

The Science Behind Brain SPECT Imaging and the Amen Clinics

By Daniel G. Amen, MD

Introduction

At the Amen Clinics we have been using brain SPECT imaging as an aide in making neuropsychiatric diagnoses and individualizing treatment plans since 1991. As I have said many times, SPECT does not give you the answer, it teaches us to ask better questions. It is an important piece of the clinical puzzle, but it is certainly not the whole puzzle.

In both medical school and during my psychiatric training at the Walter Reed Army Medical Center in Washington, DC I was taught to take a bio-psycho-social-spiritual approach to diagnosis and treatment for my patients. SPECT helps us gain a deeper understanding of the biological underpinnings of our patients' problems and then helps us formulate the biological part of our patients' treatment plans.

For example, SPECT helps us understand if an underlying head injury or toxic exposure may be contributing to our patients' problems. If a patient has an overactive brain, SPECT helps us make recommendations to calm the brain, where if a patient has an underactive brain I am more likely to make recommendations to help stimulate it. Always, the SPECT data needs to be correlated with the clinical information. SPECT is not a doctor in a box and will never replace a competent physician.

I started to order scans in 1991 on my patients after I attended a lecture on "brain SPECT imaging" at the psychiatric hospital where I worked in Fairfield, CA. Before that time I had been using neurofeedback and quantitative EEG in my clinical practice with my patients, so I was well primed to understand the implications of this new technology for psychiatry.

SPECT looks at blood flow and activity patterns. SPECT is different than CAT scans and MRIs, those are anatomy scans. They show what the brain actually, physically looks like. SPECT looks at how the brain functions. SPECT stands for single photon emission computed tomography. It is a nuclear medicine study that uses radioisotopes as tracking devices to look at living brain tissue. The radiation exposure from one SPECT study is 1/6th the level of radiation from an abdominal CAT scans, a commonly ordered procedure in medicine.

SPECT gives a three dimensional view of brain activity. Basically, SPECT measures three things:

- ◆ areas of the brain that work right,
- ◆ areas of the brain that are low in activity and
- ◆ areas of the brain that are high in activity.

Initially, I found the scans extremely useful, especially in complex cases. As I continued to use the technology in our very busy clinic and I knew functional imaging would become part of the future of psychiatry. The technology was just too useful.

Psychiatry is the only medical specialty that never looks at the organ it treats. Most psychiatrists today in 2008 make diagnoses the same way they did in 1840 when Abraham Lincoln was depressed, by looking for symptom clusters and talking with patients. I knew it was the wrong approach twenty years ago and it is even more scandalous today when we have useful techniques.

You can try to kill yourself in every major city in the world and virtually no psychiatrist will look at your brain. You can kill 6 people and prosecutors will argue to keep brain imaging information out of the court system. But I get ahead of myself.

By the early 1990s there were already hundreds of functional imaging studies (SPECT and PET, clinical cousins to each other) on Alzheimer's disease, head injuries, seizures, strokes, ADD, depression, substance abuse and schizophrenia.

Many of our critics claim there is no scientific basis for what we do. I initially heard this criticism with disbelief and wondered if these people had actually read the vast scientific literature on brain imaging. Each year more and more studies have been added. In 1992 Leonard Holman and Michael Devous wrote an article for the Journal of Nuclear Medicine titled "Functional brain SPECT: the emergence of a powerful clinical method." In the paper they outlined the science for using SPECT with vascular disease, seizures, dementia and brain trauma and suggested that many other uses would be available soon.

I kept ordering SPECT studies because they helped me be a better doctor with real patients. It wasn't something fun to do. I kept getting grief from my colleagues, who called me a quack, a charlatan and a snake oil salesman. This was not exactly why I went to medical school. It wasn't to make money. For the first 7 years of doing scans I never made any money order or reading SPECT scans. It was something that made me a better doctor.

