evaluate 34 patients who eventually underwent a temporal lobectomy for medically intractable complex partial seizures. Consistent with previous findings, patients in the interictal phase revealed decreased regional cerebral perfusion in the temporal lobe. These abnormalities corresponded with the eventual site of surgery in 73% of their patients. Ninety-three percent of their patients also displayed increased perfusion on SPECT during the ictal phase, which also corresponded with the eventual site of surgery. Sixty-nine percent of the patients had both increased cerebral perfusion on the ictal scan and decreased cerebral perfusion on the interictal scan, which corresponded to the eventual site of surgery. Duncan et. al. [95]report similar sequences of ictal (increased) and post-ictal (decreased) temporal lobe perfusion in their study of 28 patients with medically intractable complex partial seizures. Subsequent temporal lobe surgery on the hemisphere indicated by SPECT was again successful (i.e., 90% reduction in seizure frequency) in 96% [27/28] of their patients.

Brain SPECT findings in epilepsy research have correlated well with other techniques and may contribute additional information. A number of authors have evaluated the utility of brain SPECT and various structural techniques for the localization of seizure foci (96-102). Otsubo et. al. [90] reviewed EEG, CT, MRI, and SPECT imaging data obtained from 28 children with intractable seizures. In their study, brain SPECT accurately localized epileptogenic abnormalities found with MRI, CT, and EEG. However, the SPECT studies additionally showed interictal decreases of rCBF that corresponded with the temporal epileptogenic zone in 68% (15/22) of the patients. Uvebrant et. al. [102] compared the

value of SPECT to neuropediatric evaluations in their study of 79 children. Of the 56 children investigated for epilepsy, SPECT yielded clinically relevant information consistent with a diagnosis of epilepsy in 79% of their cases. MRI and CT yielded clinically relevant information in 49% and 36% of their cases, respectively. Although neither functional nor structural imaging can clarify the etiology of epilepsy, SPECT may provide information that associates the distribution of functional lesions with the behavioral manifestations associated with epilepsy. Patients with epilepsy may have functional pathophysiological deficits of otherwise grossly intact brain tissue [97-99]. In 45 patients Matsuda et al. (98) found that SPECT gave useful information about interictal cerebral blood flow around an epileptic focus and about the effects of antiepileptic drugs on brain function in TLE. Ictal SPECT may also be helpful for subclassification of temporal lobe seizures [102], whereas clinical features are relatively unhelpful. Perfusion patterns provide insight into preferential pathways of seizure propagation in the subtypes of TLE.

One of the major drawbacks of SPECT is that several studies report that interictal PET may be as sensitive as ictal SPECT [104-105]. It is easier to perform studies in the interictal phase where PET is available. Yet, it is clear that SPECT may add to the clinical evaluation of temporal lobe function by identifying an area(s) of abnormality, showing deficits not seen by EEG, and possibly by shedding light on why anticonvulsants are useful for broad neuropsychiatric indications.

CONCLUSIONS AND CAUTIONS

There is a converging body of literature on the usefulness of brain SPECT imaging in brain trauma, dementia, and temporal lobe epilepsy. However, a number of issues need be addressed before SPECT, or any other functional imaging technique, can become a standard evaluation tool. The uncertainty of false positive and false negative readings is of particular concern. As more integrative studies are conducted, the actual statistical significance of false positive and false negative readings with different diagnoses will become clearer. Furthermore, brain SPECT imaging, as with any clinical tool, should always be evaluated within the context of a patient's clinical history and examination.

Because of the variability of scan procedures and camera sensitivity, physician training and experience is of primary concern when evaluating the usefulness of SPECT. Outdated single-headed cameras do not have the same level of resolution as the multi-headed cameras. It is also possible that less experienced physicians will read a scan as "normal," while more experienced physicians will discover clear areas of concern on the same scan (or vice-versa). Although image resolution and rater variability are concerns for reading functional and structural imaging studies, the importance of experience and standardized rating scales are becoming increasingly evident when evaluating the utility of brain SPECT imaging.

In order to utilize SPECT technology effectively, three factors should be considered at minimum. It is important to have a high-resolution SPECT camera (i.e., a dual or a triple head camera), a nuclear medicine physician skilled in reading brain studies for neuropsychiatric purposes, and a psychiatrist who understands how to utilize the technology to properly integrate findings and inform treatment.

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