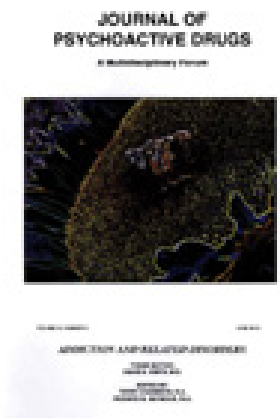

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High Resolution Brain SPECT Imaging in a Clinical Substance Abuse Practice

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High Resolution Brain SPECT Imaging in a Clinical Substance Abuse Practice

Daniel G. Amen, M.D.*

Abstract—Brain SPECT imaging is a nuclear medicine study that uses isotopes bound to neurospecific pharmaceuticals to evaluate regional cerebral blood flow (rCBF) and indirectly metabolic activity. With current available technology and knowledge SPECT has the potential to add important clinical information to benefit patient care in many different areas of a substance abuse practice. This article explores the clinical controversies and limitations of brain SPECT, plus seven ways it has the potential to be immediately useful in clinical substance abuse practice, including: adding valuable information to the prevention, evaluation, and treatment of substance abusers; helping clinicians ask better questions; helping them in making more complete diagnoses and preventing mistakes; evaluating underlying brain system pathology in individual patients; decreasing stigma and increasing compliance; visualizing effectiveness via follow-up evaluations; and encouraging the exploration of innovative and alternative treatments

Keywords—brain injuries, brain system pathology, imaging, SPECT, substance abuse

Thomas Insel, M.D., Ph.D., Director of the National Institutes of Mental Health said in a keynote address to the American Psychiatric Association in 2005 (Insel 2005) that "brain imaging in clinical practice is the next major advance in psychiatry." He went on to say that "The DSM-IV has 100% reliability and 0% validity. . . .We need to develop biomarkers, including brain imaging, to develop the validity of these disorders. . . . Trial and error diagnosis will move to an era where we understand the underlying biology of mental disorders. . . . We are going to have to use neuroimaging to begin to identify the systems pathology. . . . We need to develop treatments that go after the core pathology, understood by imaging." Dr. Insel believed in 2005 that brain imaging in clinical practice would be a reality within five years.

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Indeed, many centers around the world are using functional brain imaging technology such as SPECT and PET in the clinical setting for the assessment of cerebral vascular disease, brain trauma, differential diagnosis of dementia, epilepsy and other neuropsychiatric indications. Vasile (1996) wrote in the *Harvard Review of Psychiatry* that "The clinical utility of SPECT in neuropsychiatry is well established, and research devoted to its use in primary psychiatric disorders has been gaining momentum." Camargo (2001) wrote "Brain SPECT, in particular, with perfusion agents or with neuroreceptor imaging radiopharmaceuticals, is rapidly becoming a clinical tool in many places. The importance of this technique in nuclear medicine today should not be overlooked, particularly in cerebrovascular diseases, dementias, epilepsy, head injury, malignant brain tumors, movement disorders, obsessive-compulsive disorder, Gilles de la Tourette's syndrome, schizophrenia, depression, panic disorder, and drug abuse." Catafau (2001) concluded that

"brain perfusion SPECT has proven potential for patient management. SPECT has clinical value in the diagnosis, therapeutic management, and follow-up of patients."

Yet, the vast majority of physicians, especially psychiatric and substance abuse physicians, view functional imaging in clinical practice as experimental and something for the future after much more research is completed (Flaherty et al. 2005). It is the present author's opinion based on over 19 years of clinical experience with imaging that it is long overdue in clinical practice. Psychiatry remains the only medical specialty that rarely looks at the organ it treats. The lack of functional imaging data to help manage individual patients has kept psychiatry behind medicine's other specialties, decreasing its effectiveness and reinforcing the stigma that pervades mental illness. Nowhere is this more clear than in a substance abuse practice.

In experienced hands, brain SPECT imaging provides clinically useful information on how an individual's brain functions. It allows a more complete diagnostic picture, adding biological information about the presenting problem, and often helps to direct treatment, such as showing the need to enhance low perfusion areas or calming hyperactive ones.

