Research Sample – Violence/Suicidal

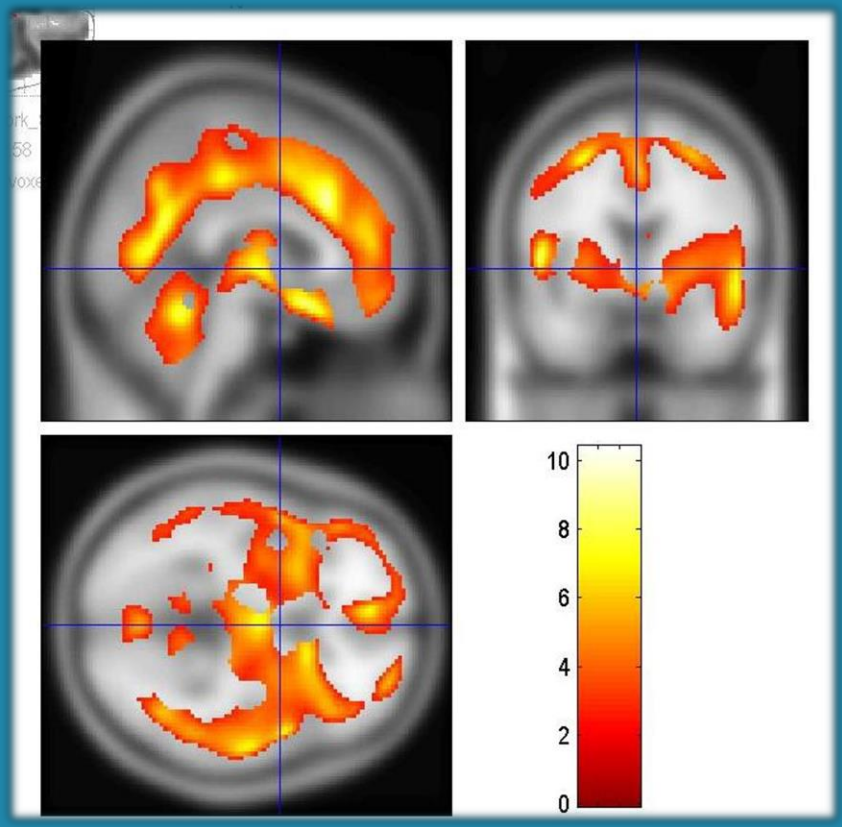
- 75 Studies, >1500 patients
- Amen, 2007, 41 murderers vs. healthy controls
  - SPECT showed significant PFC deficits, more global deficits in older adults
- Soderstrom, 2002, 32 patients
  - Aberrant frontotemporal activity most frequently seen in violent behavior.
- Hirono, 2000, 20 patients
  - Results indicated an association between aggression and decreased perfusion in the left anterior temporal cortex.

Research Sample – Violence/Suicidal

- **Bufkin, 2005, REVIEW OF 17 STUDIES**
  - **Reveals that the areas associated with aggressive and/or violent behavioral histories, particularly impulsive acts, are located in the prefrontal cortex and the medial temporal regions.**
- **Woermann, 2000, 83 patients, MRI**
  - **Patients with TLE with aggressive episodes had a decrease of grey matter, most markedly in the left frontal lobe, compared with the control group and with patients with TLE without aggressive episodes.**

Research Sample – Violence/Suicidal

- **Amen, 2009, 15 completed suicides**
  - **Marked decreases, especially in the PFC, AC and area 25**



