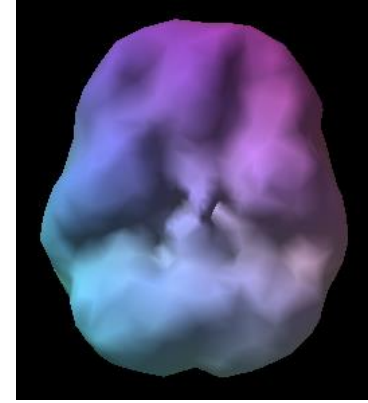




The Role of Neuroimaging in Psychiatry and Addiction Medicine

Robert Johnson, DO

Medical Director, Amen Clinics

Diplomate, American Board of Psychiatry and Neurology

Diplomate, American Board of Addiction Medicine

Bo Adler, On His Sleep Apnea Options :

“First they were going to cut out my tonsils, and if that didn’t work, they would break my jaw and reset it to reposition my tongue, and finally they would cut out the roof of my mouth.”

Sleep Apnea Options (cont)

“I had one question: ‘What if my case is *different*?’

They said, ‘Let’s try the standard course of treatment first, and if that doesn’t work, then we’ll *know* your case is different.’”

Sleep Apnea Options (cont)

What this proposal really meant:

- His doctors *wanted* to see him as a standard case, because they have assessment and treatment methods for standard cases
- They had no cure for ‘different’

But before he underwent surgery, Bo wanted some evidence that his *was* a standard case.

How often do we treat psychiatric cases as standard because of our limited ability to objectively determine 'different' ?

Why Do Neuroimaging?

“The DSM-IV has 100% reliability and 0% validity. We need to develop biological markers to develop the validity of these disorders... We can use neuroimaging to begin to identify the systems pathology in these disorders, so that treatments can go after the core pathology.”

Thomas Insel, Director of NIMH
APA Meeting 2005

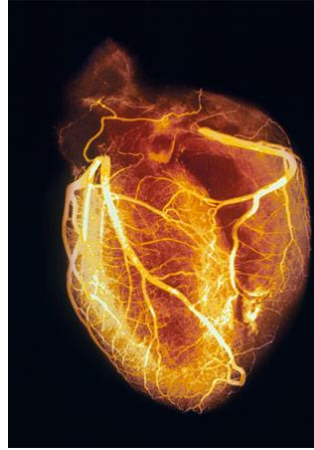
Without Imaging

- Diagnoses still made similar to how Lincoln was diagnosed with depression in 1840
- DSM is hurting us, because it is not based on underlying physiology



Psychiatrists only medical specialists who rarely looks at organ they treat

- **Cardiologists look**
- **Neurologists look**
- **Orthopedists look**
- **All other specialties look**
- **Psychiatrists... guess**





Why Do Neuroimaging?

The Truth

- Virtually all the major psychiatric illnesses (Bipolar Disorder, Major Depressive Disorder, ADHD, Autism, etc.) likely have **multiple etiologies** and **multiple subtypes**.
- **These are not single, simple, or standard disorders!**

Why Do Neuroimaging?

“Recent advances in in-vivo brain monitoring techniques such as fMRI and SPECT make it possible to visualize brain abnormalities in humans and animals... These exciting developments have translational potential to contribute to our understanding of depression and its treatment.”

From “Next Generation Antidepressants: Moving Beyond Monoamines to Discover Novel Treatment Strategies for Mood Disorders”, 2010, edited by Stahl and Beyer

Why Do Neuroimaging?

“Regarding MDD... the current classification criteria encompass a heterogeneous mix of illnesses that share similar final pathways likely reached via multiple pathophysiological processes.”

Berghorst & Pizzagalli, 2010, “Defining Depression
Endophenotypes”

Why Do Neuroimaging?

- Giving someone the standard diagnosis of “Major Depressive Disorder” is exactly like giving them the diagnosis of “chest pain” - it is a ***symptom***, not a diagnosis.
- What can cause chest pain? Heart attacks, arrhythmias, pneumonia, ulcers, hepatitis, grief, anxiety, GERD, trauma to the chest...

Why Do Neuroimaging?

- Treating Symptoms: If you give everyone the same treatment for chest pain will some people get better?
- Yes... but for many nothing will happen, and some will get *worse*
- The same is true for depression. It is a **final common pathway symptom with many different causes** (Vit B deficiency, TBI, malnutrition, substance abuse, hypothyroidism, grief/loss, anemia, pancreatic cancer, etc.)

Why Do Neuroimaging?

“With the advent of imaging technologies, it is now possible to conduct in vivo evaluations of biomarkers in “functional” psychiatric disorders... through this technology, it is possible to evaluate the underlying neurological changes at a systems level and evaluate the therapeutic response to treatment.”

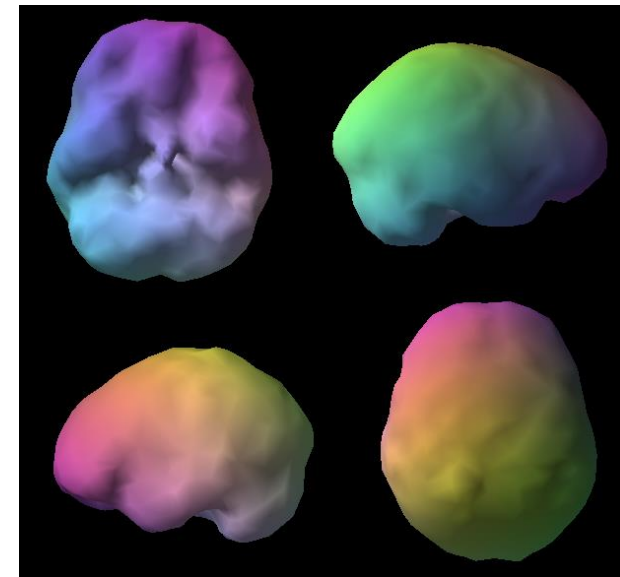
Shamy et al, 2010, “Translational research in mood disorders: using imaging technologies in biomarker research”

Why Don't We Look?

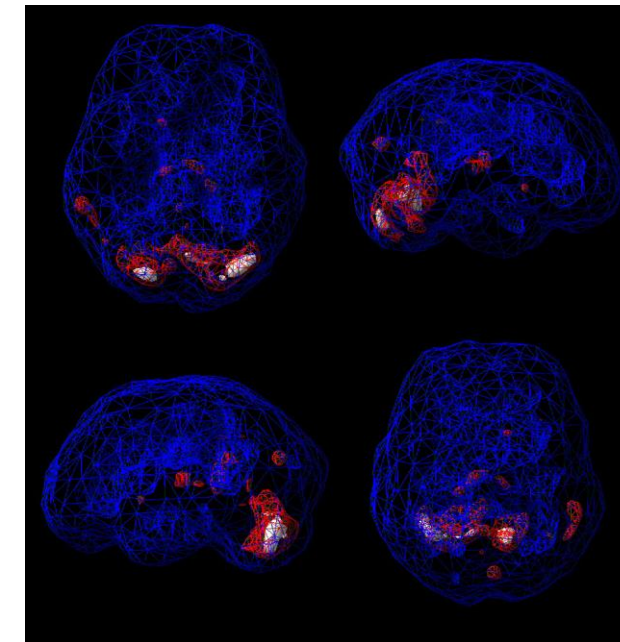
- Imaging is not part of our training or tradition
- There are residency programs (UCI, UCLA, others) who now teach residents how to order and interpret scans
- Conversation with Laszlo Mechtler, MD, American Society of Neuroradiology

SPECT

- **Single photon emission computed tomography**
- **Radioisotope, Tc99, + HMPAO or ECD**
- **Measures rCBF and activity**
- **Gives three pieces of information: good activity, too little, or too much**