So then why don't more psychiatrists and addictionologists use imaging in clinical practice? First, the clinical use of imaging is not a routine part of psychiatric or substance abuse training. Most physicians do not know when to order scans or how to use the information obtained. Doctors do not do what they are not trained to do. Another reason is the mistaken notion that brain imaging replaces physicians. Imaging should never be used alone to make a diagnosis or direct a treatment decision; but rather it is best used in the context of the whole evaluation, as an important piece of the puzzle.

Another misconception is that SPECT advocates want to perform imaging tests on every psychiatric or substance abuse patient. I think of SPECT like radar. On a clear day, radar is not necessary to land a plane. The runway is in sight. So too in psychiatry and substance abuse treatment, a careful evaluation can accurately diagnose many problems. However, radar is needed when it's stormy and there is trouble seeing the airport. SPECT imaging's best use is in complex or treatment resistant cases, where it can provide additional information, such as visualizing unidentified head trauma, early dementia, occult seizure activity, exposure to toxins, or impairment due to undisclosed drug or alcohol abuse. How do you know what is underlying a complex problem unless you look? Withholding imaging in unclear or resistant cases does an injustice to patients and may in fact harm them. Ineffectively treated neuropsychiatric disorders and substance abuse problems are expensive, hurtful and demoralizing.

Critics argue that brain imaging isn't ready for day-to-day clinical use because research has yet to find any structural or functional brain abnormality that is specific to a single psychiatric disorder (Küçük et al. 2000). These critics miss the point. Of course studies that use DSM-IV criteria as a gold standard for patient sele http://sz0159.ev.mail.comcast.net/service/home/~/Poster.tif?auth=co&loc=en&id=67200&part=2 ction will not yield a single pattern of abnormalities. That's why there are a wide range of treatments for individual diagnoses, as not every patient within a specific diagnosis responds to every treatment, and many standard treatments, such as methylphenidate or dextroamphetamine for ADHD children and adults, make many patients worse. Brain imaging evidence points to physiologic heterogeneity within DSM-IV diagnoses and SPECT helps in understanding the different types of disorders like depression, autism, OCD and ADHD, rather than diagnosing these entities.

TABLE 1
Functional Imaging Research Studies

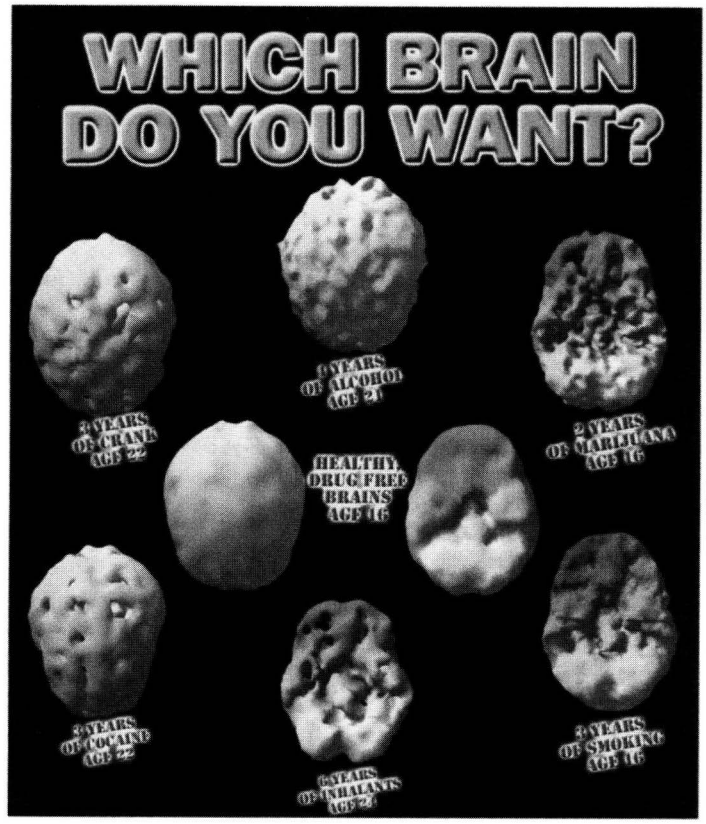
Condition	SPECT
Normal	82
ADHD	92
Autism Spectrum	93
Brain Trauma	95
Dementia	210
Drug and Alcohol Abuse	138
Epilepsy	253
OCD Spectrum	215
Treatment Effects	107
Violence	41
Total for These Categories Alone	1326