Courtesy Amen Clinics, Inc. www.AmenClinics.com

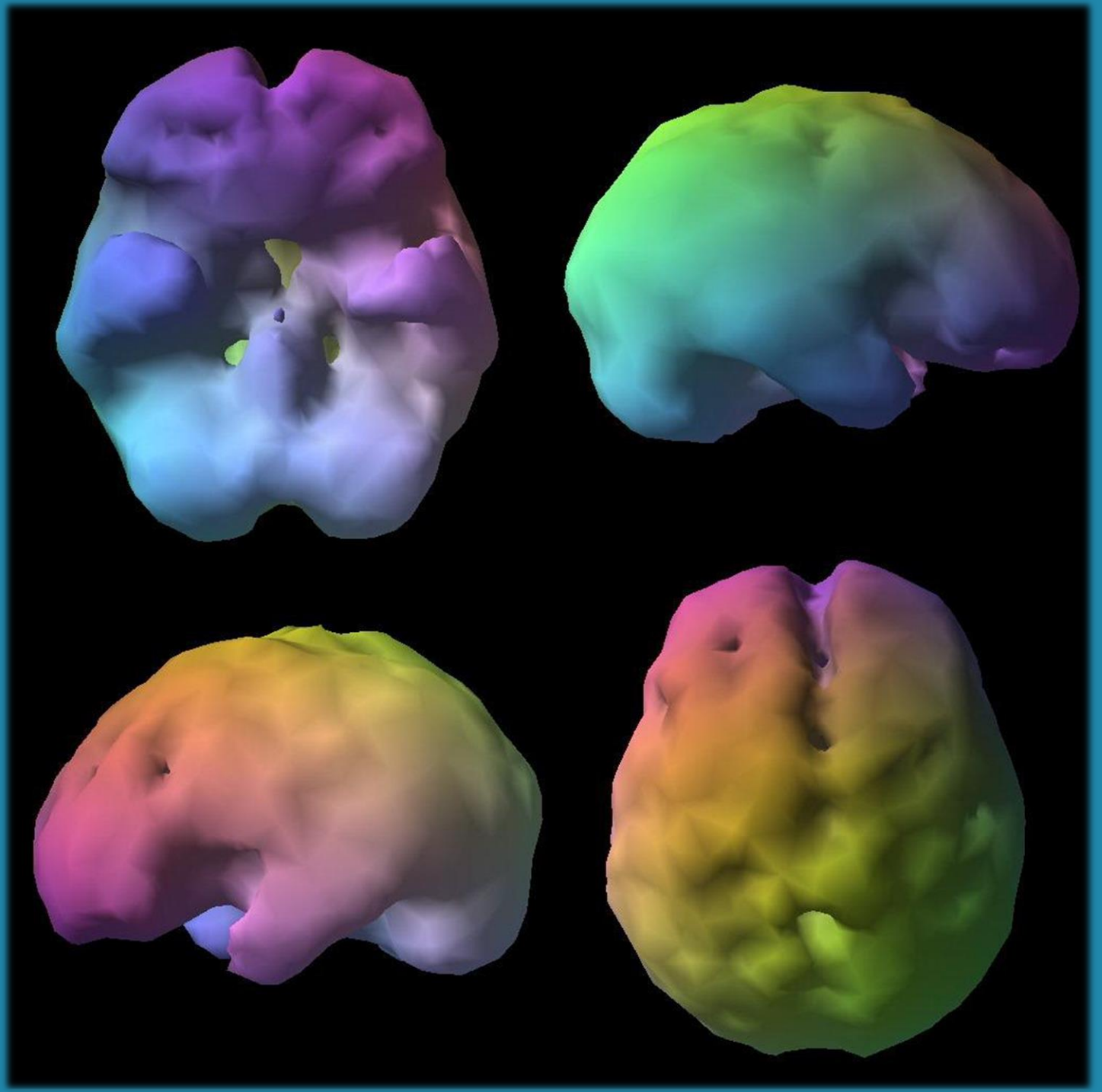
Imaging Help with Violent Behavior

- Identify systems involved with violence and direct treatment
  - Prefrontal, Temporal Lobe, Ant. Cingulate
- Optimize brain function before rehab
- Help motivate treatment
- Help understand aberrant behavior

Head Injury: Leading to Abuse

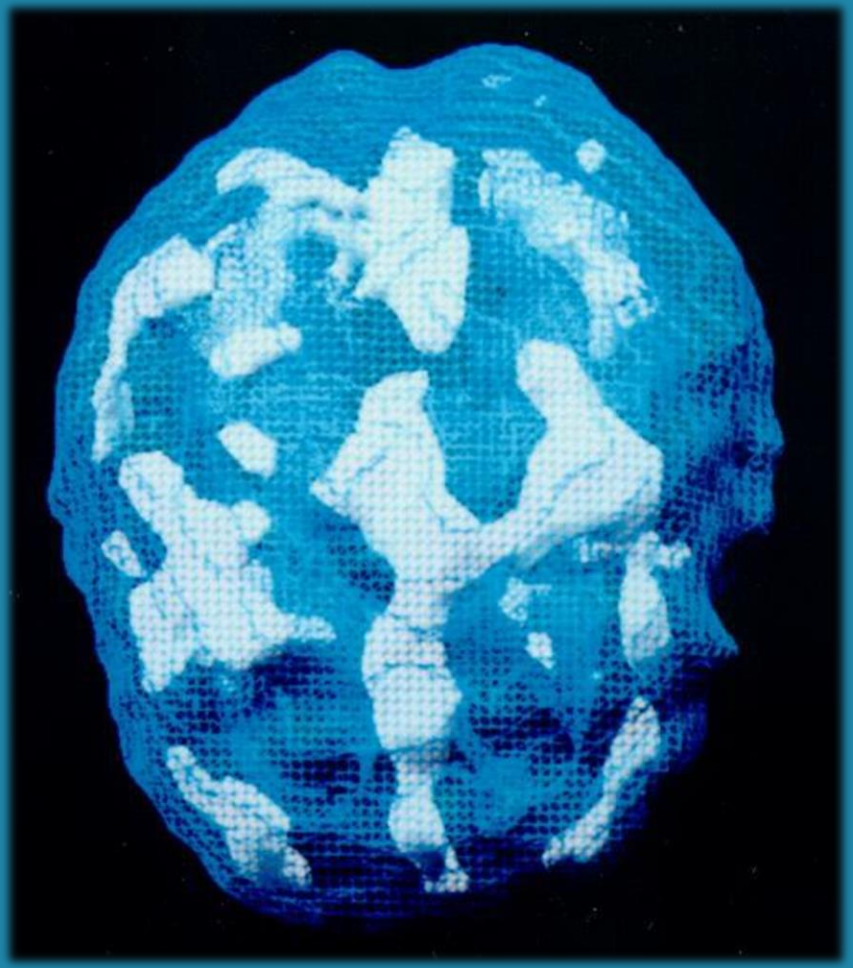
Courtesy Amen Clinics, Inc. www.AmenClinics.com

