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On Psychiatric Treatment

AN UNBIASED MONTHLY COVERING ALL THINGS PSYCHIATRIC

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Neuroimaging: A Primer

Roll up your sleeves; this is a no-nonsense article, in which we will lay out for you all the neuroimaging modalities currently available, with a little explanation on how each works, and a tidbit or two on how it can (or can't) be used in psychiatry.

CT (Computed Tomography) Scan

What it is. If you shoot an X-ray through the brain, denser structures will impede (or "attenuate") the radiation more than less dense structures. The more of the X-ray that passes through, the more exposed, or darker, that part of the image. Bone is very dense, and blocks all of the radiation, so it looks white. Water is least dense, so CSF is dark on CT and brain parenchyma is in between.

Uses in Psychiatry. Few to none. The only time you might consider ordering a CT scan is in ruling out a tumor or a stroke in someone with an atypical psychiatric presentation, but even in these instances you should choose an MRI over CT if at all possible. ER docs use CT all the time because it's cheap, quick and good for picking up acute bleeding.

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Focus of the Month:
Neuroimaging in Psychiatry

Can PET Diagnose Alzheimer's?

If you haven't had patients asking you to order them a PET scan to diagnose Alzheimer's disease yet, brace yourself. It's only a matter of time.

PET scanning for AD was recently endorsed by no less august a figure than Charlton Heston (of "Ben Hur," "Ten Commandments," and, less gloriously, "Bowling for Columbine" fame), who announced in 2002 that he had been diagnosed with AD. Heston had evidently been won over by the Academy of Molecular Imaging, a professional group that is boosting PET scanning with almost religious zeal. The actor's endorsement was accompanied by a press release quoting UCLA's Daniel Silverman's claim that PET decreases false AD diagnosis "by almost half," and that using PET would lead to a "62% decrease in avoidable months of nursing-home care and a 48% drop in unnecessary drug treatment."

Sure, they're nifty; but do PET scans add real value to a competent clinical diagnosis?

With numbers like these, who wouldn't be sold on the technology?

While *TCR* hates to be a killjoy, the story on PET scanning for AD is quite a bit more complex than this. This article will guide you through this confusing landscape, and we will--sorry to say--be discussing such dreaded statistics as "sensitivity" and "specificity."

Studies have shown that a psychiatrist's conventional low-tech approach to diagnosing dementia is quite accurate. A clinical diagnosis of "possible or probable AD" has a sensitivity of about 90%, and a specificity of about 50% (for a review of these studies, see "Practice Parameter: Diagnosis of Dementia (An Evidence-Based Review)" *Neurology* 2001; 56:1143-1153).

"Sensitivity" is defined as the proportion of true cases picked up by the diagnostic procedure. Thus, a 90% sensitivity means that you pick up most of the

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Learning objectives for this issue: 1. Recall the different types of neuroimaging techniques. 2. Describe the evidence for and against the use of PET scanning in Alzheimer's disease. 3. Cite the major regions of the brain of relevance to psychiatrists.

This CME activity is intended for psychiatrists, psychiatric nurses, and other health care professionals with an interest in the diagnosis and treatment of psychiatric disorders.

Neuroimaging: A Primer

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MRI (Magnetic Resonance Imaging)

What it is. Put a brain in a strong magnetic field, and the protons of the hydrogen atoms will align in the direction of that field. An MRI signal ("radio pulse") disturbs that alignment, and as the protons realign themselves with the magnetic field, they release energy. This energy, analyzed and transformed by computers, is the basis for the images we see in an MRI. By controlling the type of radio pulse delivered, the MRI tech can "interrogate" different types of tissues. Thus, "T-2 weighted images" are best for picturing water, which looks white on the film. Since most brain pathology involves edema, T-2 images are preferred for detecting pathology, while T-1 images are better for normal anatomy.