Another argument against imaging is that there are insufficient studies to interpret findings. Clearly much more research is needed, but there is a wealth of research studies to make reasonable assumptions about what different findings on scans may mean, such as hyperfrontality in obsessive compulsive spectrum disorders (Saxena et al. 1998) and deactivation of the prefrontal pole in ADHD (Amen, Hanks & Prunella 2008). There are literally thousands of peer reviewed imaging articles that provide a basis for interpreting findings (Amen Clinics, Inc. 2010). Table 1 shows a small sample.

Another widely held misconception is that the clinical use of SPECT is restricted by limited resolution (Kuperman et al. 1990). It has been called the "poor man's PET study." Early SPECT practice utilized single detector cameras that produced low resolution images, especially in deep areas of the brain. However, sophisticated multiheaded gamma detectors with fan beam collimators have been available for more than 15 years. George (1991) reports that multihead SPECT camera resolution is similar to PET at considerably less cost.

With adequate training it is also the author's opinion that functional brain imaging, particularly high resolution SPECT, has the potential to be clinically useful in at least nine different ways in a substance abuse practice. Before

FIGURE 1
Which Brain Do You Want?



these ways are explored here is a list of what SPECT scans cannot do.

WHAT SPECT SCANS CANNOT DO

1. SPECT scans cannot give a diagnosis in the absence of clinical information. Findings always have to be correlated to the clinical presentation. For example, low prefrontal cortex perfusion has been seen with ADHD, but is also seen with schizophrenia. Giving a schizophrenic patient ADHD medication can worsen symptoms.

2. SPECT scans cannot date a head injury. SPECT scans can give evidence of a past trauma, but it cannot tell when it occurred unless a prior scan was obtained.

3. SPECT scans cannot date a toxic exposure. SPECT scans can show evidence of toxic exposure, but it cannot tell when it occurred unless a prior scan was obtained.

4. SPECT scans cannot assess or evaluate IQ, although in the author's experience mental retardation is often associated with global decreases in perfusion (Kabakus et al. 2006).

5. SPECT scans cannot assess or evaluate the guilt, innocence, motivation or sanity of a criminal defendant, although SPECT has been used in court to give more information on the state of a defendant's brain and how the information might related to the crime.

SEVEN WAYS SPECT HAS THE POTENTIAL TO BE HELPFUL IN A SUBSTANCE ABUSE CLINICAL PRACTICE

1. SPECT Can Add Valuable Information to the Prevention, Evaluation, and Treatment of Substance Abusers

Substance abusers have demonstrated a number of cerebral perfusion abnormalities in brain areas related to behavior, especially in the frontal and temporal lobes. Psychoactive stimulants such as cocaine and methamphetamine have rapid uptake in the dopaminergic system of the basal ganglia, causing short-term cerebral activation. Volkow and colleagues (1993) evaluated 24 users of high-dose stimulants, and found that these subjects had significant decreases in dopamine receptors after long-term use of cocaine and methamphetamine. The authors reported that these decreases can cause acute and chronic disruptions of the orbital frontal system. Over time, many amphetamine and cocaine abusers display multiple cerebral perfusion defects on SPECT (Mendelson et al. 1995; Kao, Wang & Yeh 1994; Levin et al. 1994; Mena et al. 1994; Miller et al. 1992; Holman et al. 1991; Tumeh et al. 1990). Inhalants also demonstrate significant areas of hypoperfusion on SPECT (Ryu et al. 1998). Simultaneous use of multiple psychoactive drugs

has been shown by SPECT to have particularly detrimental effects on cerebral blood flow (Levin et al. 1994).

Three-dimensional SPECT images demonstrating brain damage from substance abuse may have a positive educational effect on deterring children and teenagers from drug abuse (see Figure 1). SPECT studies may also help to break though the denial that often accompanies substance abuse. When patients are faced with abnormal brain SPECT scans it may be hard for them to remain in denial. The effects of drug abuse are detected by SPECT, so that patients can see how their drug use has damaged their own brain function.