Here is one of my favorite examples:

Matilda was brought to the hospital by her family after she nearly burned down her house by forgetting something on the stove. Her family was at their wits end. At age 69 she had been diagnosed with Alzheimer's disease and had been getting worse. She had also lost her driver's license because she had been in four minor accidents. Five of her six children thought she should be in a care facility for her own safety. One of her daughters, however, had heard about me and brought her to the hospital for more testing. "One more try," she told me. When I first met Matilda I thought she had Alzheimer's Disease, but the results of her SPECT scan were very different. She had good activity in the areas usually affected by Alzheimer's. Her scan was more consistent with depression. Sometimes in the elderly it can be difficult to distinguish Alzheimer's disease from depression, so I put Matilda on the antidepressant Wellbutrin. Within three weeks

Matilda's memory was better, she became more talkative and even started to help other patients on the ward. After a month I was ready to discharge her from the hospital. Everyone was so excited by her progress. Before she left she asked if I would write the DMV to help her get her driver's license back. I told her, "I drive on the same highways you drive. I need you to take your medicine, do the other things we discussed and if in 6 months you are still better and your scan is better than I will write the DMV. Six months later she remained improved. I repeated her SPECT study, which was now completely normal. I wrote the letter to the DMV and they gave her back her license! As a psychiatrist before I ordered SPECT scans I had virtually no experiences as powerful as this one. After I started ordering scans they started to happen regularly.

If you really knew me you would know I tend to be fairly anxious and I like people to like me. Stirring up this controversy was anything but fun. After 1993 when I received intense criticism from my colleagues I limited talking about our work in public for the next two years.

Then Andrew came to my clinic. It was late one night in April 1995 when my sister-in-law Sherrie called me at home to tell me that my nine year old nephew Andrew had attacked a little girl on the baseball field that day, for no apparent reason, out of the blue. Stunned, I asked her what else was going on with Andrew?

"Danny," she said, "he is different. He is mean and surly, and today I found two pictures in his room that he drew: in one picture he was shooting other children, in the other one he was hanging from a tree. I asked Sherrie to bring Andrew to see me the next day.

As I sat with him I said, "Buddy, what is going on?"

He said, "Uncle Danny, I don't know. I am mad all the time."

"Is anyone hurting you," I asked?

He said NO.

"Is anyone teasing you?"

He said NO.

"Is anyone touching you in places they shouldn't be touching you?"

He said NO. I don't know why I feel this way.

As part of his evaluation I ordered a SPECT study. I had suspected he had a problem in his left temporal lobe. The temporal lobes, which are underneath our temples and behind our eyes are very important structures in the brain involved with language, memory and mood stability. By 1995 researchers had already correlated some types of violence to this part of the brain. I held Andrew's hand while he had the scan. He held a teddy bear in his other hand. He was 9 years old.

On his scan Andrew was missing the function of his left temporal lobe. I had never seen anything like that before. He had a cyst the size of a golf ball occupying the space of his left temporal lobe. After Andrew's surgery to drain the cyst I got two phone calls. One, from his mother who said Andrew did great with the surgery and that when he woke up from the anesthesia he smiled at her. "Danny," she said, "he hadn't smiled at me for a

year.” The next call was from the neurosurgeon, Jorge Lazareff who said, “I am so glad you sent Andrew to me, the cyst had put so much pressure on Andrew’s brain that it had actually thinned the bone over his temporal lobe. If he would have been hit in the head by a baseball it would have killed him instantly. Either way, without the surgery he would have been dead within 6 months.”

Without the cyst pressing on Andrew’s brain he went back to being the sweet, loving boy he always wanted to be. Since Andrew’s surgery I couldn’t stop talking about what we did and the need to do imaging in psychiatry. Most of my colleagues, and me before doing our brain imaging work, would have found a psychological explanation to make sense of Andrew’s behavior and completely miss the real cause of his trouble.

That was no longer acceptable to me. I had to speak up. Since Andrew, we have seen 15 other children and adults with temporal lobe cysts who had problems with aggression. Kip Kinkle, the school shooter in Oregon who murdered his mom and dad and then shot 25 people at his high school had severe problems in the same part of the brain.

One of the Big Lessons

One of the most important lessons I learned early on from our imaging work is that most psychiatric illnesses, such as ADD, anxiety, depression, autism or bipolar disorder, are not single or simple disorders.

They all have multiple types. **This was the major reason why most researchers did not understand how useful imaging was in clinical practice.** Researchers would gather a group of ADD, bipolar or depressed patients and look for the underlying signature pattern for them on imaging. But when they did not find the pattern they declared imaging was not yet useful in psychiatry.