Uses in Psychiatry. Debatable. Early research led to excitement about "white matter hyperintensities" in psychiatric patients, but later studies found these same blips in normal brains. At this point, the main use of MRI is to exclude potentially reversible causes of psychiatric symptoms (such as tumors and normal pressure hydrocephalus). However, the yield is extremely low. In a survey of 6200 psychiatric inpatients at McLean Hospital, 99 patients, or 1.6%, had MRI findings that might theoretically have led to a change in clinical management (Renshaw PF, Rauch SL: Neuroimaging in clinical psychiatry. In: Nicholi AM, Jr, ed. The Harvard Guide to Psychiatry, Third Edition. Cambridge, Massachusetts: Belknap Press; 1999.) A shotgun approach to ordering MRIs is likely to lead to coincidental findings of unclear significance that might lead patients down a road of unneeded diagnostic procedures. Most authorities limit their MRI recommendations to the following scenarios: pre-ECT workup, atypically late age of onset of a psychiatric condition, history of head trauma, presence of delirium, and focal neurological signs accompanying psychiatric symptoms.

PET (Positron Emission Tomography)

What it is. See this issue's interview with Dr. Darin Dougherty for plenty of PET information. PET scanners use radioactive isotopes to measure metabolic activity or to identify neurotransmitter receptor sites. The downside of PET is that you need an on-site cyclotron, a very large and expensive ($2 million) machine that allows you to accelerate protons and smash them into target atoms in order to create the isotopes required for PET scanning.

Uses in Psychiatry. At this point, there is no reimbursable use of PET scan in psychiatry. In neurology and oncology, PET is covered for localizing the focus of a seizure before planned neurosurgery and for diagnosing and staging most cancers. Many researchers believe that it should be approved for early diagnosis of Alzheimer's Dementia, but the data are not yet compelling enough to convince either *TCR* or the Gods of Medicare (see the article in this issue).

SPECT (Single Photon Emission Computed Tomography)

What it is. SPECT can be thought of as PET's poorer cousin. Like PET, it depends on radiopharmaceuticals to detect brain activity, but it measures photons shot in one direction rather than gamma rays shot in two directions. This means that SPECT cannot produce the same degree of spatial resolution as PET. On the positive side, SPECT scans are cheaper, because they can use isotopes with longer half-lives, and therefore don't require an on-site cyclotron.

Uses in Psychiatry. Like PET, there are no reimbursable uses in psychiatry.

fMRI (Functional Magnetic Resonance Imaging)

What it is. This is an adaptation of basic MRI techniques that uses a measure of blood oxygenation to visualize blood flow and neuronal activity. Unlike PET, which does basically the same thing, fMRI is noninvasive, and therefore easier to perform and less risky for patients.

Uses in Psychiatry. There are no clinical uses in psychiatry, but it is used frequently in research. One of the more fascinating fMRI experiments was one published recently in *Science*, in which subjects were given a list of words and then asked to suppress the memory of certain words. fMRI was used to identify the neural substrate of suppression; perhaps predictably, many prefrontal brain regions were more active during memory suppression than retrieval (*Science* 2004 Jan 9; 303:232-5).

MRS (Magnetic Resonance Spectroscopy)

What it is. MRS measures brain chemistry safely and noninvasively. The technique allows you to measure levels of specific compounds in specific brain regions. Each compound has its own "frequency signature," and amazingly enough, MRS can detect these compounds without the need to inject any radioactive tracers.

Uses in Psychiatry. No approved clinical uses yet, but you'll start to see more and more studies reporting levels of various compounds in the brains of patients with various disorders. Understanding these results, however, is not for the biochemically faint of heart. A recent study, for example, found elevated lactate levels in the gray matter of medication-free patients with bipolar disorder. The authors concluded that the findings "suggest a shift in energy redox state from oxidative phosphorylation toward glycolysis" (*Arch Gen Psychiatry*. 2004;61:450-458). Toto, I have a feeling we're not in Kansas anymore. ❖

TCR VERDICT:

Neuroimaging: Use it for Ruling Out, Not for Ruling In

Neuroanatomy: A Very Short Course

Five of the last six covers of the *American Journal of Psychiatry* have been chock-full of brains. We have learned from these issues that depressed patients have lower hippocampal volumes (*Am J Psychiatry* 2004 161: 598-607), that schizophrenics have "a pattern of prefrontal cortex underactivation and parahippocampal overactivation" when recognizing words (*Am J Psychiatry* 2004 161: 1004-1015), and that long term abstinence from methamphetamine abuse normalizes metabolism in the thalamus but not in the striatum or nucleus accumbens (*Am J Psychiatry* 2004 161: 242-248).

While these articles are of dubious clinical relevance for practicing psychiatrists, they do have the effect making us feel inferior to neurologists and the small cadre of academic psychiatric researchers who actually understand this stuff. And that may be a good thing, because it motivates us to bone up on our neuroanatomy, knowledge that impresses our patients as we try to convince them to take their meds.