2. SPECT has the Potential to Help Clinicians Ask Better Questions

Harold Bursztajn, M.D., cofounder of the Psychiatry and Law Program at Harvard, says that SPECT scans do not give you the answer, they teach you to ask better questions (Bursztajn 2002). The results from a scan do not give a diagnosis per se, they are involved in the investigation of the problem. For example, if a brain injury pattern is seen but not given by history it informs the clinician to ask more pointed questions about brain injury, or if a toxic pattern is noticed it guides the clinician to explore further for any possibilities for toxicity.

H, age 44, had failed six drug treatment programs and was referred for a SPECT scan to help understand why. Her scan (Figure 2) showed a toxic pattern consistent with substance abuse, but it also showed clear evidence of a brain injury. Even though the patient initially denied any history of brain injury, on further detailed questioning she remembered falling off a horse at age ten and being knocked unconscious. The information on the past brain injury helped the family understand why she was having such trouble staying sober, and lead to more specific brain injury treatments.

3. SPECT has the Potential to Help Clinicians Give More Complete Diagnoses and Not Miss Important Clinical Information

Without imaging data clinicians may miss important pieces of biological information, such as brain injuries, toxic exposure, early dementia vulnerability, and potential seizure activity. Scans also show if there is hyperfrontality, hypofrontality or significant asymmetries in function. SPECT also helps physicians not miss anatomical lesions that may be contributing to the problems. I feel that starting with a SPECT scan is more practical than starting with CT scans or MRIs because functional data is also obtained. Here is an example.

J, 17, came for evaluation with extreme mood swings, suicidal and homicidal thoughts, and explosive outbursts. He had spent 18 months in a residential treatment facility at a cost of more than a $100,000 and had been evaluated by a number of psychiatrists and multiple mental health professionals and tried on multiple medications without success. He failed residential treatment. When he was discharged he entered into a drug treatment facility for 30 days, but used drugs the day he was discharged. The drug counselor recommended a SPECT scan.

His SPECT scan was severely abnormal (Figure 3), with a very large defect cyst occupying nearly 25% of the left prefrontal and temporal regions of his brain. Subsequently, an MRI revealed that he had a cyst the size of a tennis ball, causing a hemispheric shift and compression of ventricles. His neurological exam was normal.

As happened with J, most psychiatrists would diagnose him with bipolar disorder and conduct disorder, a prelude to antisocial personality disorder, and place him on medication. When he is treatment resistant, those treating him then wonder about his character and family environment. This all seems backwards. No amount of medication or family therapy will help this child until the pressure in his brain is relieved.

4. SPECT has the Potential to Help Evaluate Brain System Pathology in Individual Patients

One of the criticisms of SPECT is that it does not have signature patterns associated with each psychiatric illness. Yet, that is precisely the reason to order scans to learn about individual patient brains. It is useful to know how your patient's brain specifically works so that you can better target treatments to the areas of the brain that are abnormal. For example, in our work at the Amen Clinic we have found that there are at least six different types of ADD (Amen 2002) and seven different types of depression (Amen & Routh 2004). Giving someone the same treatment for these illnesses invites failure and frustration. For example, some patients with ADD have low prefrontal cortex perfusion, while others have low cerebellar perfusion; some patients with ADD have diffuse increased perfusion, while others have diffuse decreased perfusion. Some patients with depression are hyperfrontal, while others are hypofrontal. Some patients have anterior cingulate hyperperfusion, while others have hypoperfusion in that area of the brain.