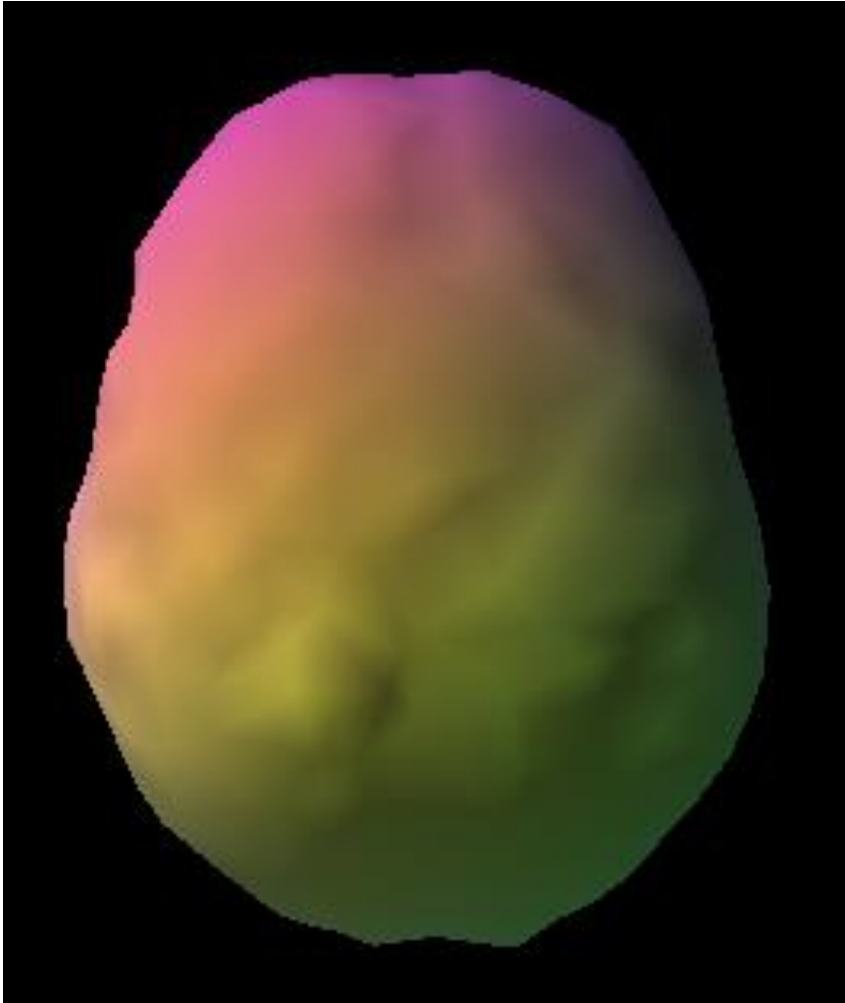


Healthy surface view

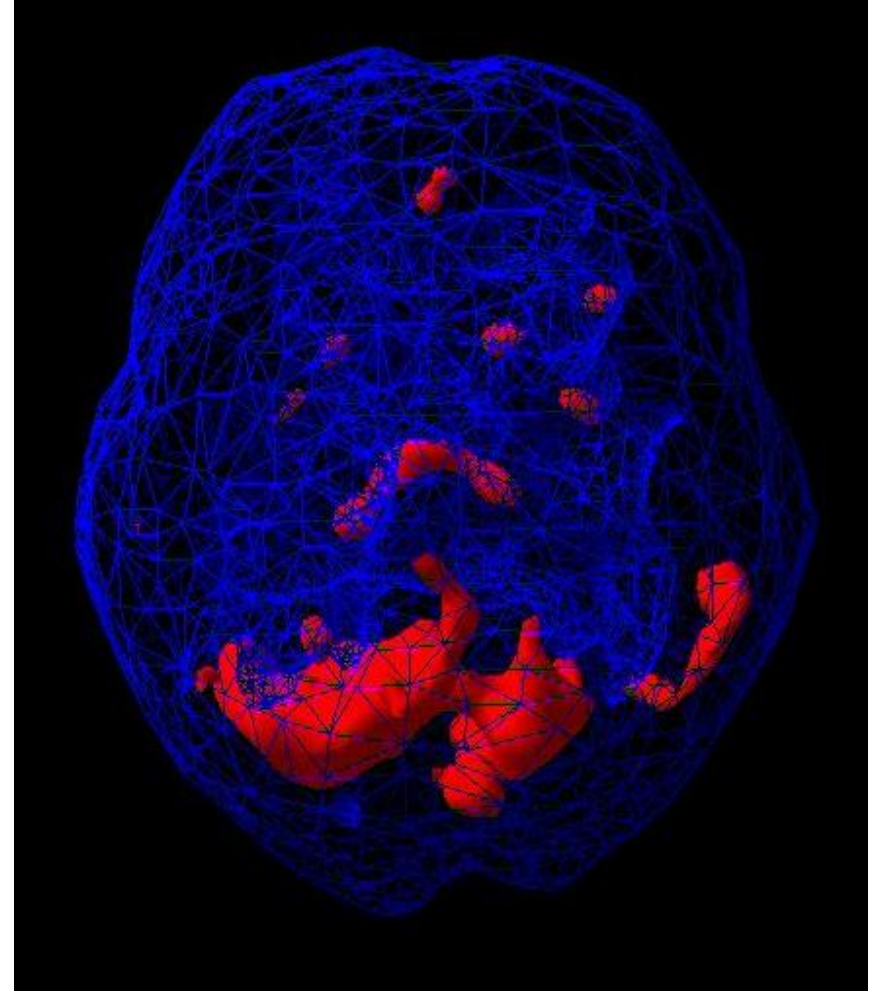


Healthy active view

Healthy Brain SPECT Scans

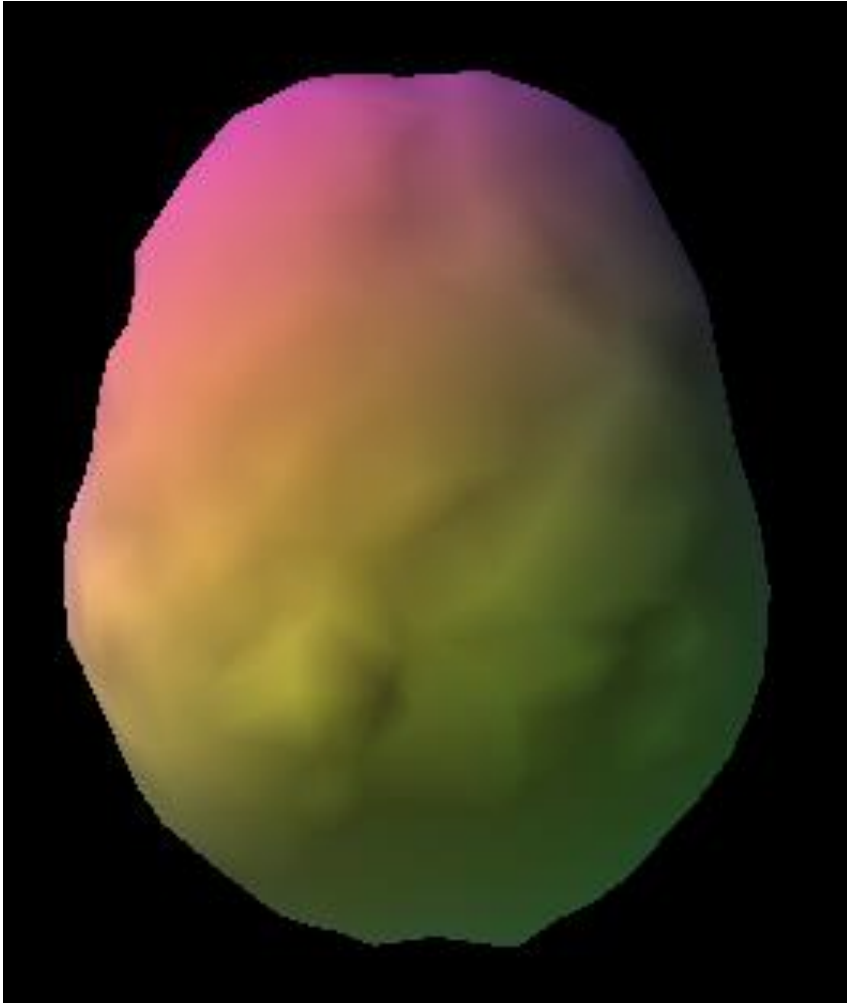


Surface View

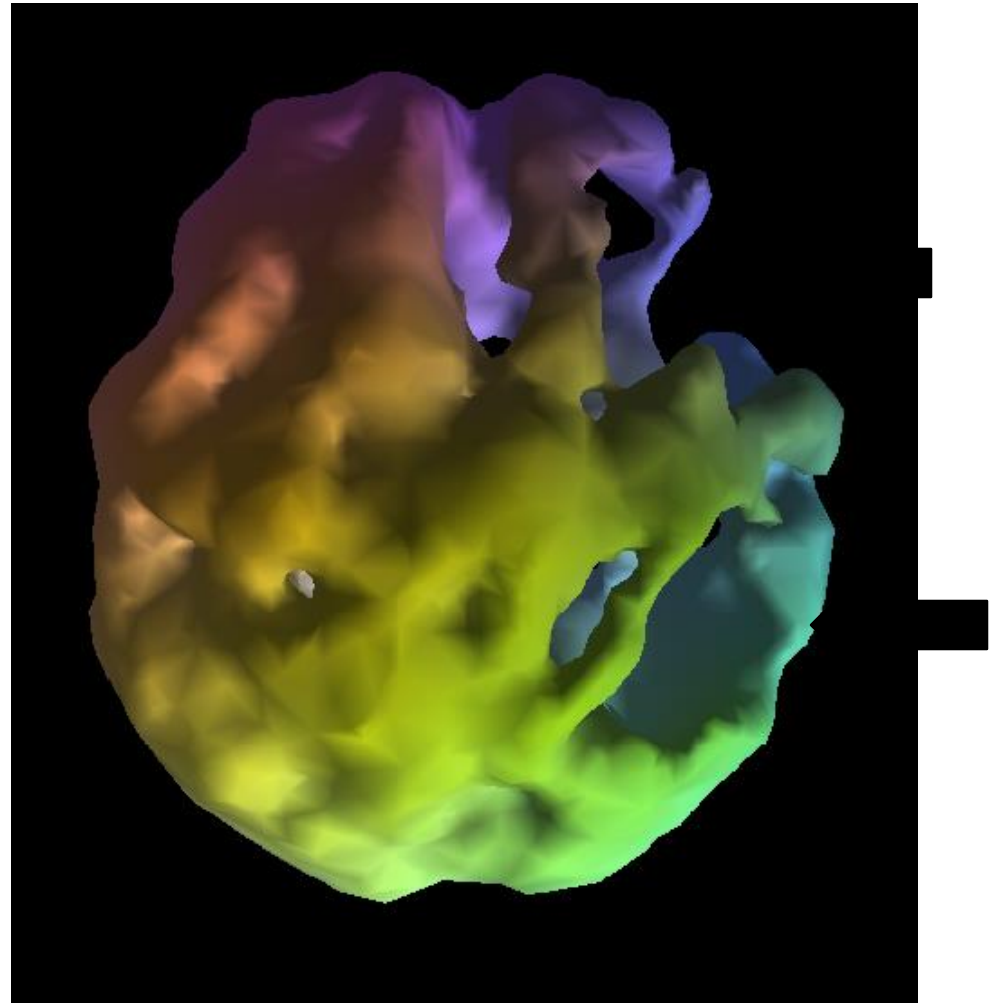


Active View

Healthy vs 2 Strokes

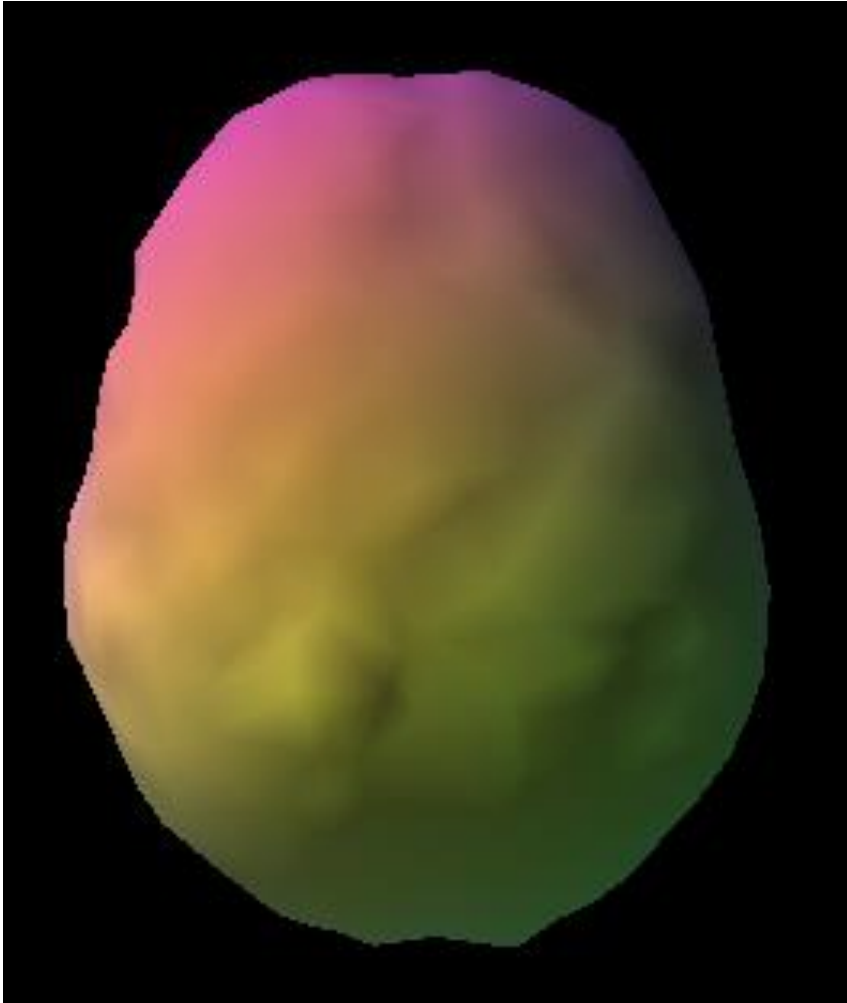


Healthy

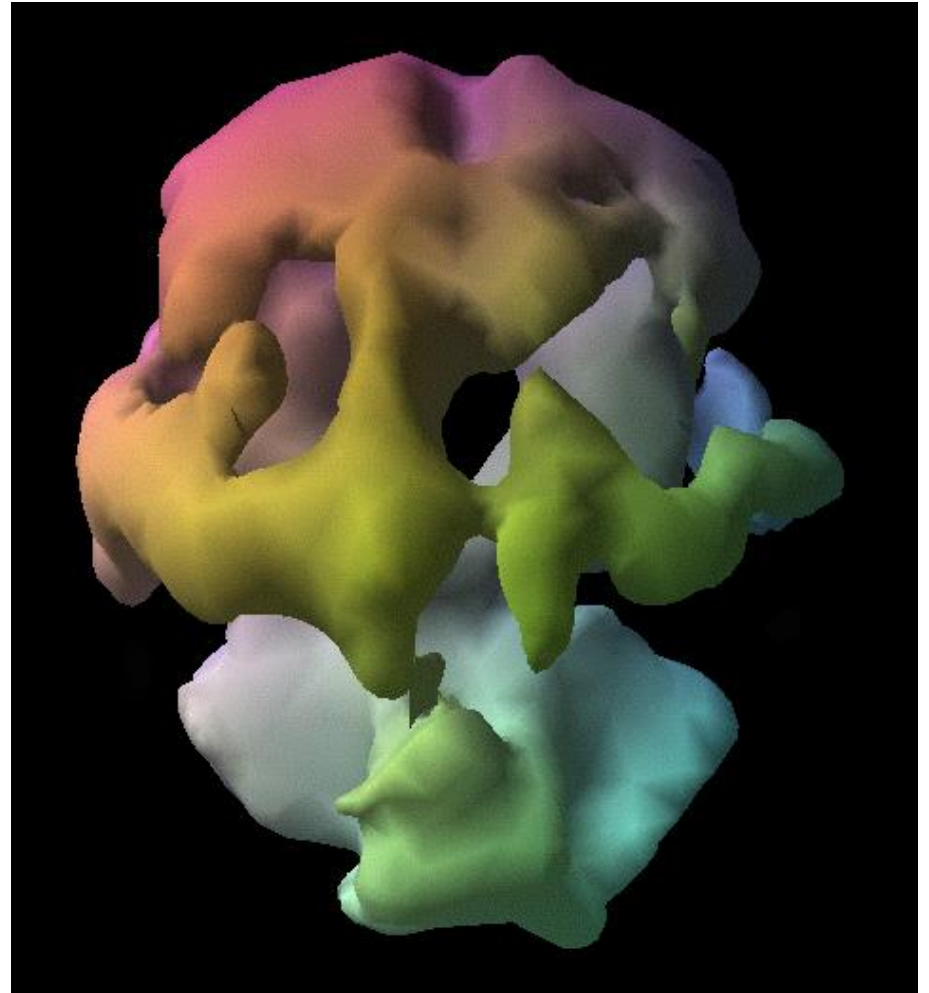


Stroke

Healthy vs Alzheimer's Disease

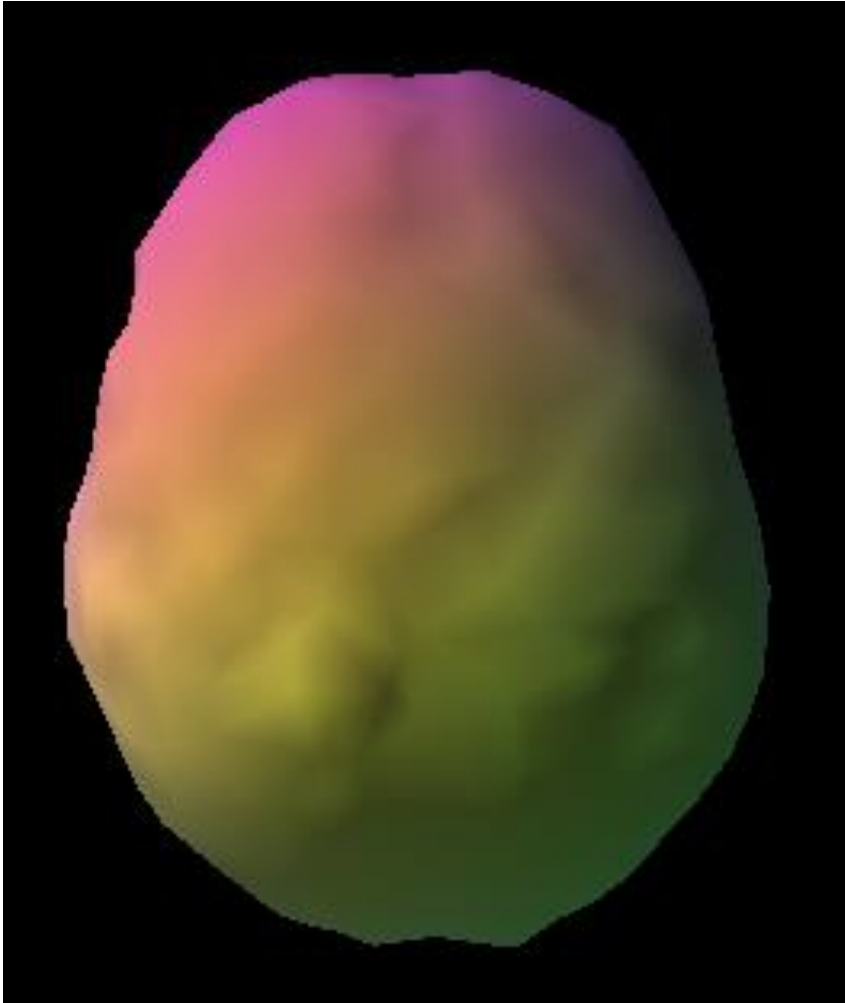


Healthy

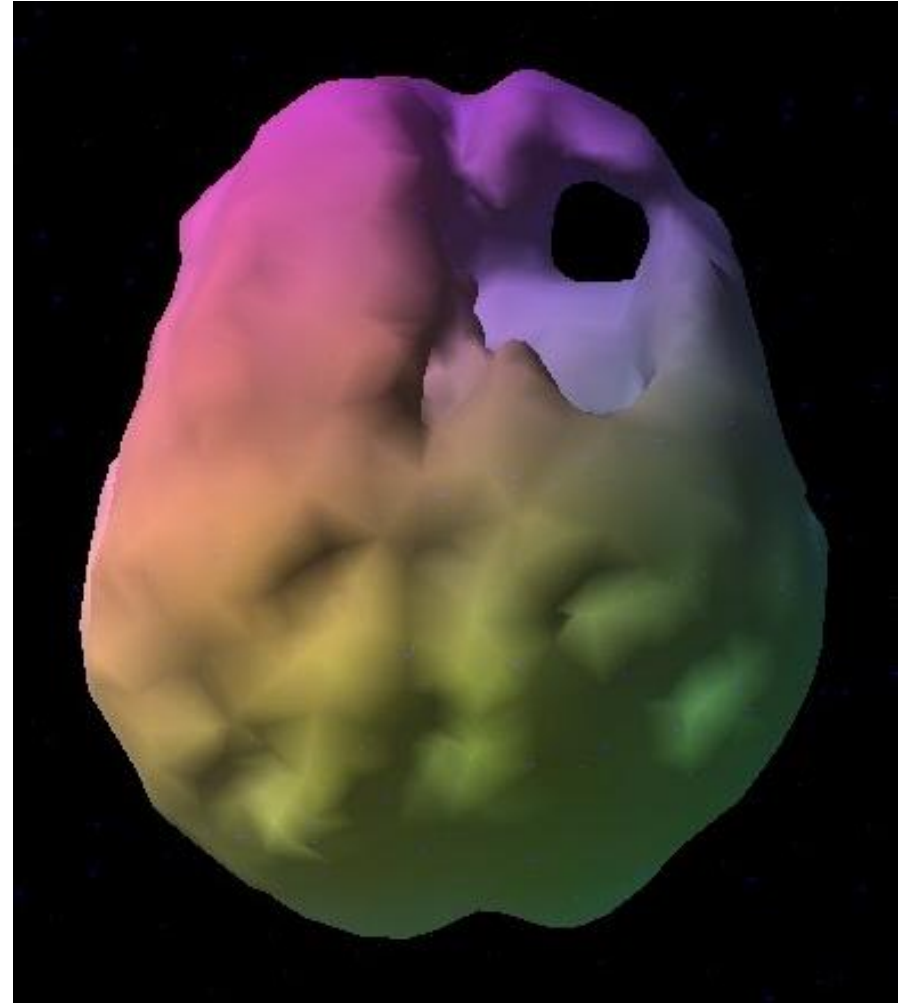


Alzheimer's

Healthy vs Traumatic Brain Injury

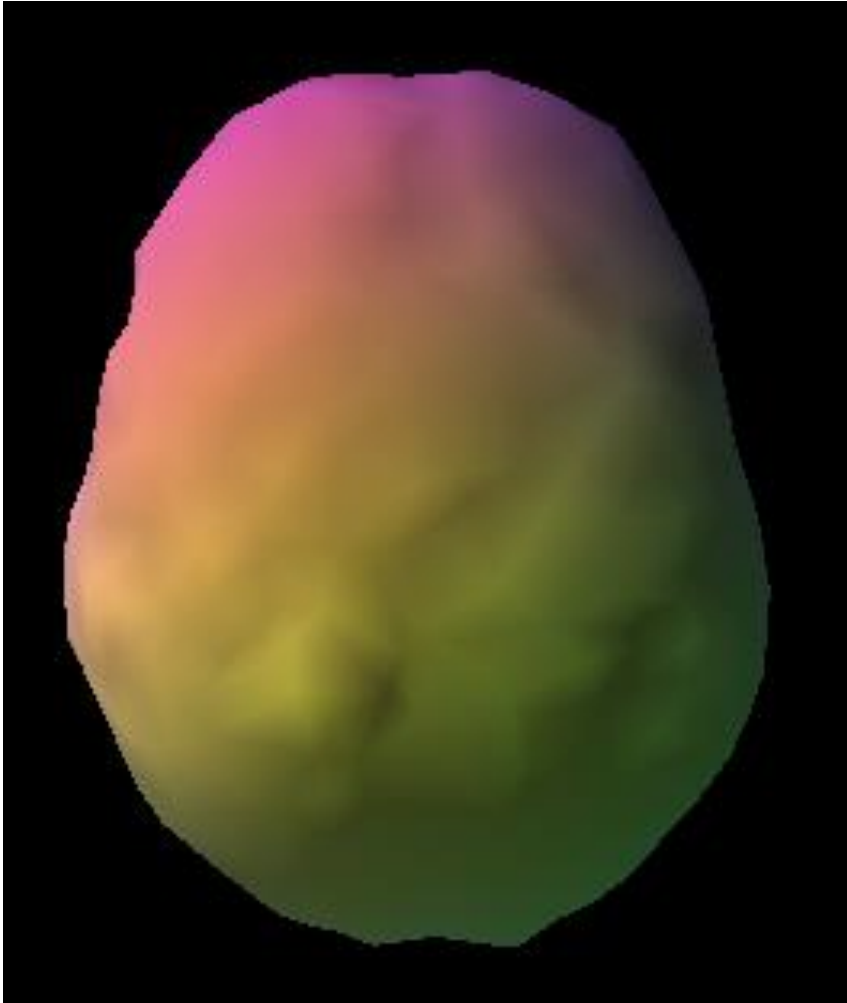


Healthy

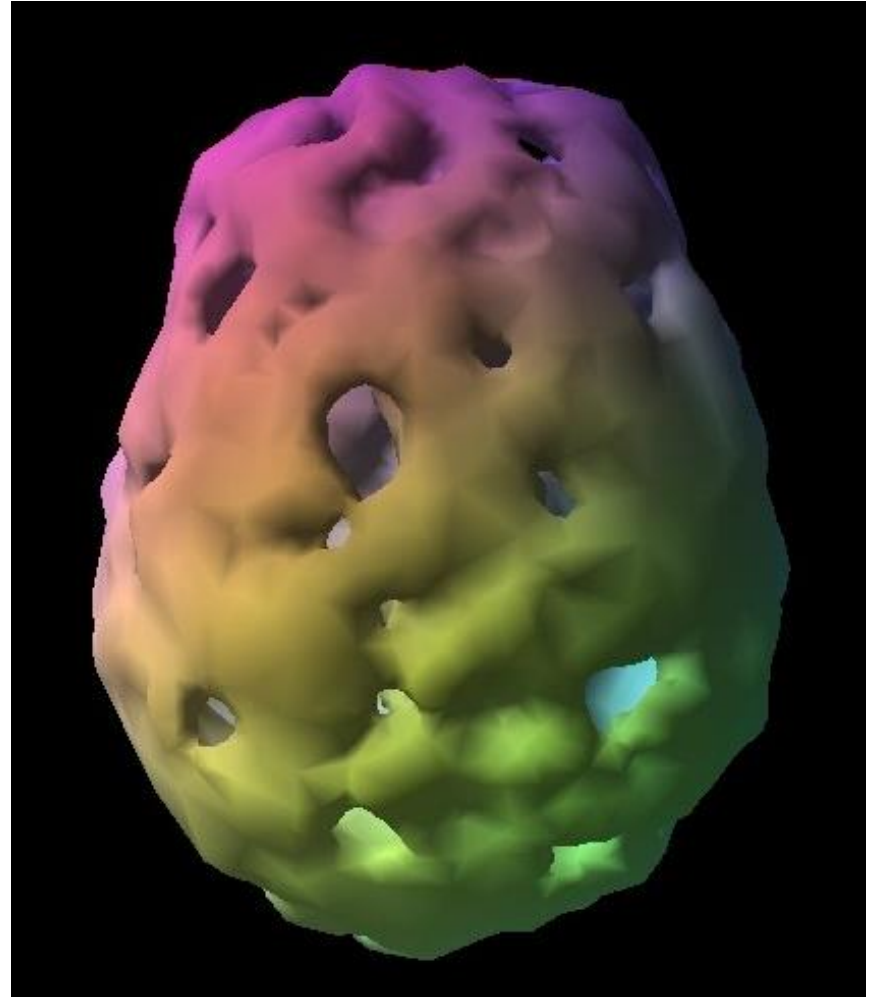


TBI

Healthy vs Drug Abuse

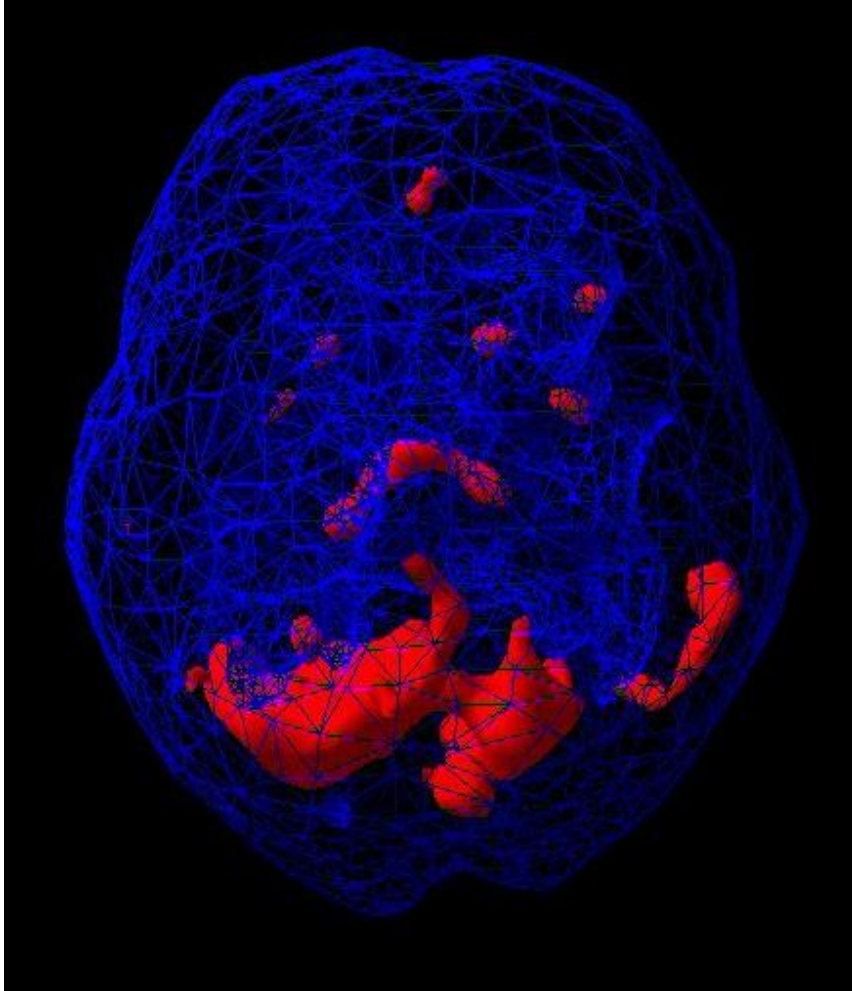


Healthy

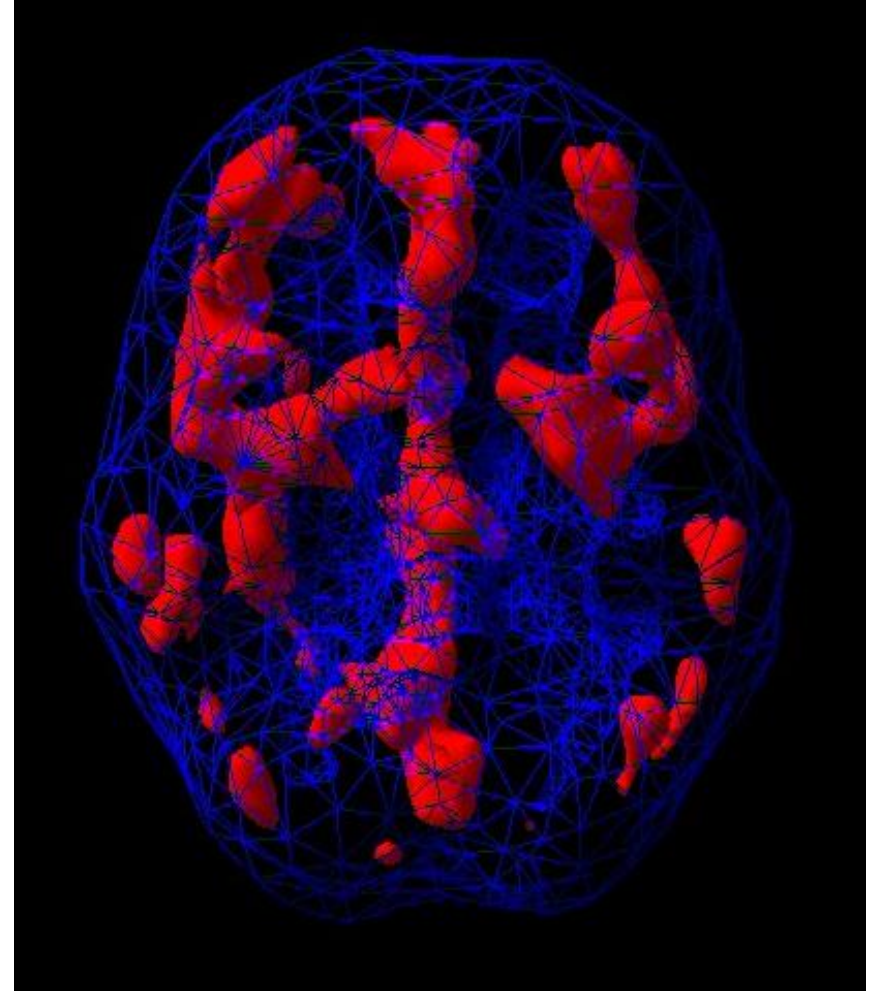


Drug Affected

Healthy vs OCD

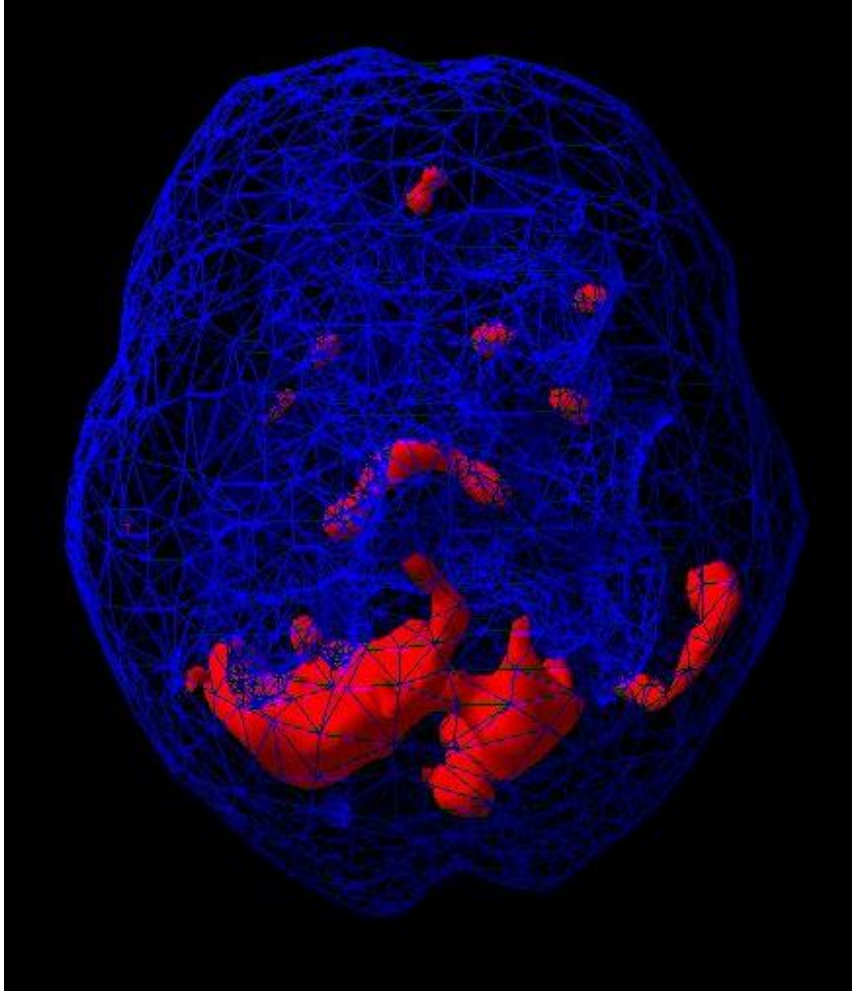


Healthy

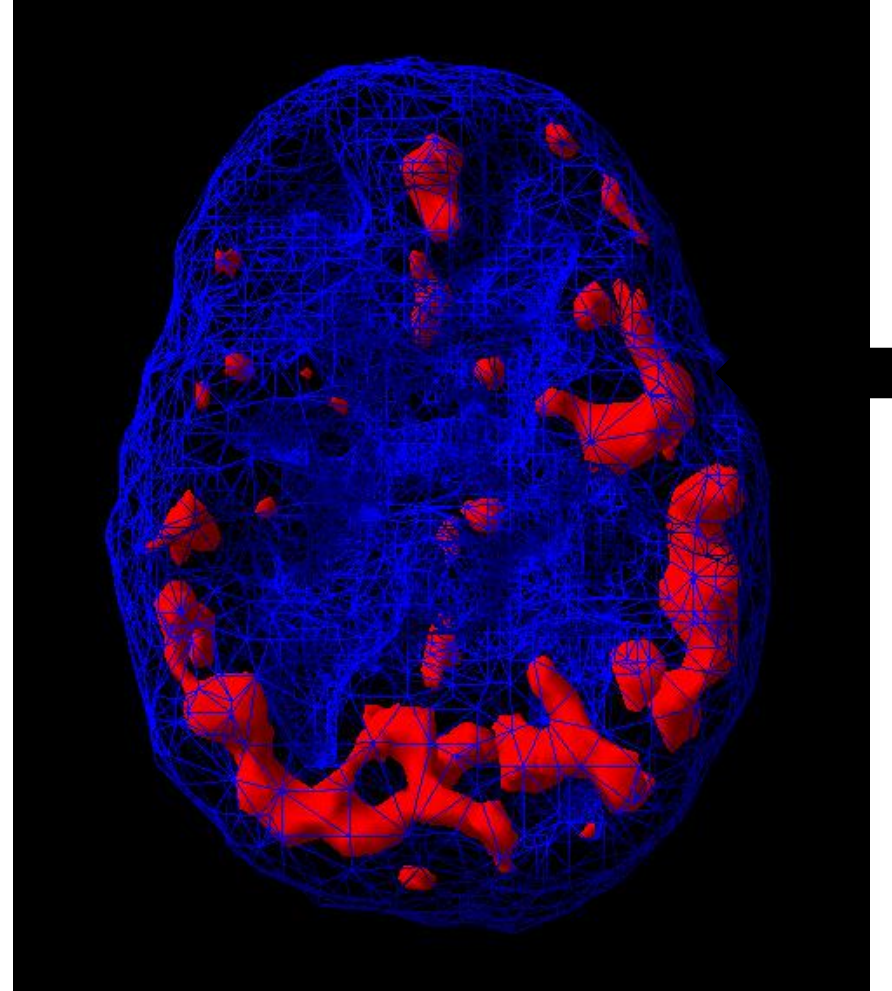