What follows is a very basic neuroanatomy course for psychiatrists.

Weighing in at about 3 pounds, we all have **brains**, which are composed of the **forebrain** (two hemispheres, four lobes, and subcortical structures--more details below), the **midbrain** (part of the brainstem--cranial nerves, substantia nigra for dopamine, and the raphe nucleus for serotonin), and the **hindbrain** (the pons and cerebellum--cranial nerves and balance and the locus coeruleus for norepinephrine). The forebrain is where most of the action is in psychiatry, so we'll focus on that. It's covered by a 4 mm layer of **cortex** that is composed of nerve cell bodies, also known as **gray matter.** Axons connect to the interior from the cortex; they are covered with a white fatty myelin sheath, and make up the **white matter**. The cortex is very wrinkled in order to fit our billions of neurons into a small skull; if ironed out, it would cover a king-sized bed. Don't try that at home.

The folds of the cortex are **gyri** and the creases are **sulci**. The **central sulcus** is a nice landmark, as it separates the fontal lobe from the parietal lobe. The strip of cortex in front of the central sulcus is the **motor strip** (remember the motor homunculus with the giant hand?) and the strip behind it is the **somatosensory strip**.

Now, to **lobes**. Lobes are big chunks of brain, and are somewhat arbitrary ways of dividing something very complicated into four regions. The **frontal lobe** is the neuro-superego. The **"frontal cortex"** is not the same as the **"frontal lobe,"** rather, it just refers to the gray matter covering of the lobe. The **prefrontal cortex** is the most forward part of the frontal cortex; prefrontal lobotomies (no longer done) and prefrontal strokes cause a variety of **frontal lobe syndromes**, such as disinhibition, inappropriate behavior, and apathy.

If you read too many psychiatric journal articles, you will come across confusing terms denoting various parts of the frontal cortex, including **"orbital gyrus"** (a fold of the FL above the eyes) and **"cingulate gyrus"** (a fold tucked away in the medial part of the FL).

The **temporal lobe** is an overachieving lobe and as a consequence is always mentioned. The famous **Wernicke's** area (receptive aphasia) area is on the cortex, and tucked deep in the **medial temporal lobe** is the **limbic system** (LS). The LS is particularly confusing because researchers find another brain structure connected to it yearly, so it's quite the moving target to learn. It's the emotional circuit, and it includes the **amygdala**, the **hippocampus**, the **mammilary bodies**, the **thalamus**, the **parahippocampal gyrus** (just a fold of temporal cortex next to the hippocampus), and maybe even the frontal lobe's **cingulate and orbital gyri**. A threatening stimulus is first perceived by our senses, then gets transmitted to the thalamus (our sensory switchboard), then on to the amygdala, which judges the degree of danger and can send a quick message to the motor strip to MOVE. The amygdala is conveniently located next the memory-rich hippocampus, allowing for quick scanning of the memory banks to assess degree of danger.

Ah, the **basal ganglia**. It's mostly for control of movement, but it gets involved in emotions too. It comprises the **striatum** (the **caudate** plus **putamen**), the **globus pallidus**, and the **nucleus accumbens**. It gets degenerated in Parkinson's disease, and it's famous for causing EPS (extrapyramidal symptoms) as a result of over-exuberant dopamine blockade from antipsychotics.

Oh--almost forgot the **parietal lobe**, good for fine-tuned sensation, and the **occipital lobe**, great for vision.

Phew! Done. Simplistic? Sure. But I'm no brain surgeon! ❖

Q&A With the Expert

This Month's Expert:

Darin Dougherty, M.D., M.Sc.
On Research in Neuroimaging

Assistant Professor of Psychiatry, Harvard Medical School
Assistant Director, Psychiatric Neuroimaging Group
Massachusetts General Hospital

Financial Disclosure: Dr. Dougherty has disclosed that he has no significant relationships with or financial interests in any commercial companies pertaining to this educational activity.

TCR: Dr. Dougherty, it looks like you've now literally "written the book" on neuroimaging in psychiatry (Essentials of Neuroimaging for Clinical Practice, Dougherty, Rauch, and Rosenbaum, eds., Wash D.C.: APPI, 2004). Congratulations! How did you get interested in this field, originally?