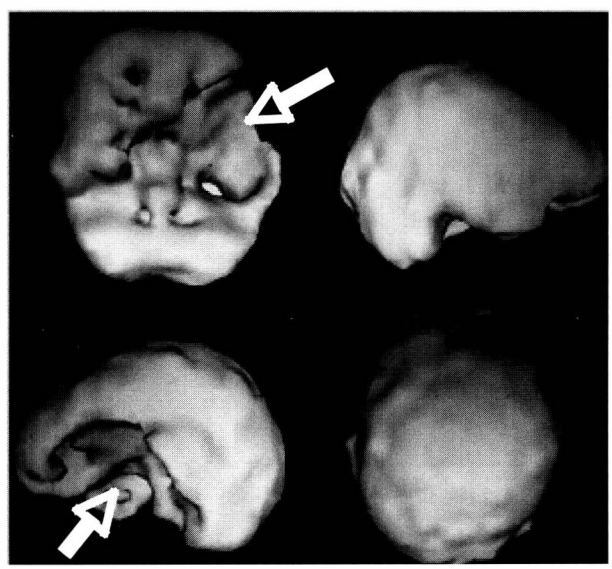
A study from UCLA on differentiating compulsive hoarders from checkers highlights this point (Saxena et al. 2004).

> The findings demonstrate how neurobiological testing [imaging] could improve diagnosis and treatment of psychiatric disorders. Lower activity in the anterior and posterior cingulate areas [rather than the typical high activity seen on OCD] may not only underlie compulsive hoarding symptoms, but also their poor response to standard treatments for OCD. The results suggest cognitive-enhancing medications commonly used in patients with age-related dementia may be more effective at treating compulsive hoarding behaviors than standard OCD medications such as serotonin reuptake inhibitors. . . . Our work shows that hoarding and saving compulsions long associated with OCD may spring from unique, previously

FIGURE 2
SPECT Scan Showing Toxic Exposure and Brain Trauma

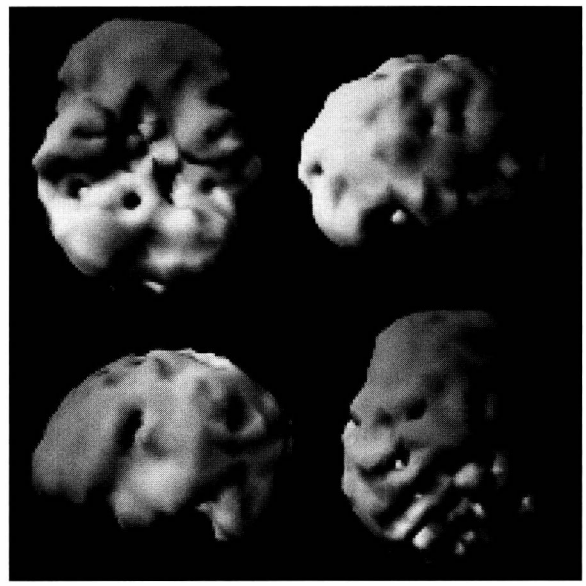
The Swiss cheese, shriveled appearance is consistent with toxic exposure, and marked decreased frontal perfusion is consistent with brain trauma.

FIGURE 3
Tennis Ball Sized Cyst Occupying the Left Prefrontal and Temporal Regions



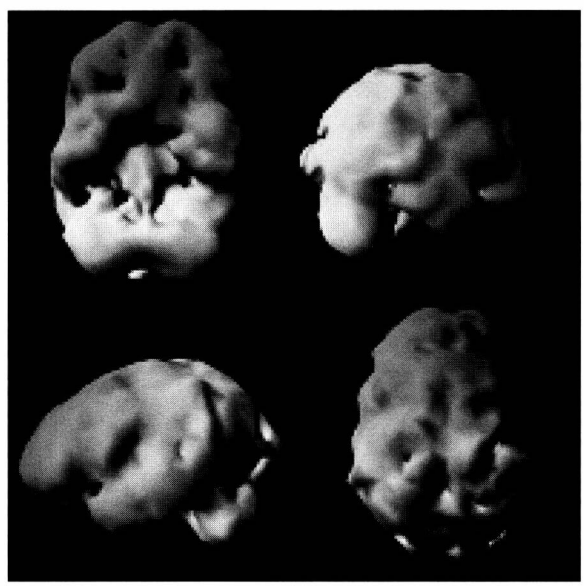
Large defect inleft hemisphere

FIGURE 4
Chronic Benzodiazepine Use



Decreased perfusion, scalloped appearance

FIGURE 5
Chronic Hydrocodone Use



Decreased perfusion, scalloped appearance

unrecognized neurobiological malfunctions that standard treatments do not necessarily address. . . . *In addition, the results emphasize the need to rethink how we categorize psychiatric disorders. Diagnosis and treatment should be driven by biology rather than symptoms.* [emphasis added]