Yet, as a clinician I knew that giving people the diagnosis of depression is exactly like giving them the diagnosis of chest pain.

Why don’t doctors give people the diagnosis of chest pain? Because it is a symptom! There are too many different causes. What can cause chest pain? Heart attacks, heart arrhythmias, pneumonia, ulcers, hepatitis, grief, anxiety, reflux, being hit in the chest. Doctors do not give people the diagnosis of chest pain because it doesn’t tell you what causes it or what to do for it. Now, if you give everyone the same treatment for chest pain will some people get better? Yes, but for many nothing will happen or they will get worse.

The same thing is true for depression. It is a symptom with many different causes. One treatment does not fit everyone. What can cause depression? So many different things, from chronic stress, relationship problems, financial losses, head injuries, drug abuse, low thyroid, chemical imbalances, genetic tendencies and grief. On scans you can have too much activity in the front part of your brain and overthink or worry yourself sick. Or,

you can have too little activity in this part of the brain and have trouble thinking or controlling your impulses.

Depression is not one thing and giving everyone the same treatment for it invites disaster. Yet, that is exactly what is happening across our country everyday. No wonder psychiatric medications are controversial; they make some people better and a lot of people worse!

Many patients tell their doctor that they are depressed or anxious and leave the office after a 5 minute appointment with samples of the latest drug to treat depression, without any sense of the type of depression they are treating.

Here is an example.

Jan, a minister's wife left her family physician's office with a prescription for Prozac. She told him that she had been under a lot of stress and was feeling sad. Within three days Jan started to feel much better. After a week she was feeling really great.

While stopped at a traffic light, a man in a pick up truck pulled up beside her. He winked at her, as she was an attractive woman. That was not an unusual event for Jan. But what happened next was very unusual. Jan then proceeded to unbutton her blouse and show the man her breasts. Horrified at her own behavior she sped off, as the man tried to follow her. She had never done anything like that before. That is when she stopped the medicine and came to see me. When we scanned her, we found low activity in the front part of her brain, which is the wrong brain pattern for Prozac. This is the scan you see on the screen. Prozac and medications like it, lower activity in the front part of the brain. Prozac works well when that part of the brain works too hard and we can't let go of bothersome thoughts. It can be a disaster for people who start with low activity in this part of the brain because it will make them more impulsive, like Jan.

Knowing the type of depression, ADD, autism or bipolar disorder that you have is critical to getting the right help so that your treatment doesn't make you worse.

Research Based

Some of our critics say if what we do at the Amen Clinics is so good why haven't we published our work in the scientific literature? I scratch my head when I hear this because since 1993 my team and I have published 23 scientific articles on our work, including papers on ADHD, , predicting treatment response with stimulants, marijuana, aggression, murder, criminal recidivism, brain injury, EMDR and posttraumatic stress disorder, oppositional defiant disorder, before and after treatment response with clomipramine and Subtyping ADHD. We currently have papers under review for our work with suicide and comparing suicide and murder. In addition, I have written four book chapters on SPECT including one with Joseph C. Wu in the Comprehensive Textbook of Psychiatry on the clinical application of brain SPECT imaging, the most

respected psychiatric textbook in the world.

In addition to our own research, we list over 2300 scientific abstracts on a wide variety of neuropsychiatric conditions on our website at www.brainplace.com so that clinicians and researchers can see the incredible depth of scientific knowledge underlying the application of the imaging work we do.

For example, this abstract was published in the Journal of Nuclear Medicine by EE Camargo in 2001.

“Structural and functional images of the brain play an important role as powerful adjuncts in the management of an increasing number of neurologic and psychiatric diseases. Brain SPECT, in particular, with perfusion agents or with neuroreceptor imaging radiopharmaceuticals, is rapidly becoming a clinical tool in many places. For many neurologic and psychiatric conditions, this imaging modality has been used in diagnosis, prognosis assessment, evaluation of response to therapy, risk stratification, detection of benign or malignant viable tissue, and choice of medical or surgical therapy. 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.”

Or from Y Krausz and colleagues in the European Journal of Radiology in 1996.