OCD

Healthy vs Seizure Activity

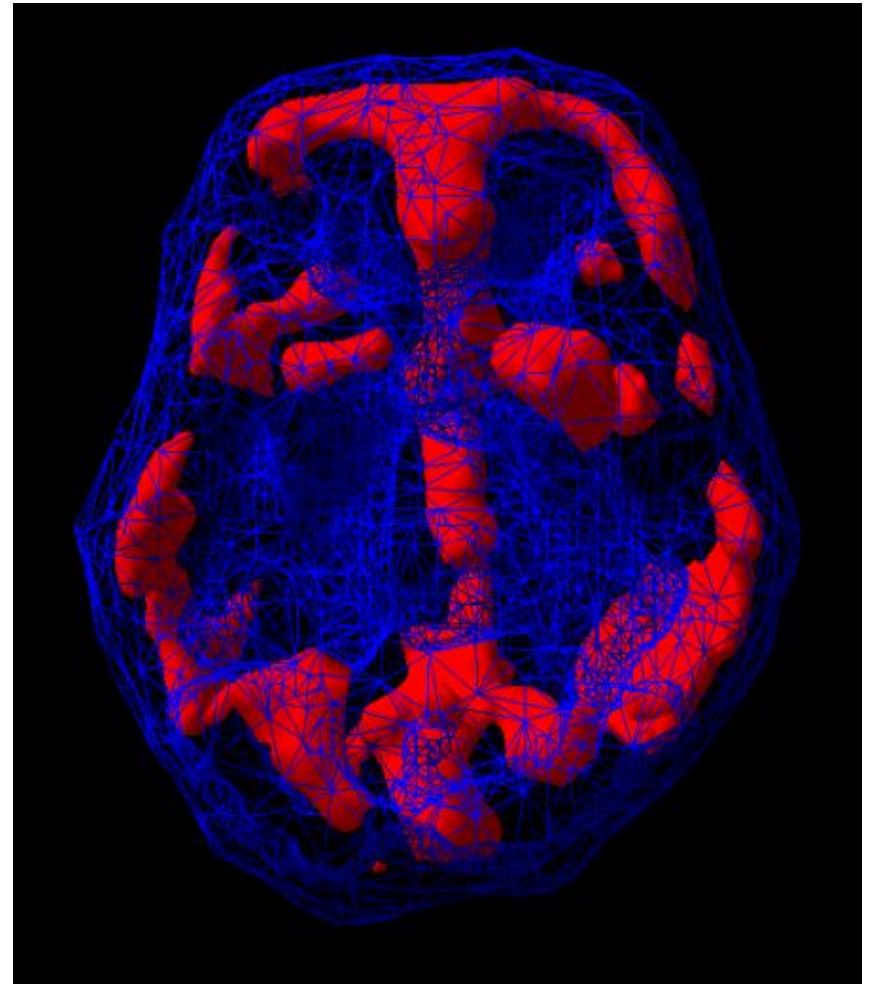
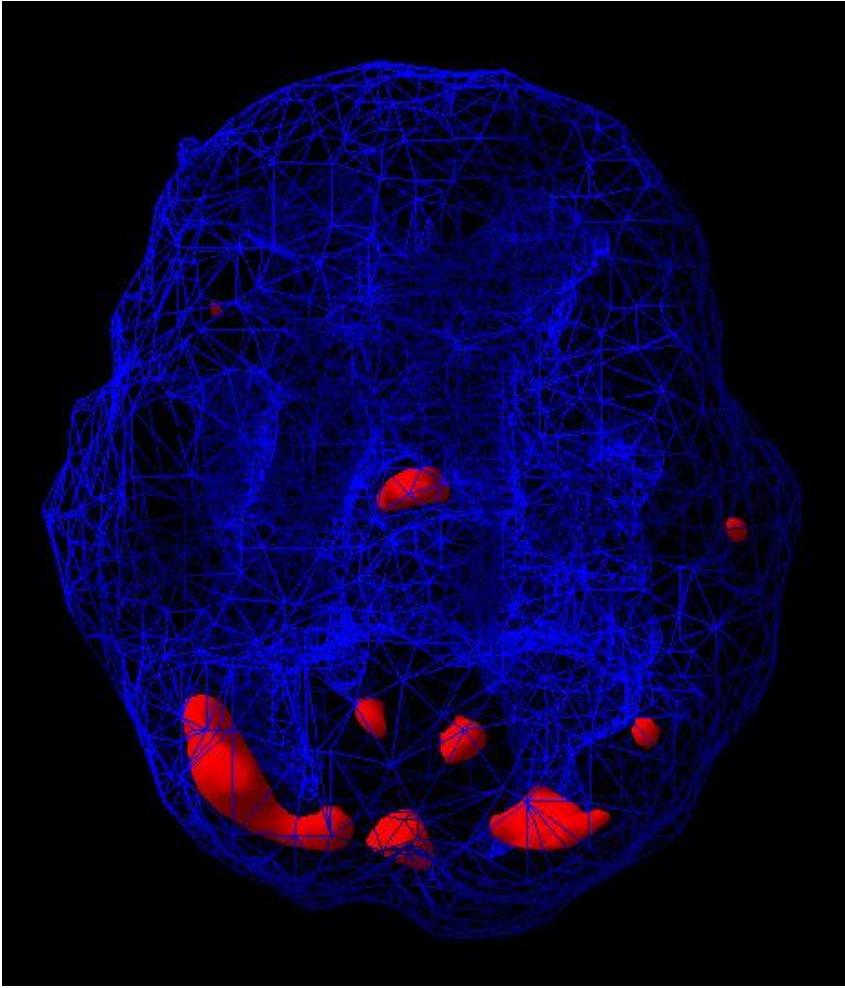


Healthy



Seizure Activity

Two Patients with Depression



Rx needs to be tailored to individual brains

The DSM-V Workgroup, on the link between diagnostic classification and etiology across the four major anxiety disorders:

“The DSM anxiety categories do not map neatly onto simple, consistent, and distinct etiological pathways... given this complexity and our current extremely incomplete stage of knowledge, we are unlikely, at this point in time, to define a significantly ‘truer’ anxiety nosology.”

Fyer and Brown, From “Stress-Induced and Fear Circuitry Disorders: Advancing the Research Agenda for DSM, edited by Gavin Andrews, MD et al, 2009

The DSM-V Workgroup, on the link between diagnostic classification and etiology across the four major anxiety disorders:

As a result, they note that “plans to make major modifications in the classification should probably be undertaken with some degree of caution.”

Current Paradigm

Symptoms = Diagnosis = Treatment

➤ Depressed	Depression	Antidepressant
➤ Attent/Impulse	ADHD	Stimulant
➤ Panic attacks	Panic Dis	Anti-anxiety
➤ Explodes intermittently	I. E. D.	???

There Is A Better Way

Comprehensive Clinical Assessment

(thorough history + focused psychometric testing

+ Detailed Lab Work

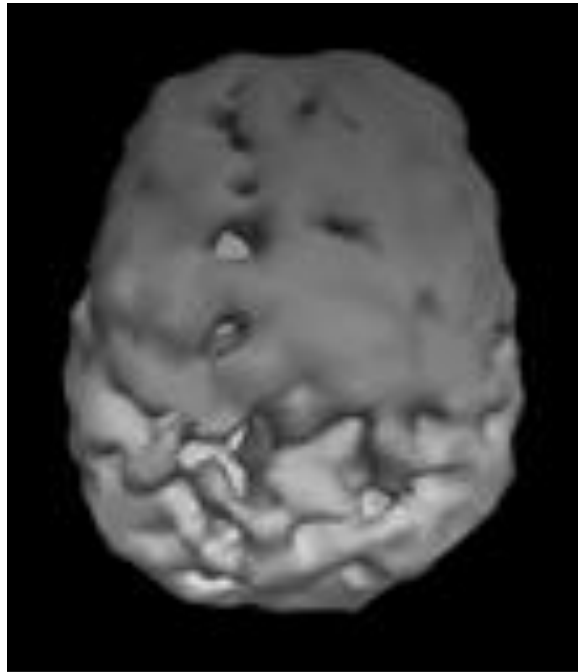
+ Functional Imaging

= Revolution

**→ More *targeted* treatment and significantly
improved patient outcomes**

Why Do Neuroimaging?

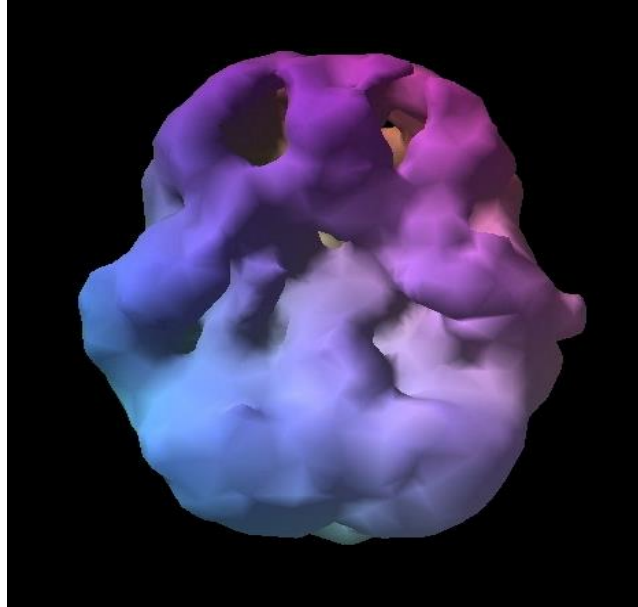
Enhance Motivation and Compliance: *“This is a real wake-up call”*



Why Do Neuroimaging?

Decrease Stigma:

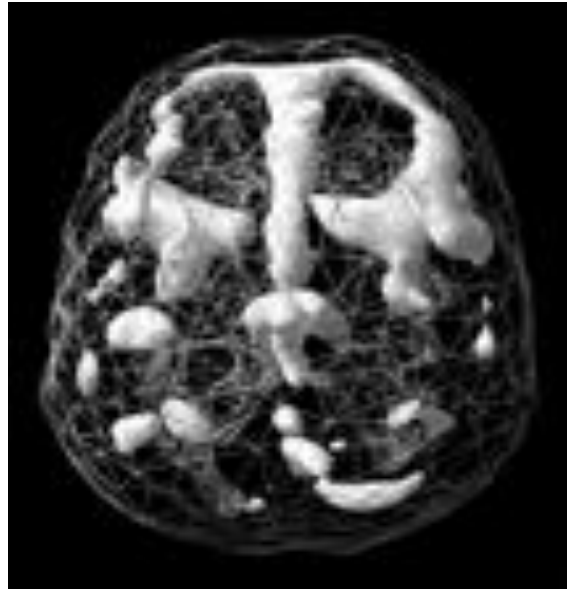
*“I have a **medical** illness”*



Why Do Neuroimaging?