Dr. Dougherty: When I was a medical student at the University of Illinois I worked in a lab labeling receptors in rat brains, and then when I came to Mass General for psych residency, I learned that you can use PET and SPECT to look at receptors in vivo and I thought, "Wow that is really cool." So after residency I did a two-year research fellowship in radiology and nuclear medicine, and I've been doing research ever since.

TCR: I know that neuroimaging is a huge topic, but perhaps we could start with PET scanning, which has gotten plenty of press lately. How does the PET scan work exactly, in not too complicated terms?

Dr. Dougherty: It isn't like a CT scanner that creates radiation and shoots it through you. You have to actually inject the patient with a radioactive tracer which is then detected by the scanner. Usually, this tracer is a form of glucose labeled with an unstable isotope of fluorine (F-18), and it's abbreviated "FDG." FDG goes wherever glucose normally goes, and the scanner detects the radiation.

TCR: OK, but PET stands for "positron emission tomography." You haven't even mentioned positrons--how do they get involved?

Dr. Dougherty: F-18 and other unstable isotopes release positrons which are just very small subatomic, positively-charged particles, sort of the opposite of electrons. Very quickly, the emitted positron finds an electron and they smash into one another, causing what is called an "annihilation event." Gamma rays then shoot off in opposite directions from this little apocalypse, and that is what the PET camera detects.

> **"Researchers have found that in depression, the limbic system in the brain tends to be hyperactive, while the higher cortical areas tend to be under-active."**
>
> **— Darin Dougherty**

TCR: So PET imaging allows you to detect where the most glucose metabolism is taking place at any given time.

Dr. Dougherty: Exactly. For example if you had someone do a visual task and then took a picture, you would see a lot of visual cortex activity compared to the rest of the brain. Or if someone squeezes a tennis ball with the left hand, you would see the right motor strip light up.

TCR: How is PET changing how we conceive of depression?

Dr. Dougherty: PET has helped us understand which brain regions are affected in depression. In simplistic terms, what researchers have found is that the limbic system in the brain tends to be hyperactive, while the higher cortical areas tend to be under-active. We all have strong affective experiences throughout the day, but most of us have a good functioning cortex to squelch much of this, allowing us to go about our business. But in depression, you have a double whammy in which your limbic system is heightening affective experience, but your cognitive cortical areas are not as well prepared to dampen that, so you get hit from both sides.

TCR: A recent study in *Archives of General Psychiatry* has gotten a fair amount of press in which researchers PET-scanned patients who had recovered from depression and found differences between those who took medications versus those who improved with cognitive behavior therapy alone.

Dr. Dougherty: Right, and in that study the antidepressant seemed to have its effect by dampening the limbic system, whereas the cognitive therapy seemed to increase metabolic activity in the dorsal cortex. But it seems that repair of either brain region reciprocally leads to repair of the other area as well. So for treating depression, you have the choice of coming in from the

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Q & A With the Expert

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"bottom" (the limbic system) with meds or from the "top" with cognitive behavioral therapy--or most ideally, with both.

TCR: You've also done research using PET to visualize receptor occupancy for neurotransmitters. How is this work affecting our view of the neurobiology of depression?

Dr. Dougherty: We have found that the conventional idea that there are abnormalities of serotonin, norepinephrine, and dopamine in depression is probably true. But PET is allowing us to pinpoint exactly how these abnormalities arise.

TCR: Okay, let's talk about serotonin. The simplistic view is that depression is a disorder of low levels of serotonin.

Dr. Dougherty: Right, and the prediction was that this would lead to a higher density of receptors because of upregulation.

TCR: So when there is low serotonin, the brain responds to that by synthesizing more receptors because it's kind of "thirsty" for more serotonin.

Dr. Dougherty: Exactly. There are more receptors on the receiving neuron, so those receptors have a better chance of being hit by the little serotonin that is there. Up until recently, however, the studies weren't really supporting this theory.

TCR: So how are the newer PET techniques helping us to understand this issue?

Dr. Dougherty: We are now developing specific ligands that can attach to different subclasses of serotonin receptors. There are some fourteen different receptor subclasses of serotonin and different drugs we use affect different parts of the serotonin system. For example, BuSpar affects 5HT1A, the SSRIs affect the reuptake pump, nefazodone affects 5HT2 in addition to the reuptake pump. All of these drugs work a little differently. And what has been interesting is that many of the earlier studies were using ligands to look at 5HT2 receptors, and they were finding that depressive cohorts didn't differ much from controls in the density of 5HT2 receptors.