“Brain imaging has become an integral part of the evaluation of neurological and psychiatric disorders. Functional imaging techniques, SPECT and PET, together with structural modalities, CT and MRI, are widely employed. Functional imaging studies are routinely used in the diagnostic workup of patients with well-characterized neurological disorders, such as epilepsy and brain tumors, and have a growing role in research on psychiatric disorders without known mechanisms such as depression and schizophrenia....”

The table below summarizes the depth of research on the major categories where we use SPECT at the Amen Clinics. You can find these research tables at www.brainplace.com.

Functional Imaging Research Table Summary with Emphasis on SPECT

Condition	# Patients	# Studies	SPECT
Normal	4,111	76	59
ADHD	1,988	92	43
Autism +	2,051	63	18
Brain Trauma	3,145	96	72
Dementia	13,261	210	210
Drug and alcohol	2,975	138	100
Epilepsy	7,382	253	253
OCD Spectrum	2,200	99	41

Treatment effects	2,695	107	107
Violence	1,468	41	14
Total for these categories alone	41,276	1,137	862

How Imaging Helps from our article Why SPECT

For physicians and mental health clinicians:

1. A SPECT scan shows the underlying cerebral blood flow and consequently metabolic activity patterns of the brain. A scan can show:
 - a. specific areas of the brain that are implicated with specific clinical problems, such as the prefrontal cortex with executive function and the medial temporal lobes with memory (2).
 - b. unexpected findings that may be contributing to the presenting problem(s), such as toxicity, potential areas of seizure activity, brain trauma, or brain pathology.
 - c. underlying potential seizure activity that may be contributing to the problem, more accurately seen by SPECT than standard EEG, especially in the areas of the medial temporal lobe.
 - d. specific target areas for treatment, such as an overactive basal ganglia, anterior cingulate gyrus (seen on anxiety and OCD spectrum disorders) or an underactive temporal lobe (seen in seizure disorders and other disorders such as brain trauma).
 - e. the specific effect of medication on the brain, and subsequently how to adjust medication dosages. Often patients report that SSRIs are helpful but also cause demotivation or memory problems. SPECT studies can show when SSRIs are causing excessive decreased prefrontal or temporal lobe activity that clinical evaluation only hints at.
 - f. how the brain actually functions on the specific medical treatment. See the many before and after scans at www.brainplace.com .

2. A SPECT scan's image occurs (as opposed to PET or fMRI) while the patient is sitting upright in an injection room, not while he or she is lying in the camera. Within 2 minutes of injecting the radiopharmaceutical for SPECT it locks in the brain where it stays fixed and measurable for 6 hours. Thus the SPECT image occurs in a more normal state (in the injection room), rather than while a person is lying in an MRI tube listening to what sounds like machine gun fire (MRI tubes are noisy and can be frightening) or a PET scanning device. Furthermore, PET images occur as isotope is slowly assimilated over a 30 – 45 minutes window of time. This is very different from a SPECT scan that locks in within a window of 2 minutes post injection.

Because the image occurs at the time of injection outside the imaging camera, it gives SPECT several significant advantages. Most notably, we are able to sedate people after they have been injected so that they can lie still for the scan and not affect the images. Often hyperactive or autistic children or demented adults have difficulty lying still for the scan, which is essential for a high quality scan (motion artifact ruins the scan in all of these imaging techniques). Furthermore with the 6 hour half life of the SPECT isotope we can easily retake films if we find motion artifact without further injection of isotope.

PET Isotopes are more radioactive and require shielding of the patient.