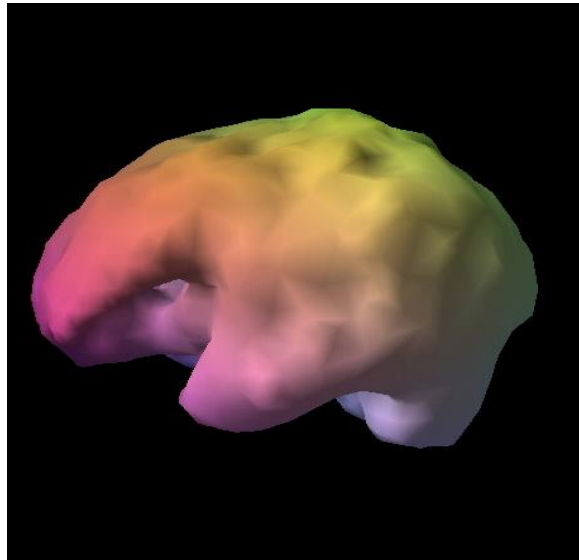
Promotes Compassion, Understanding, and Patience in Family Members:

*“Oh, you have a **medical** illness”*



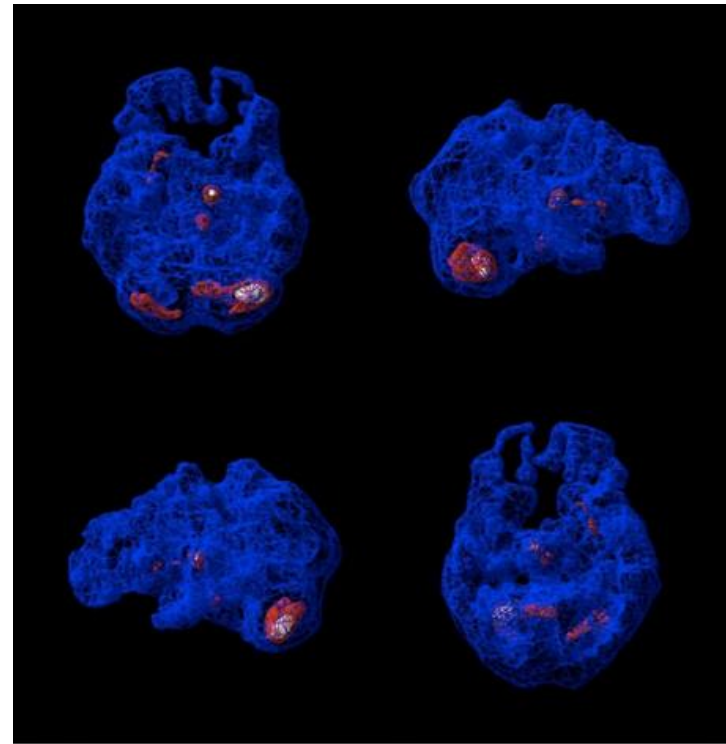
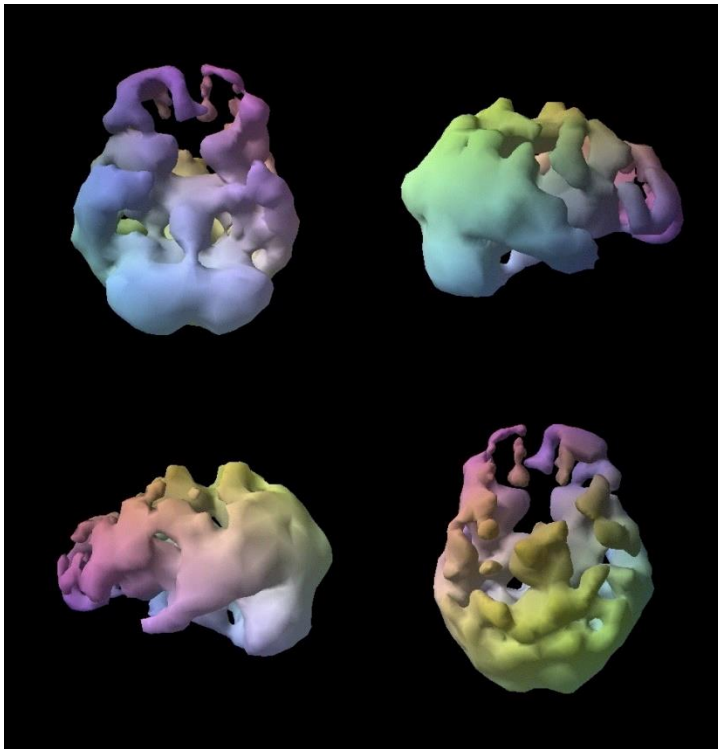
Why Do Neuroimaging?

Discover unforeseen findings that are contributing to problems - like strokes, seizures, or traumatic brain injury: *“Wow, I didn’t expect that”*



Why Do Neuroimaging?

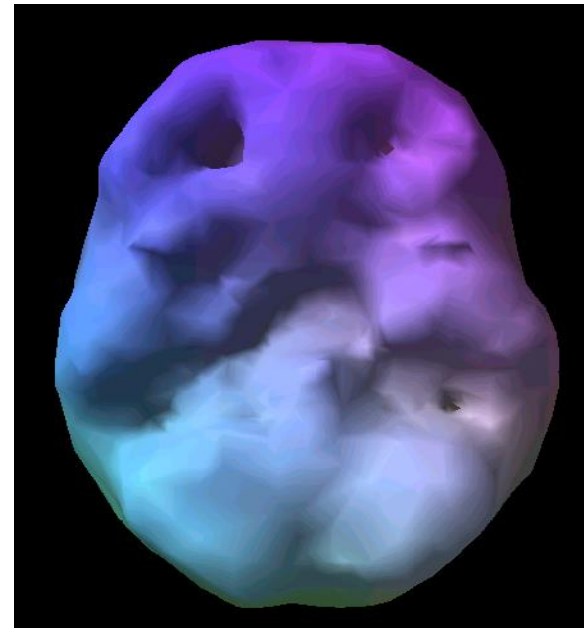
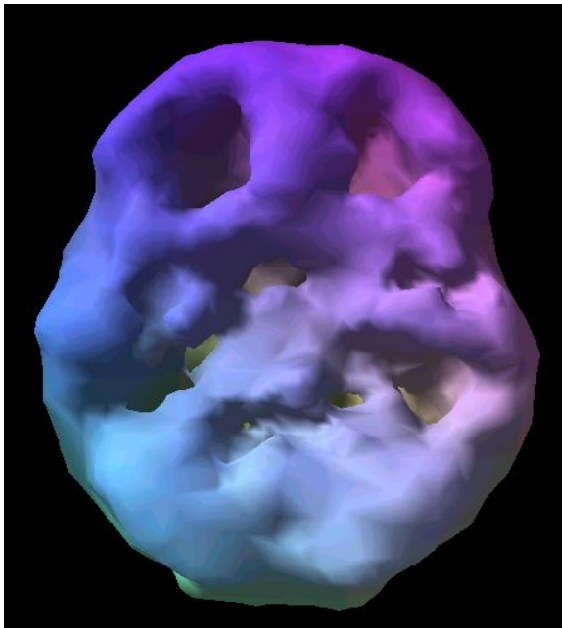
Clarify Co-Occurring Illnesses



Why Do Neuroimaging?

Enhance Our Effectiveness:

“The treatment is really making a difference!”



How Does SPECT Change Clinical Practice?

- **109 consecutive patients**
- **SPECT changed diagnosis &/or treatment 79%**
- **22% unexpected brain injury**
- **22% unexpected toxicity**
- **60% new targets for medication or other Tx's**

(Amen DG, et al. J Psychoactive Drugs 2012)

Better Outcomes

➤ **500 consecutive patients**

➤ **On average our patients have 4.2 diagnoses, 3.3 prior providers and 6 medications failures**

➤ *75% significantly improved across all measures*

➤ *QOLI significantly increased in 85%*

➤ *Cleveland Clinic QOLI in <50%*

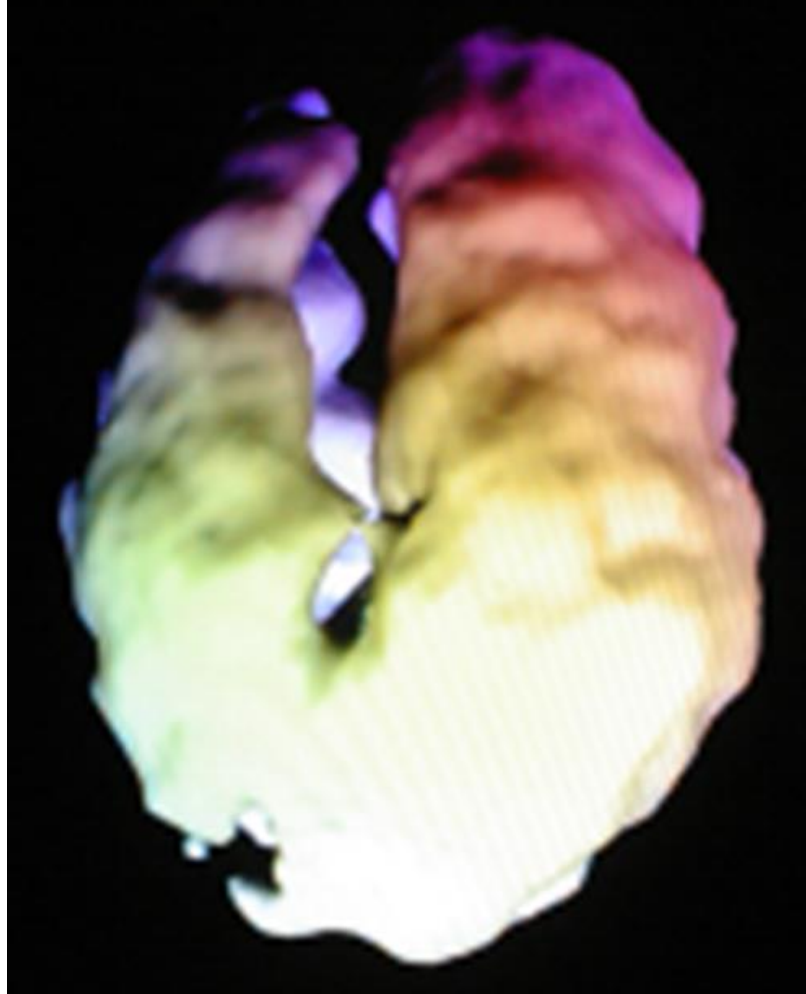
Multisite, 6-Month Outcome Study of
Complex Psychiatric Patients Evaluated
with Addition of Brain SPECT Imaging

Daniel G. Amen, MD; Melissa Jourdain, MS; Derek V. Taylor;
H. Edmund Pigott, PhD; and Kristen Willeumier, PhD

Early Lesson

- **Mild traumatic brain injuries are a major cause of psychiatric illness**

Mild Traumatic Brain Injury



Mild?

Undiagnosed Brain Injuries Are a Major Cause of:

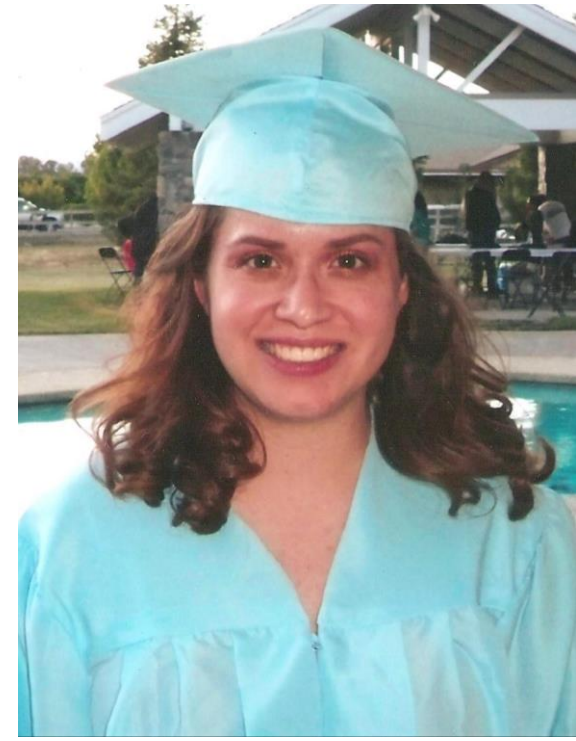
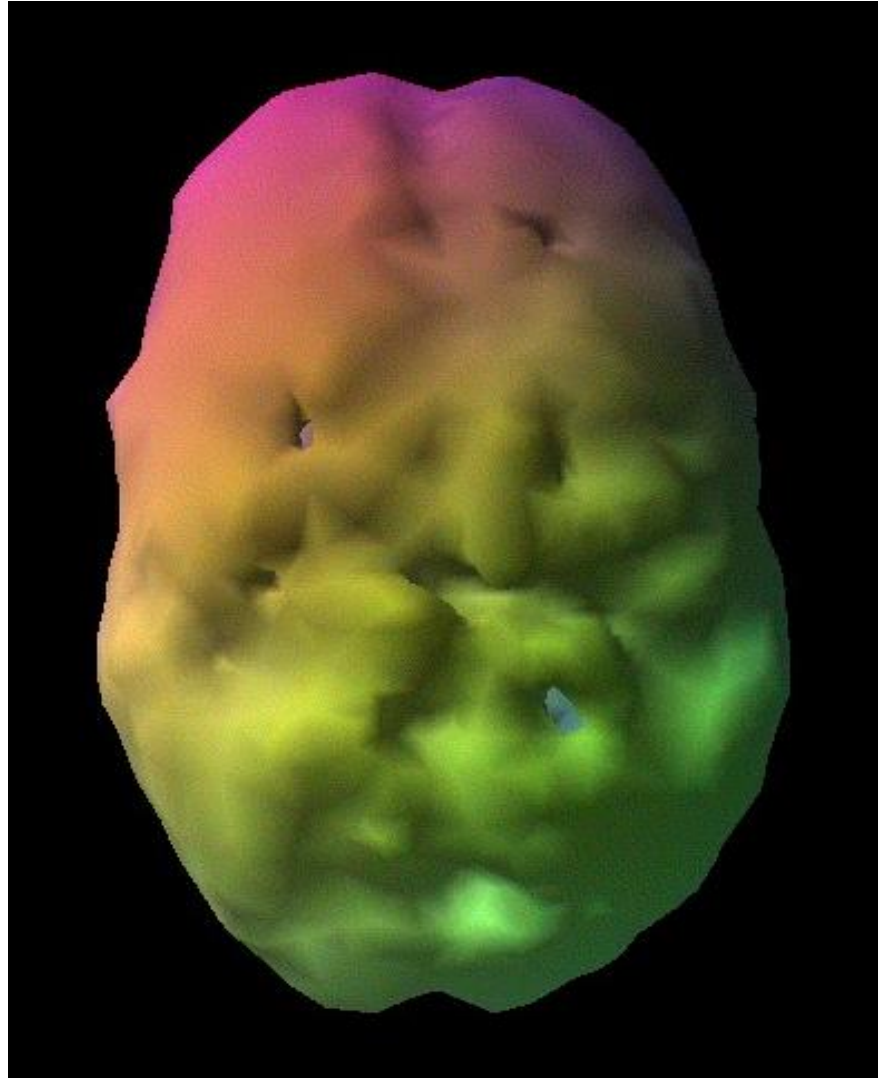
- **Homelessness**
- **Drug/alcohol abuse**
- **Depression**
- **Panic attacks**
- **ADHD symptoms**
- **Suicide**



Early Lesson

- **Infectious diseases are a common cause of psychiatric symptoms**

Adrianna



More Lessons

- **Judges and defense attorneys sought our help to understand criminal behavior**
- **> 500 convicted felons, including 90 murderers**
- **Our work taught us that people who do bad things often have troubled brains**
- **Many of these brains could be rehabilitated**

Radical Idea?

- **What if we evaluated and treated troubled brains**
- **Rather than simply warehousing them in toxic, stressful environments? (Bruce Alexander)**
- **We could save tremendous \$\$ by making people more functional**
- **→ So when they got out of prison they could work, support their families and pay taxes.**

Fyodor Dostoevsky

“A society should be judged not by how it treats its outstanding citizens, but by how it treats its criminals.”



Instead of just **Crime and Punishment**

→ **Crime, Evaluation and Treatment**

Could functional neuroimaging have prevented this tragedy and others like it?