TCR: A finding that directly contradicts the idea of receptor upregulation in depression.

Dr. Dougherty: Right. The problem was that most of the ligands being used in these studies were for 5HT2A and 5HT2B. But now there is a whole new branch at the NIMH just to develop new ligands for use in PET imaging studies. And there are new ligands to look at other parts of the serotonin system like the 5HT1A receptor, which--in contrast to 5HT2--shows huge differences between depressives and controls. So the research is still rather nascent, but we are beginning to be able to tease apart what components of the neurotransmitter systems may be disordered in depression.

TCR: You also do some work with OCD, and I know there are some interesting PET findings there as well.

Dr. Dougherty: The PET findings in OCD have been replicated so many times that the neurocircuitry of the disease is now pretty clear. And what is going on essentially is that OCD patients have hyperactivity in the orbital frontal cortex, the caudate, the thalamus, and the anterior cingulate cortex. All of these areas are connected via a circuit, and the whole circuit is hyperactive. When I treat patients, I use the analogy of a treadmill that is going too fast and I explain that treatment slows down the treadmill enough so that patients can step off it. Neurologically, this is in fact what happens--the degree of hyperactivity in the orbital frontal cortex gradually normalizes, and this correlates with subsequent response to both behavioral therapy and medication. OCD as a disorder is probably the star in terms of psychiatric illnesses in which we have really been able to tease apart the neurobiology.

TCR: Alzheimer's dementia is another area in which there are some promising PET findings. We review some of the studies on this in another article in this issue, but can you describe some of the typical PET findings in patients with AD?

Dr. Dougherty: In AD you get decreased metabolism in temporal and parietal areas first, and then it gradually moves forward into the frontal regions. The areas that are spared are the somatosensory cortex on each side. So in the worst cases you have what is called the "earmuff sign" because as you look at the brain the only areas that are lit up correctly are the two somatosensory cortices.

TCR: And radiologists have enough experience with normal PET patterns that they can fairly easily recognize a pattern suggestive of AD?

Dr. Dougherty: Yes they can, and while the sensitivity and specificity aren't perfect, patients sometimes pay for these scans out of pocket, and I expect that sometime in the not too distant future insurance companies will pay for them as well.

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Can PET Diagnose Alzheimer's?

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genuine AD patients you see, allowing very few patients to go undiagnosed. "Specificity" is a measure of the *precision* of your diagnosis. A specificity of only 50% means that half of the patients you diagnose as having AD don't actually have it. You're being overly inclusive, and you generate a lot of "false positive" diagnoses.

Is this such a bad thing? Not necessarily. By far the majority of the patients you've falsely diagnosed with AD have some other form of dementia, usually vascular dementia, and often some mixture of AD, vascular dementia, and Lewy Body Disease (*J Am Geriatr Soc* 1999; 47:564-569). The evidence is increasingly clear that all such patients benefit from immediate treatment with cholinesterase inhibitors, so the false AD label is unlikely to harm them in any way.

Now, the question we have to ask about PET is: Does a $1,500 PET scan add anything of value over and above what we can accomplish with the conventional workup?

The largest study reported to date relevant to this question involved 284 patients who were PET-scanned as part of the evaluation of cognitive deficits between 1984 and 1998 (*JAMA* 2001; 286:2120-2127). At least two years of clinical follow-up was obtained (via chart review) on about half of these patients (the UCLA portion of the study); the other half were treated at other sites, both in and out of the U.S., and researchers obtained autopsy data on these patients.

A nuclear medicine specialist read all the scans (he was, of course, blinded to the eventual outcome) and divided them into two categories: 1. "progressive scans" (a scan indicating dementia of some type) and 2. "nonprogressive scans" (no abnormal findings or nonspecific findings such as generalized cerebral atrophy).

How good were these two categories at predicting subsequent decline and diagnosis? Let's look first at the 146 patients who were followed clinically at UCLA, and for whom we do not have autopsy data. Of these 146 patients, 86 of them subsequently experienced some type of dementia over an average of 3.2 years of follow-up. Researchers had correctly put 78 of those 86 PET scans in the "progressive" pile, for a diagnostic sensitivity of 91%. Thus, based on PET findings alone, 8 of 86 patients would have been falsely reassured that their memory would not get worse (i.e., false negative rate of 9%).