3. A SPECT scan helps **provide real, demonstrable answers to refractory symptoms and, in addition, helps clinicians ask** better and more targeted questions – about toxic exposure, brain injuries, anoxia, inflammation, or infection, that patients may have initially denied or forgotten.
4. A SPECT scan helps clinicians prevent mistakes or hurting patients by prescribing the wrong treatments, such as unnecessarily stimulating an already overactive brain or, on the other hand, unnecessarily calming an underactive one.
5. A SPECT scan can help evaluate those who may be at risk for dementia – the brain often shows changes before people have clinical symptoms of dementia. One study reported that there has to be a loss of 30% in the hippocampus before symptoms occur. Using autopsy data in 54 patients Bonte reported that brain SPECT had a positive predictive value for Alzheimer’s disease of 92%.
6. SPECT scans can also help to differentiate between types of dementia (Alzheimer’s disease, frontal temporal lobe dementia, Lewy body dementia, and multi-infarct dementia early in the disease each have their own patterns.
7. SPECT scans help clinicians understand why they use certain medications such as anticonvulsants to stabilize temporal lobe function or calm focal areas of marked hyperactivity, or stimulants to enhance decreased prefrontal perfusion, or SSRIs to calm basal ganglia and anterior cingulate hyperactivity.
8. A SPECT scan can identify specific areas of the brain hurt by trauma to better target treatment and help deal with insurance, legal and rehabilitation issues.
9. A SPECT scan **can** often demonstrate **a** specific brain malfunction that may contribute to recovering alcoholics, drug addicts, eating disordered or sexual addicts **relapsive behaviors**. **For example: the patient may have suffered an** injury in the prefrontal cortex or temporal lobes, or have overactivity in basal ganglia, limbic system, or prefrontal cortex, each of which could contribute to their relapsive behaviors.

10. A SPECT scan is also useful to determine if further adjustment of medication is needed. SPECT scans of patients already on medication can reveal areas of the brain that need to be further addressed for overactivity or underactivity.

For patients and their families:

1. A SPECT scan can help take modern psychopharmacology from mystery and unknown consequences to reality and more predictable outcomes.
2. A SPECT scan allows patients to have a specific physical representation of their problems that is accurate and reliable.
3. A SPECT scan helps develop a deeper understanding of the problem and leads to decreased shame, guilt, stigma and self loathing. Scans can increase self forgiveness. Patients can see that their problems are, in part, a medical problem.
4. A SPECT scan helps to increase compliance – pictures are powerful. Scans can provide a very powerful influence in determining a patient's willingness and ability to accept and adhere to a treatment program. They can realize that not taking medication for their problems of anxiety, depression, rage, ADD, etc. is similar to not wearing the "right" prescription for their eyes. Medication compliance becomes less an experiment, and more scientific.
5. A SPECT scan helps families understand when specific symptoms may not get better, such as having permanent brain damage from an injury. Such an understanding allows patients and families to accept the condition and work effectively with the measurable handicap.
6. A SPECT scan helps substance abusers decrease denial and become motivated for treatment by seeing the damage they have done to their own specific brain. A SPECT scan can help motivate recovering alcoholics and addicts continue in sobriety as it becomes clear to patients that further use will cause increased brain scalloping and further damage.
7. A SPECT scan physically shows patients how treatments have impacted (improved or worsened) brain function.
8. A SPECT scan helps motivate verbally and physically abusive spouses to follow medication protocols by seeing they have a physical abnormality that may be contributing to their problems.
9. A SPECT scan is useful for the patient that is post cancer chemotherapy and is suffering with "a chemotherapy toxic brain." It gives them insight into their cognitive struggles and may also help their doctors see the physical results of chemotherapy

problems as differentiated from the emotional, traumatic consequences of dealing with cancer.

10. A SPECT scan allows patients to understand why specific treatments are indicated, which medications are helpful, and why certain medical interventions are chosen.

As Clinicians at Amen Clinics:

1. We use SPECT in a clinical environment to observe patterns of activity, to guide us in re-balancing a brain whose activity patterns are clearly abnormal. Biology drives our pharmacologic recommendations.
2. A SPECT scan can guide us in the application of specific medications or other treatments such as supplements, neurofeedback, transcranial magnetic stimulation, and hyperbaric oxygen therapy.
3. We recognize the fact that SPECT is never the complete or final answer. It is part of the answer, that when used with a good clinical history and examination gives clinicians and patients more information for diagnosis and to tailor treatments to the specific patient.

What SPECT Scans Cannot Do

1. Give a diagnosis in the absence of clinical information
2. Give the date of a head injury
3. Give the date of an infection or toxic exposure
4. Assess or evaluate IQ
5. Assess or evaluate the guilt, innocence, motivation or sanity of a criminal defendant

Lots to Learn

There is no question that we have much to learn. This is the most exciting time to study psychiatric medicine because of all the medical professions we have the most potential for progress and meaningful change.

We at the Amen Clinics will continue to push for change and using imaging in psychiatry to better serve our patients.

Our biggest referral source over time has always been our own patients. That is gratifying because they are the ultimate judge of what we do to help people.

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