In 1994 NFL Formed Concussion Committee



- In 2009 Goodell said to Congress: “We (NFL) don’t yet know if playing football causes long term brain damage. *We are still studying the issue.*”
- NFL never sponsored a functional brain imaging study for players ... instead studied rats
- NFL acted like many employers: delay... deny... and blame the employee when they’re hurt

Problem with NFL's Position

- **If you don't admit you have a problem, you cannot do anything to solve it!**
 - ➔ **Many brain damaged NFL players were left without help or hope**
- **2009-2011 Amen Clinics with the LA Chapter of NFLPA performed first large functional imaging study on players**
 - ➔ **Brain SPECT imaging helped to change *everything***

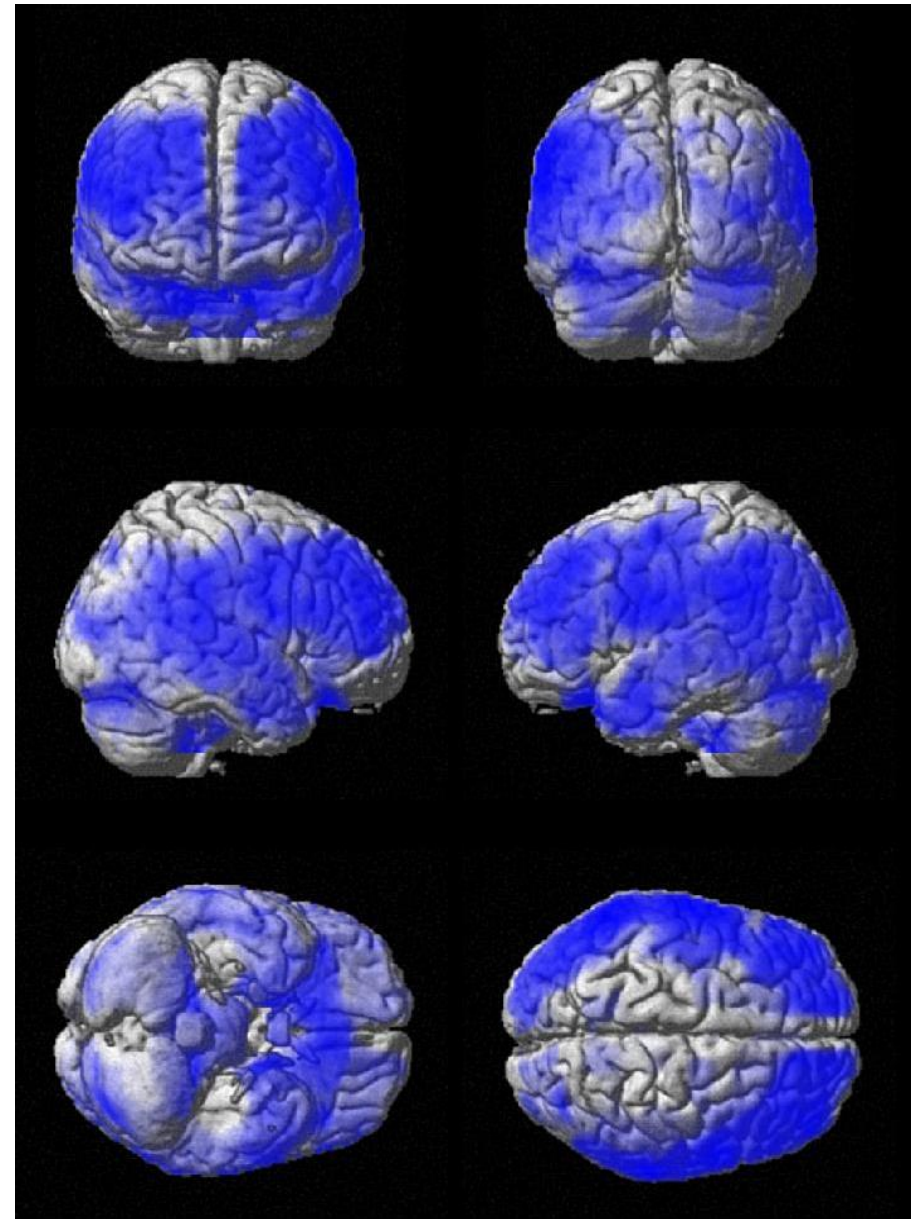
Damage Seen Across Whole Brain

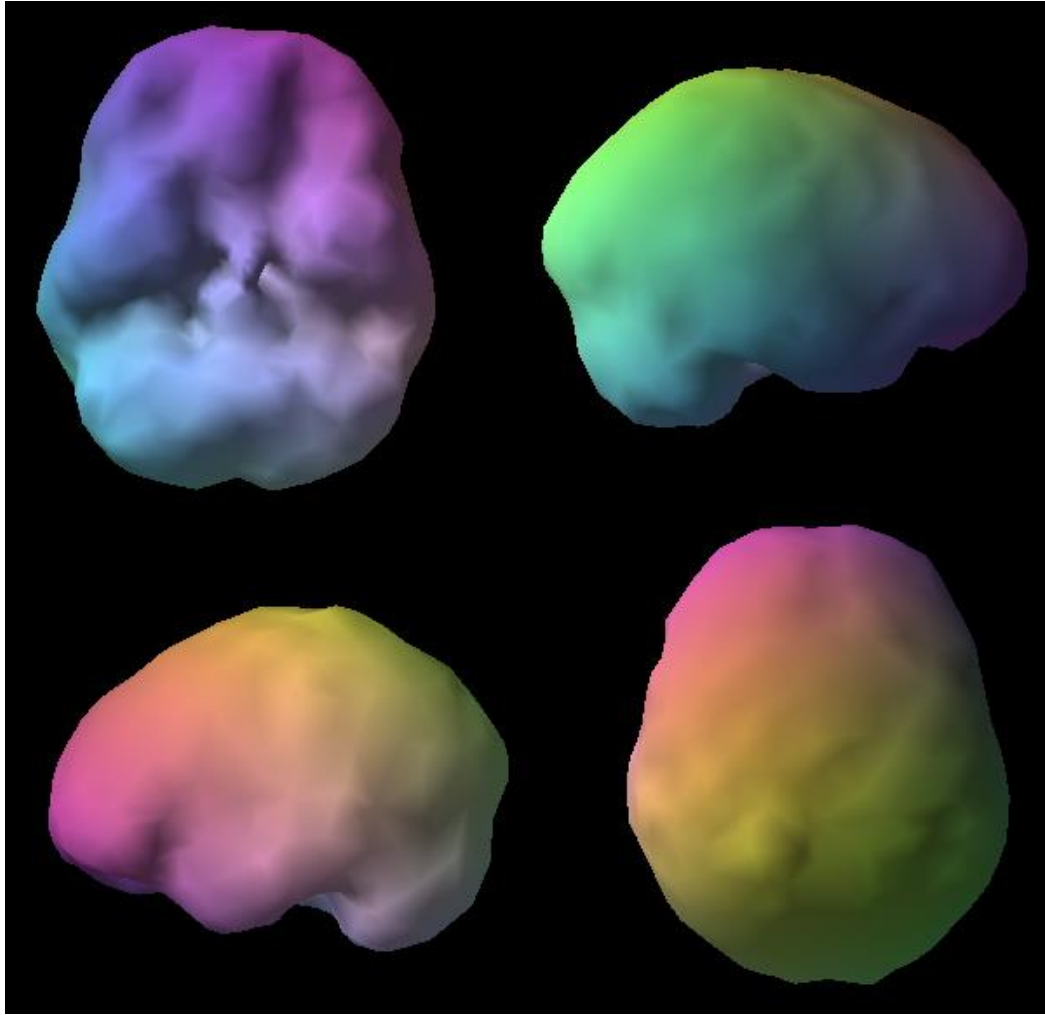
CLINICAL AND RESEARCH RE

Impact of Playing American Professional Football on Long-Term Brain Function

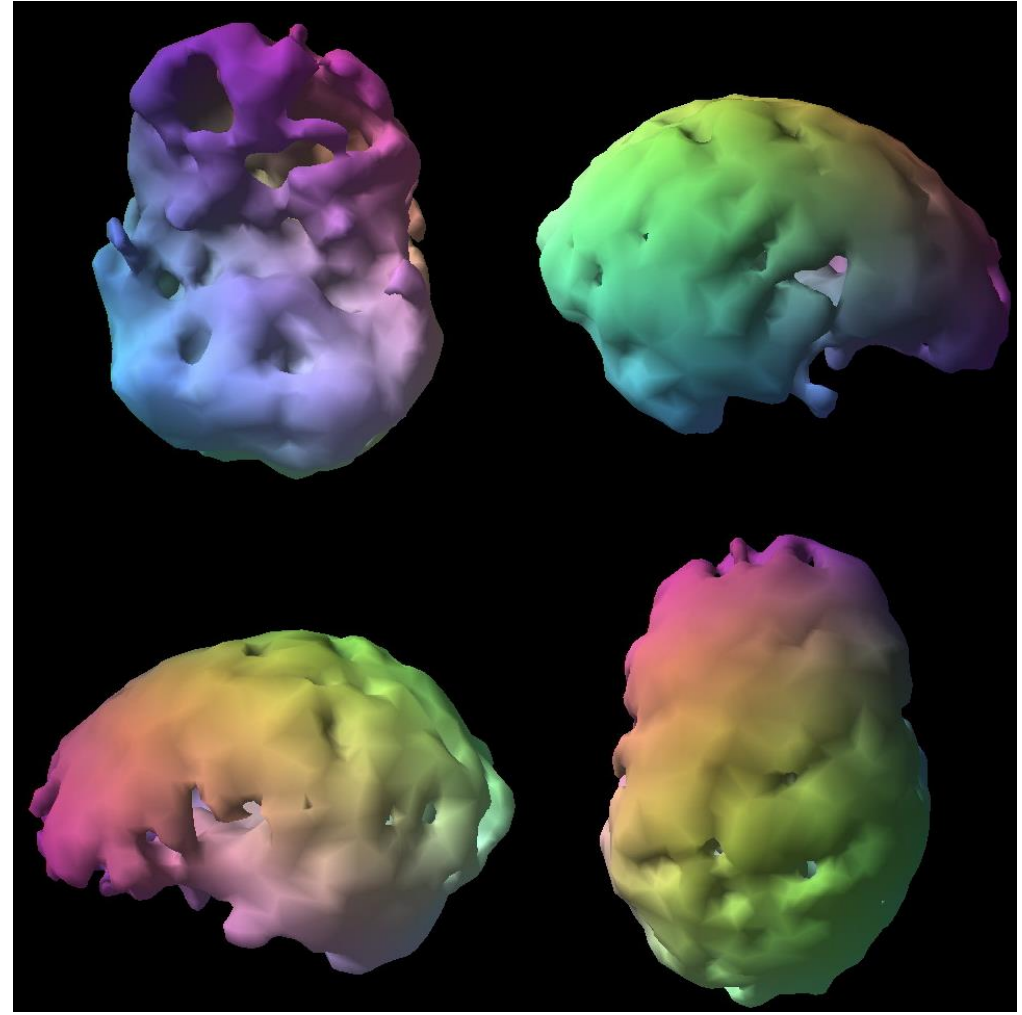
Daniel G. Amen, M.D.
Andrew Newberg, M.D.
Robert Thatcher, Ph.D.
Yi Jin, M.D.
Joseph Wu, M.D.
David Keator, M.C.S.
Kristen Willeumier, Ph.D.

The authors recruited 100 active and former National Football League players, representing 27 teams and all positions. Players underwent a clinical history, brain SPECT imaging, aEEG.





Healthy



16 Year Guard

2011 ... NFL Radically Changed Its Position On TBI

None of this was
possible without the
clinical application of
neuroimaging.



CONCUSSION

A Must Read for NFL Players

Let's Take Brain Injuries Out of Play



Concussion Facts

Concussion is a *brain injury* that alters the way your brain functions

Concussion can occur from a blow to the head/body:

- following helmet to helmet contact, and / or
- contact with the ground, object or another player

Most concussions occur without being knocked unconscious

Severity of injury depends on many factors and is not known until symptoms resolve and brain function is back to normal

All concussions are not created equally. Each player is different, each injury is different and all injuries should be evaluated by your team medical staff

Concussion Symptoms

Different symptoms can occur and may not show up for several hours. Common symptoms include:

- | | |
|------------------------------------|-------------------------------------|
| - Confusion | - Feeling sluggish, foggy or groggy |
| - Headache | - Sensitivity to noise |
| - Amnesia / Difficulty remembering | - Sensitivity to light |
| - Balance problems | - Double / fuzzy vision |
| - Irritability | - Slowed reaction time |
| - Dizziness | - Feeling more emotional |
| - Difficulty concentrating | - Sleep disturbances |
| - Nausea | - Loss of consciousness |

Symptoms may worsen with physical or mental exertion (e.g. lifting, computer use, reading)

Why Should I Report My Symptoms?

- Practicing or playing while still experiencing symptoms can prolong the time to recover and return to play.
- Unlike other injuries, there may be significant consequences of "playing through" a concussion. Repetitive brain injury, when not treated promptly and properly may cause permanent damage to your brain.

What Should I Do If I Think I've Had a Concussion?

Report it. Never ignore symptoms even if they appear mild. Look out for your teammates. Tell your Athletic Trainer or Team Physician if you think you or a teammate may have had a concussion.

Get Checked Out. Your team medical staff has your health and well being as its first priority. They will manage your concussions according to NFL / NFLPA Guidelines which include being fully asymptomatic, both at rest and after exertion, having a normal neurologic examination, normal neuropsychological testing, and clearance to play by both the team medical staff and the independent neurologic consultant.

Take Care of Your Brain. According to the CDC*, "traumatic brain injury can cause a wide range of short- or long term changes affecting thinking, sensation, language, or emotions". These changes may lead to problems with memory and communication, personality changes, as well as depression and the early onset of dementia. Concussions and conditions resulting from repeated brain injury can change your life and your family's life forever.



Work smart. Use your head,
don't lead with it. Help make
our game safer. Other athletes
are watching...