What about specificity? Of the 60 patients whose memory held steady over three years, PET correctly predicted 45 of them (specificity 45/60=75%). This means that 15 patients would have falsely been given the nasty news that the brain scan indicated that they had dementia (25% false positives). The autopsy portion of the study produced similar figures. At autopsy, 97 patients were diagnosed with AD. PET predicted 91/97 = 94% of these, and correctly predicted no AD in 30/41 = 73%.

So how do we interpret these figures? How likely is it that PET scan data added something of value to these patients's subsequent management? Well, the patients who had true dementia would likely have been picked up by a standard clinical exam anyway (since the sensitivity is comparable to PET). Scan or no scan, they would have received a prescription for a cholinesterase inhibitor and been scheduled for follow-up in a month.

The patients whose scans accurately predicted lack of dementia could breathe a $1,500 sigh of relief. But we psychiatrists can produce that same sigh much more cheaply with a careful clinical exam.

Where PET scans caused problems was for those 15 "false positive" patients whose scans were read as indicating dementia but who turned out to be fine 3 years later. In clinical practice, patients whom we falsely label AD generally have another type of dementia, so the treatment they get is actually helpful, despite the misdiagnosis. But PET has a nasty habit of finding AD-like perfusion defects in cognitively normal people. Thus, PET risks causing a lot of normal patients to become extremely anxious, not to mention leading to unnecessary further workup and medication. So even though there are fewer false positive diagnoses with PET scan, they are clinically more significant.

It appears, then, that PET scans are not yet "ready for prime time," an opinion seconded by the Agency for Health Research Quality (AHQR), which just concluded that PET does not add significant information to a competent clinical exam (http://www.cms.hhs.gov/coverage/download/ADTAFinalReport-042904-2.pdf). This federal opinion constitutes a death knell for those seeking Medicare coverage for PET in evaluating AD.

It's too bad. Those images sure are pretty. ❖

TCR VERDICT:

PET Scans: Too Much Bad News for the Absent-Minded

Tales from the History of Psychiatry: The First MRI

In 1977, Raymond Damadian and a team of graduate students put together the first whole-body MRI scanner, which they dubbed the "Indomitable." Damadian volunteered himself as the first guinea pig. With veiled trepidation, he sat down on the movable platform inside his shiny, 1 1/2-ton contraption and turned it on. After hours of tinkering, there was no signal. Eventually it occurred to the team that Damadian's corpulence might be preventing the creation of an image, and, with disappointment, they called a halt. For seven weeks after the test, graduate student Larry Minkoff keenly monitored his boss, watching for any odd behavior or ailment. Detecting none, he offered his own, leaner, torso to science. On July 3, 1977, nearly five hours after the start of this test, Indomitable achieved the first human scan and became the first MRI prototype.

Source: http://www.smithsonianmag.si.edu

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Please identify your answer by placing a check or "X" mark in the box accompanying the appropriate letter.

1. The main difference between PET and SPECT is:
- [ ] a. Only SPECT can accurately diagnose Alzheimer's disease.
- [ ] b. PET requires an on-site cyclotron, while SPECT does not.
- [ ] c. SPECT releases more radioactivity.
- [ ] d. Only PET is reimbursed by Medicare for psychiatric indications.

2. A true statement about fMRI is:
- [ ] a. It requires the injection of tracers.
- [ ] b. It is more like CT than MRI.
- [ ] c. It is used for measuring neurotransmitter receptor density.
- [ ] d. It provides similar information as PET but is non-invasive.

3. PET and clinical judgement are of comparable sensitivity for diagnosing Alzheimer's disease.
- [ ] a. True [ ] b. False

4. The orbital gyrus is:
- [ ] a. A component of the basal ganglia.
- [ ] b. A part of the frontal cortex.
- [ ] c. The center of dopamine production.
- [ ] d. Located in the midbrain.

5. The limbic system includes both the amygdala and the basal ganglia:
- [ ] a. True [ ] b. False

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This Month's Focus:
Neuroimaging in Psychiatry

Next Month in *The Carlat Report*: Pain and Psychiatry, including articles on fibromyalgia, pain meds, and how to dose antidepressants for pain relief.