5. SPECT has the Potential to Decrease Stigma and Increase Compliance

A SPECT scan helps patients develop a deeper understanding of their problems, see their problems from a

FIGURE 6
NFL Brain Trauma

Decreases in prefrontal and temporal lobes

FIGURE 7
After Fish Oil, Gingko, Huperazine

Improved perfusion in the prefrontal and temporal lobes

medical point of view and dramatically decrease shame, guilt, stigma and self-loathing. Scans also help increase self-forgiveness and the forgiveness and understanding of others. Patients can see that their problems are, in part, a medical problem and not moral or willful. SPECT scans are also powerful for families and help to mobilize them in a similar way as when medical illnesses, such as cancer or heart disease, are present. There is nothing else in psychiatry that results in such an immediate and strong intervention to decrease stigma.

A SPECT scan helps to increase compliance—pictures are powerful. These are very powerful influences in determining a patient's willingness and ability to accept and adhere to a treatment program, as they realize that not taking care of their brain or treating underlying illnesses is similar to not wearing the "right" prescription for their eyes.

6. SPECT has the Potential to Visualize How Effective Treatments are Working Through Follow-Up Scans

Follow-up scans can provide evidence of a treatment's effectiveness or ineffectiveness for both clinicians and patients. Once a plastic surgeon does a procedure he and the patient can visualize the outcome and see a positive or negative effect of the work. SPECT provides a similar opportunity. For example, one of the most important lessons learned from SPECT is that benzodiazepines, such as alprazolam or lorazepam, and opiate pain medications can have toxic effects on brain function (Figures 4 and 5).

This finding led me to strongly recommend using psychotherapeutic interventions such as biofeedback and hypnosis for anxiety, and alternative treatments such as acupuncture, fish oil and SAMe for pain syndromes if possible instead of benzodiazepines or pain medications to prevent this toxicity from occurring.

Follow-up scans also make clinicians more responsible. When a follow-up scan shows the patient's brain is worse, rather than blame the patient, clinicians can redesign the plan. Follow-up scans have also taught me that one treatment (such as stimulants or antidepressants or even natural supplements) does not work the same for every patient who suffers from a certain disorder. Psychostimulants, for example, stimulate the prefrontal cortex in some patients, while they cause deactivation of the prefrontal cortex in others. Knowing how a certain treatment or alternative intervention works in an individual patient's brain is useful clinical information.

7. SPECT has the Potential to Open the Mind to New, Innovative and Alternative Treatments

Another benefit to scans, and especially doing follow-up scans, is that they open the clinician's mind to new, innovative or alternative treatments. When a clinician can see the effect of omega three fatty acids, St. John's Wort, SAMe, GABA, gingko biloba, acupuncture, hyperbaric oxygen treatment, meditation, and psychotherapy (such as cognitive therapy or hypnosis) on functional imaging it adds more credibility and more excitement for these treatments and leads to an increase in their usage.

Here is an example:

AD is a retired NFL football player. He retired at the

age of 28 due to several concussions. Years later he came for evaluation to prevent the cognitive problems he saw in other retired football players. Figure 6 shows clear evidence of brain damage. Six months later on fish oil, gingko, and huperazine his brain looked much better (Figure 7) and he said he felt more energetic and was better able to focus and remember.

CONCLUSION

There is a converging body of literature and clinical experience on the usefulness of brain SPECT imaging in a number of areas relevant to psychiatric medicine. Some authors have written that it is unethical to order scans when there is not yet enough consensus or research on the clinical use of imaging (Bush 2008). This author believes that it is not only unethical to withhold potentially valuable information from clinicians, patients and families, it also hurts our profession and our society at large.

Still, there is much work to do to bring widespread use of brain imaging into clinical practice for substance abuse practitioners. The next two decades will see a radical shift in the way substance abuse treatment and psychiatry is practiced, and imaging will play an important role in the change.

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