*for more information about traumatic brain injury and concussion, go to <http://www.cdc.gov/concussion>

Brain Rehab Program

- Damage so severe, we performed a “real-world” rehabilitation study
- Brain healthy strategies (**healthy nutrition, sleep, exercise, sobriety, weight loss if needed**)
- Brain boosting supplements (**5.6 grams fish oil, B6, B12, folic acid, ginkgo, vinpocetine, huperzine A, NAC, carnitine, and alpha lipoic acid**)

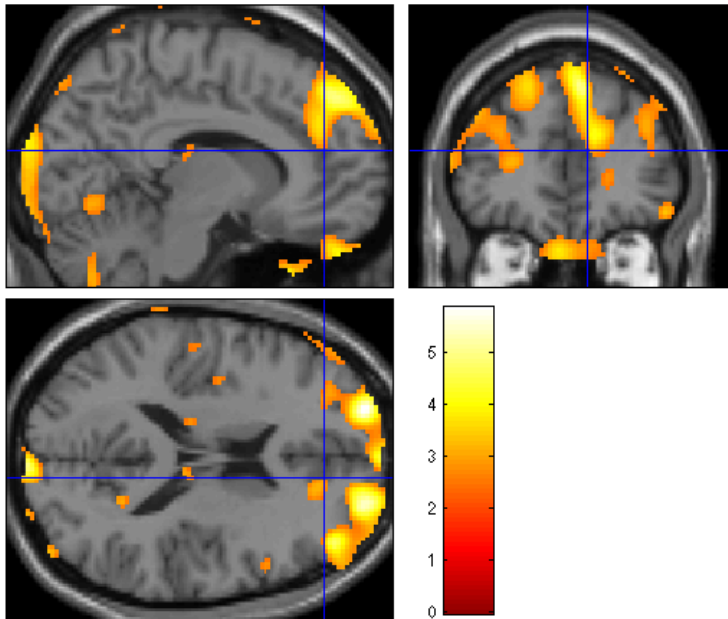
Significant Rehabilitation Possible

Journal of Psychoactive Drugs, 43 (1), (insert page range of article here), 2011
Copyright © Taylor & Francis Group, LLC
ISSN: 0279-1072 / 2159-9777 online
DOI: 10.1080/02791072.2011.566489



Reversing Brain Damage in Former NFL Players: Implications for Traumatic Brain Injury and Substance Abuse Rehabilitation†

Daniel G. Amen, M.D.*; Joseph C. Wu, M.D.**; Derek Taylor*** & Kristen Willeumier, Ph.D.****



➤ **65 players**

➤ **80% statistically
significant
improvement**

➤ **Especially in:**

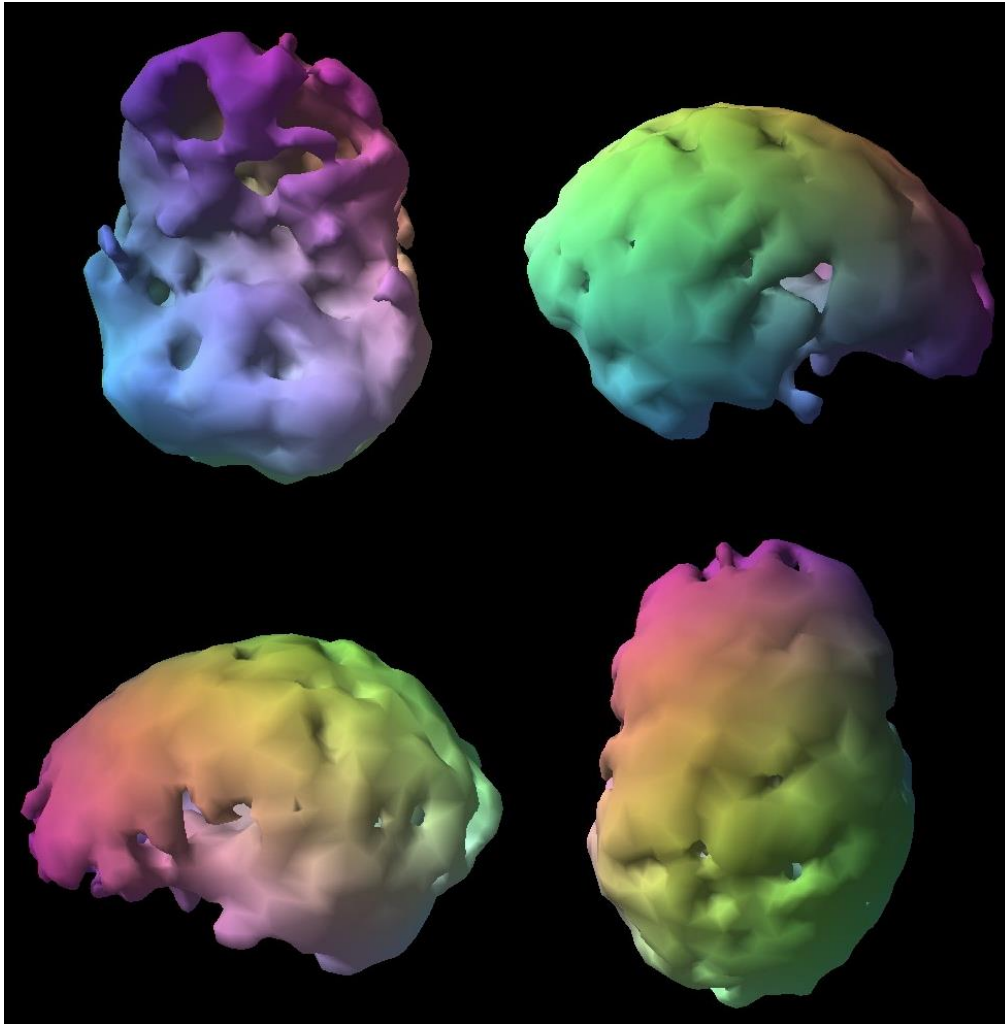
❖ **Memory 69%**

❖ **Attention 53%**

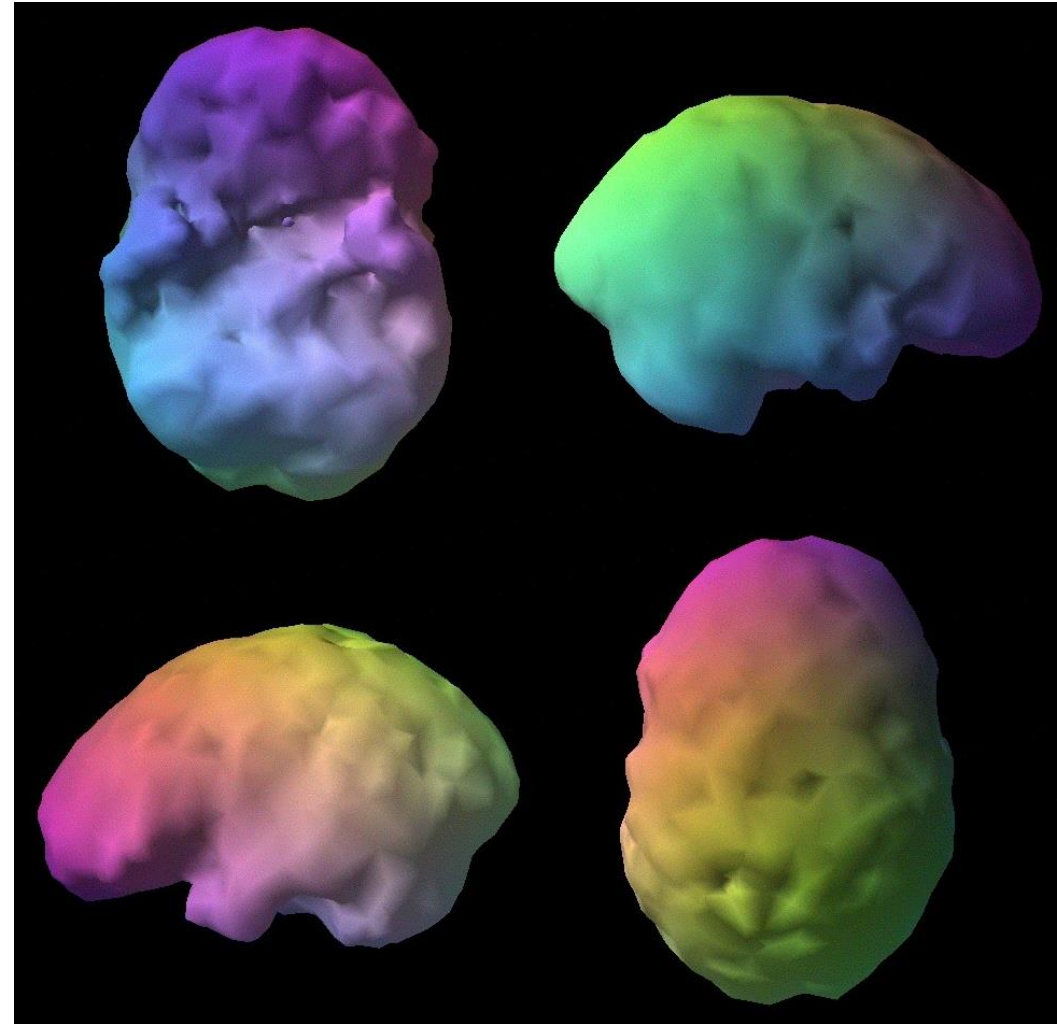
❖ **Mood 40%**

❖ **Motivation 40%**

Guard for 16 Years

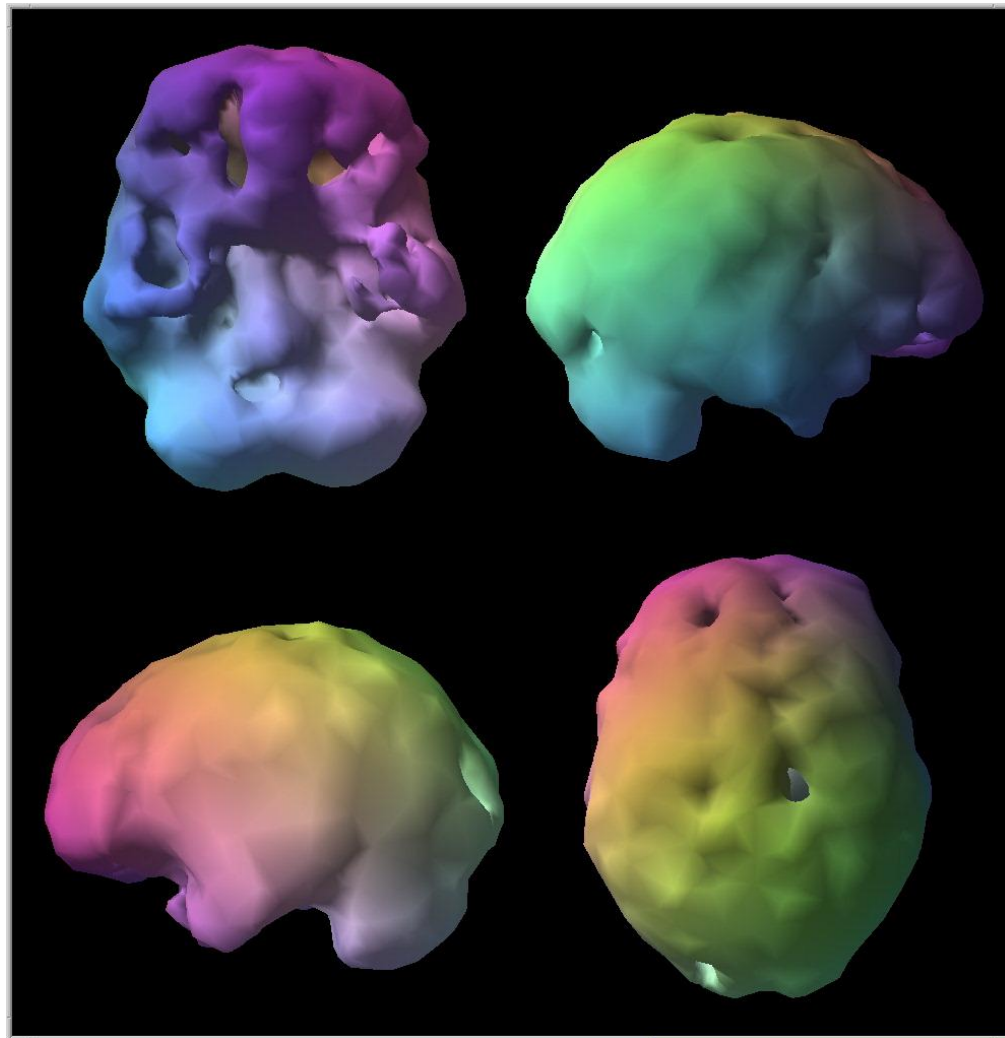


Before

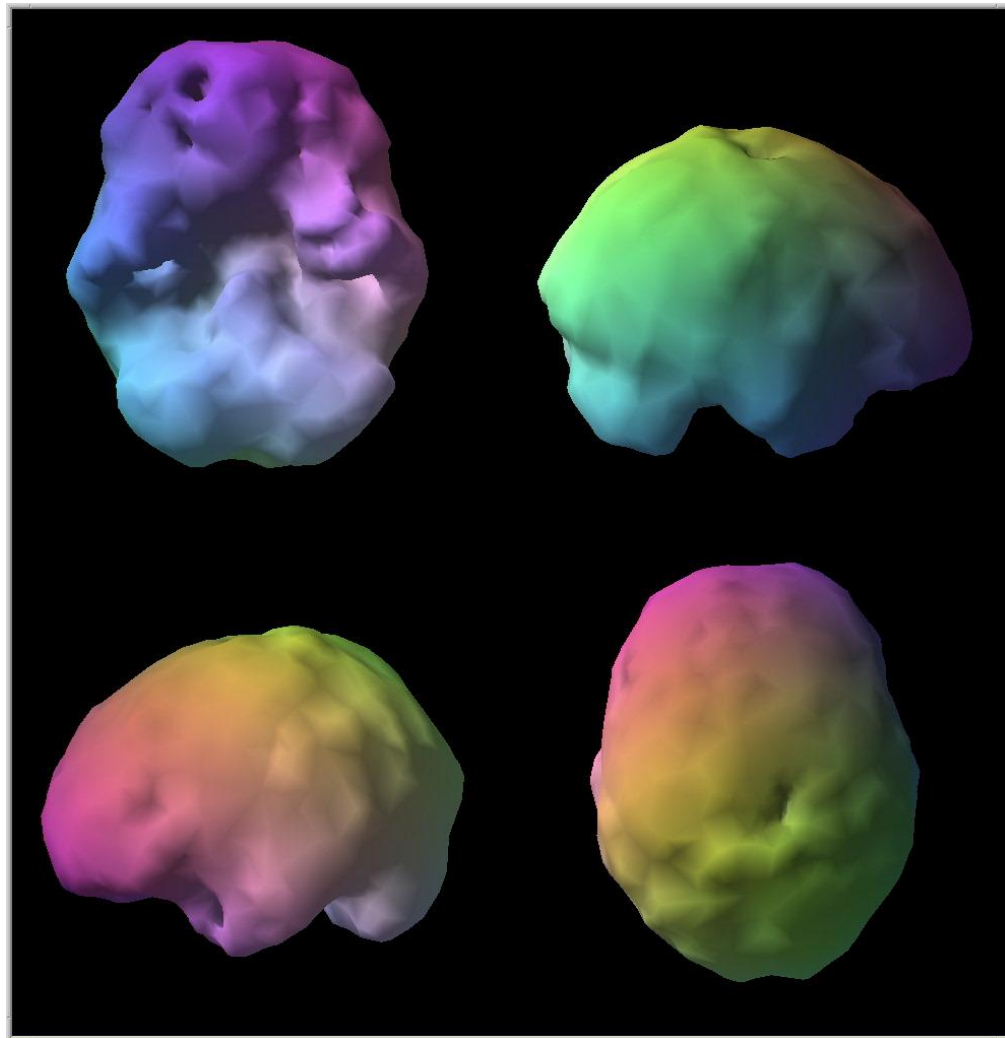


After 18 mos

Tight End for 12 Years



Before

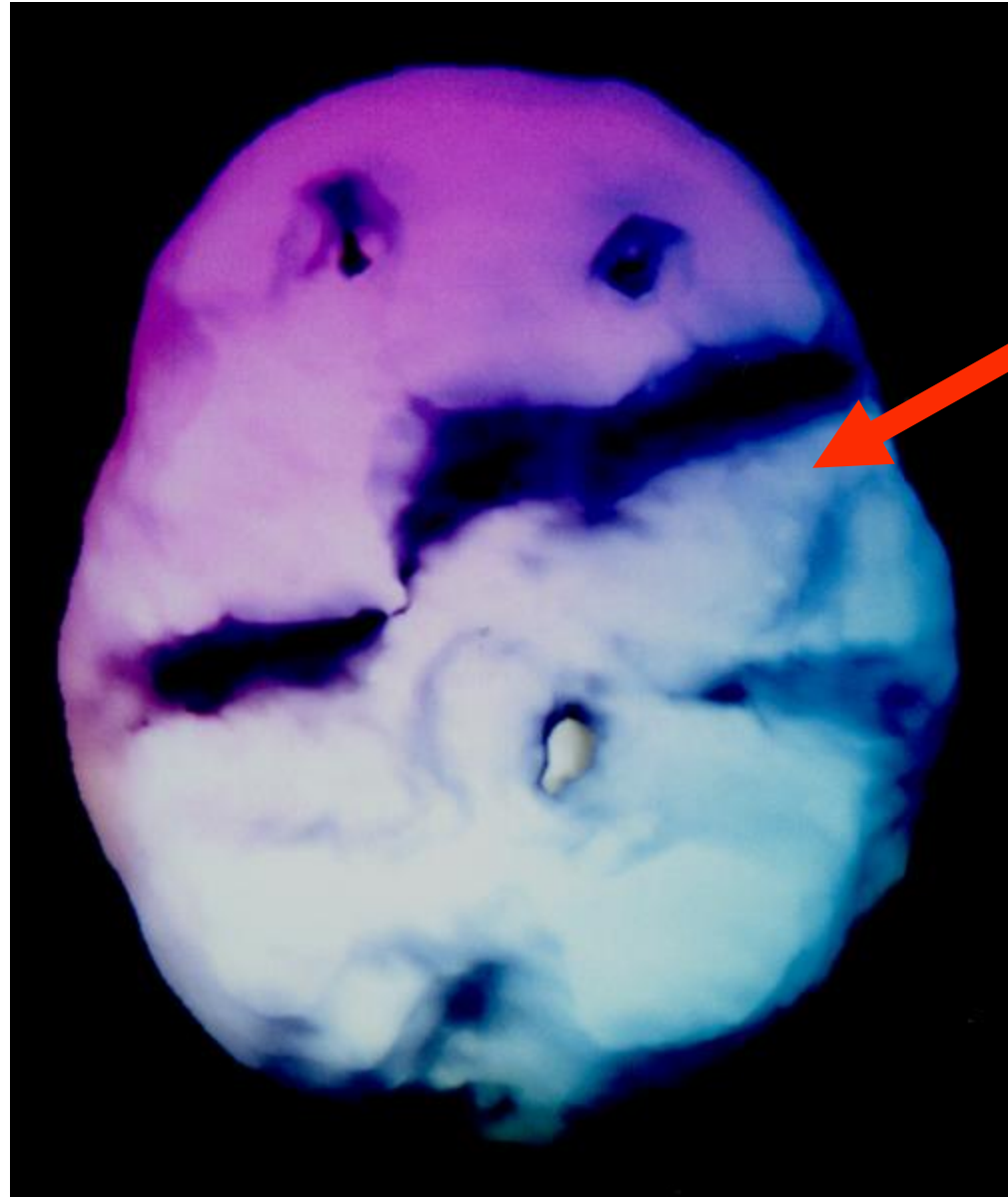


After 18 mos

**Reversing Brain Damage Is An Exciting
New Frontier, But the Implications Are
Wider**

Andrew

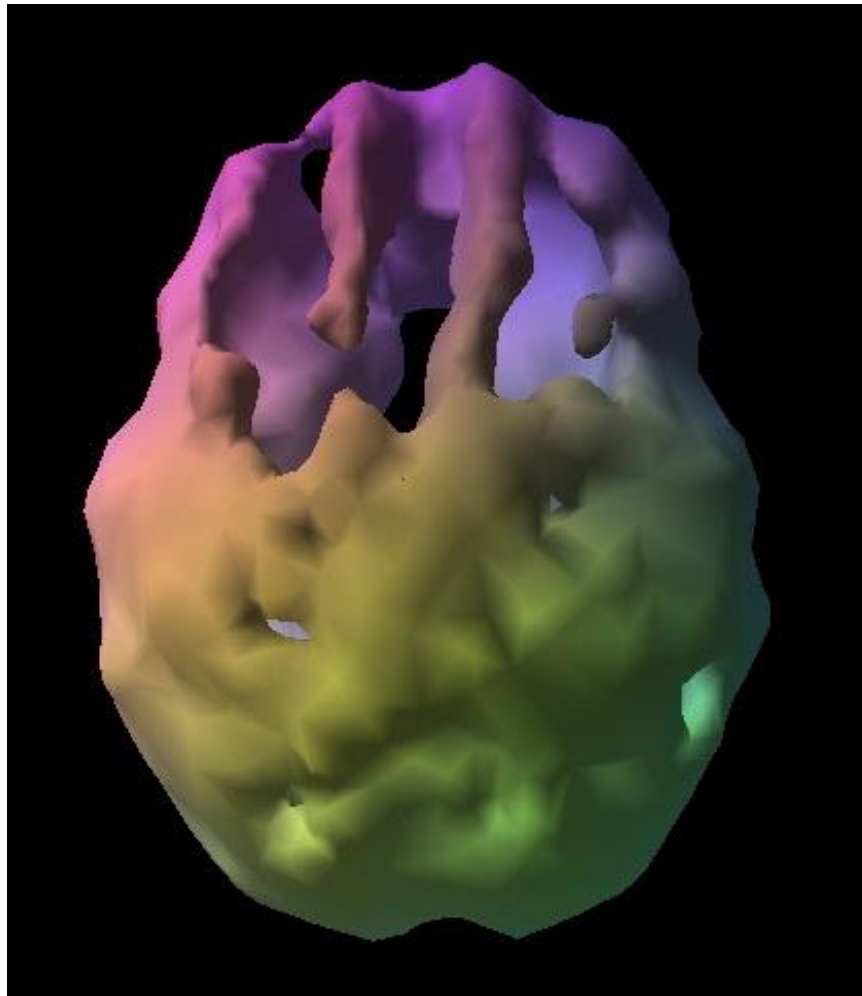






Ray and Nancy

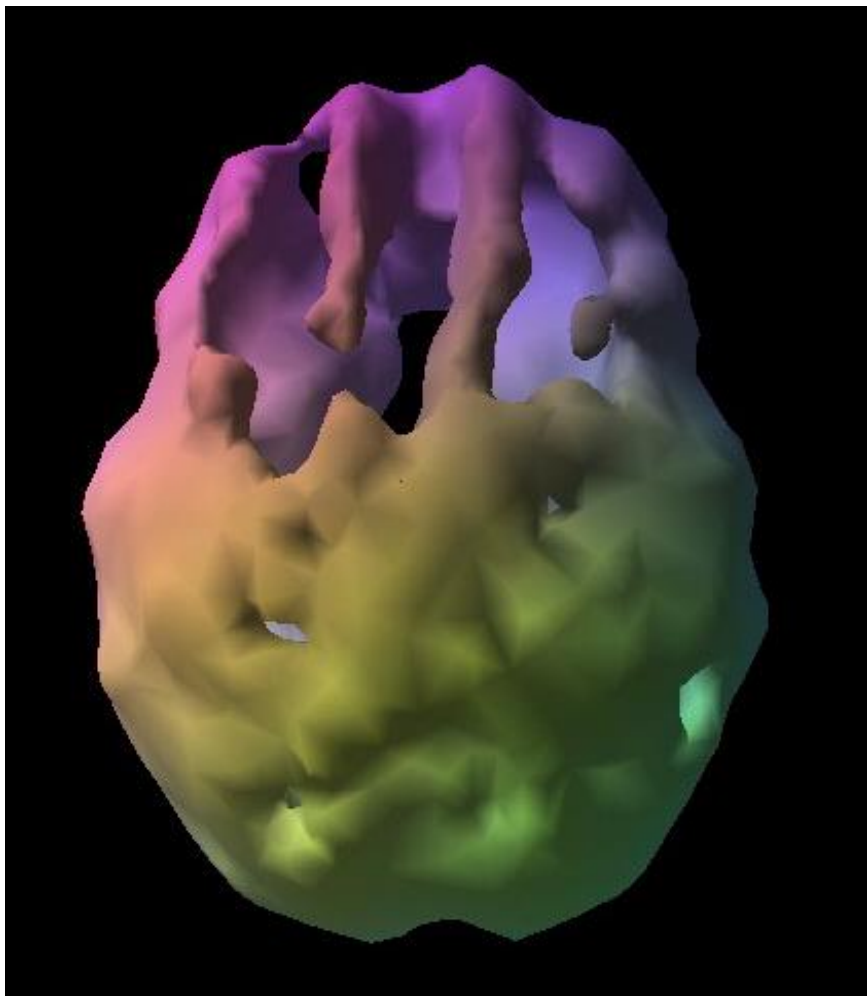




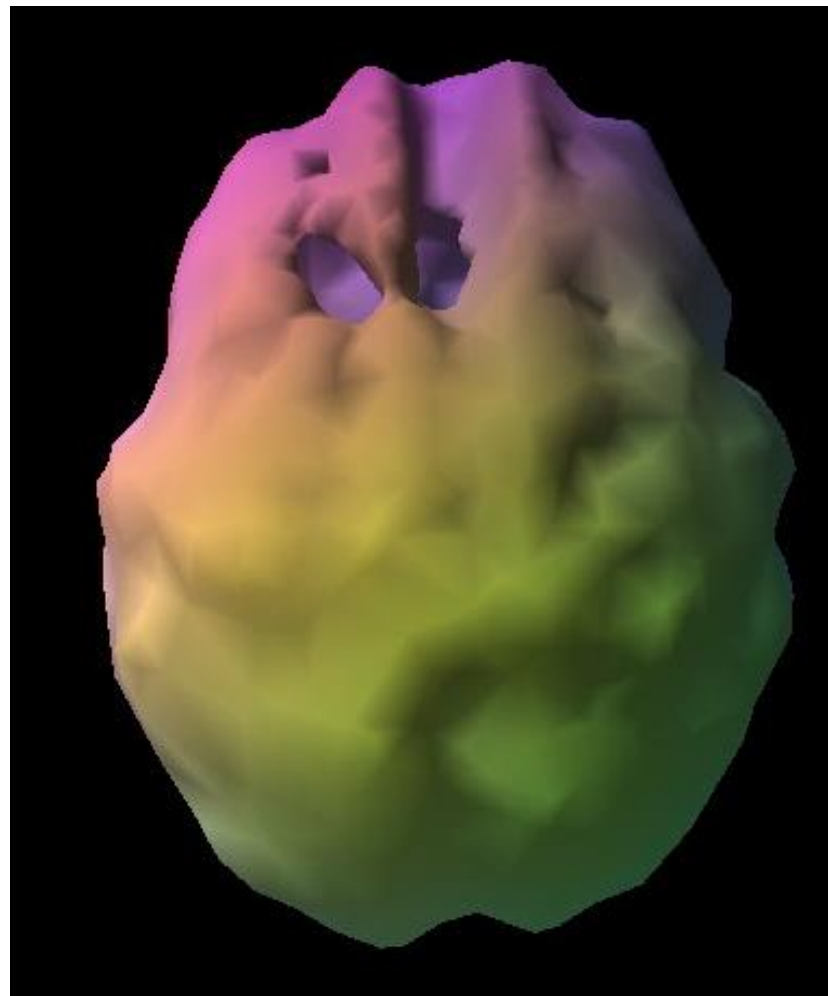
Nancy

Ray and Nancy

- Aggressive treatment program:
 - Aricept, Namenda
 - HBOT
 - Neurofeedback
 - Brain-directed nutraceuticals
 - High dose Omega-3 FA's
 - Anti-inflammatory diet
- Ray lost 30# via same nutritional plan



Before



After 10 Weeks

Ray and Nancy Now



SPECT Treatment Prediction Biomarkers

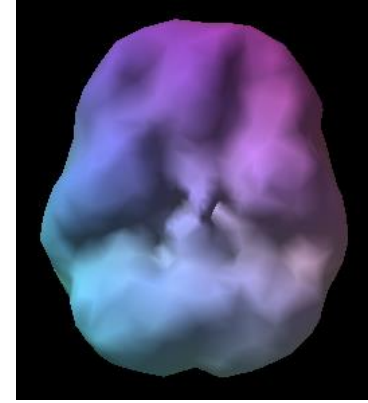
- **Cho 2007 (n34)** -- *ADHD children non-responders to stimulants had higher rCBF in AC and right BG. 88% classified correctly*
- **Amen 2008 (n157)** – *ADHD deactivation PFC pole +with concentration stimulant, activation associated with – stimulant response*
- **Navarro 2004 (n47)** – *Late onset severe depression, left frontal-cerebellar perfusion ratio positive predictive value of treatment 94%*
- **Brockmann 2009 (n93)** – *Depression hyperfrontality + SSRI response, low – SSRI*
- **Langguth 2007 (n24)** – *Depression rTMS responders ↑↑AC rCBF*
- **Richieri 2011 (n18)** – *Depression rTMS non-responders with lower PFC rCBF*
- **Hanada 2013 (n45)** – *Depression, older, non-responders lower middle frontal cortex and insular rCBF*

SPECT Treatment Prediction Biomarkers

- **Hoehn-Saric 2001 (n16)** – *OCD treatment responders to SSRIs higher pre-treatment PFC rCBF*
- **Noel 2002 (n20)** – *Alcoholics ↓↓PFC rCBF predicts relapse*
- **Warwick 2006 (n31)** – *Social Anxiety Disorder treatment response lower insular cortex citalopram (also AC) and moclobemide*
- **Tanaka 2004 (n70)** – *Alzheimer's ↑↑temporal-parietal predicts positive response to donezepil*
- **Kanetaka 2008 (n91)** – *Alzheimer's ↑↑PFC perfusion predicts positive response to donezepil*
- **Jobst 1997 (n391)** – *Predict Alzheimer's 89% sensitivity, 80% specific, 83% accurate, with CT 80% sensitive, 93% specific, and 89% accurate*

SPECT Treatment Prediction Biomarkers

- **Bonte 2006 (n49)** – *Autopsy confirmed Alzheimer's, sensitivity 87%, specificity 89%, ppv 93%, npv 83%, accuracy 88%*
- **Bonte 2004(n20)** – *95% separates Alzheimer's & FTLN PC sign*
- **Guedj 2007 (n17)** – *Fibromyalgia ↓↓bilateral medial PFC rCBF predicts negative response to ketamine (100%ppv, 91% npv)*
- **Eturgul 2009 (n22)** – *Schizophrenia, treatment responders showed higher frontal basal ganglia perfusion with treatment*
- **Rodriquez 1997 (n39)** – *Schizophrenia ↑↑thalamus, left basal ganglia, right prefrontal predicts positive response to clozapine*
- **Kao 1994 (n18)** – *Childhood viral encephalitis – early healthy SPECT predicts positive outcome at 1 year*
- **Jacobs 1996 (n136)** – *mTBI predicts outcome at 1 year, sensitivity 100%, specificity 85%, 83/89% positive/negative predictive value*



The Role of Neuroimaging in Psychiatry and Addiction Medicine

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