Chiesa

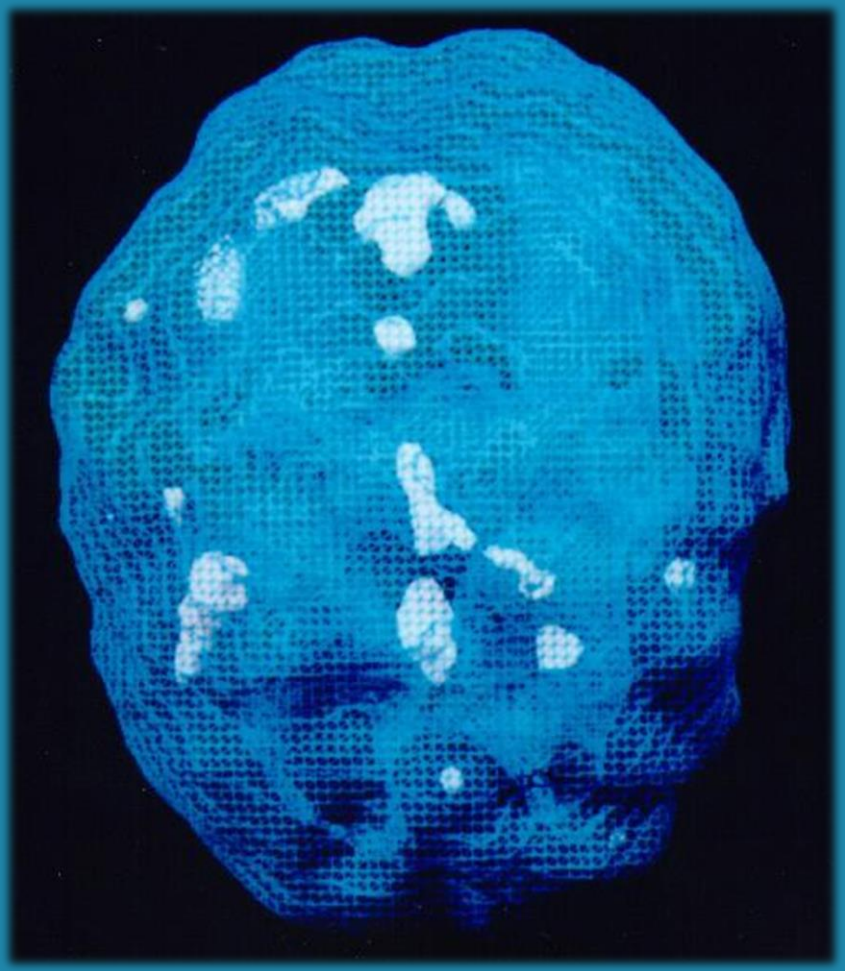


Courtesy Amen Clinics, Inc. www.AmenClinics.com

WHAT DOES HIS SOUL LIKE?



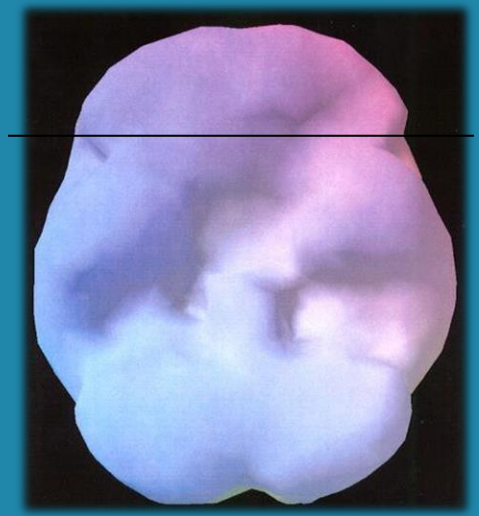
Before Treatment



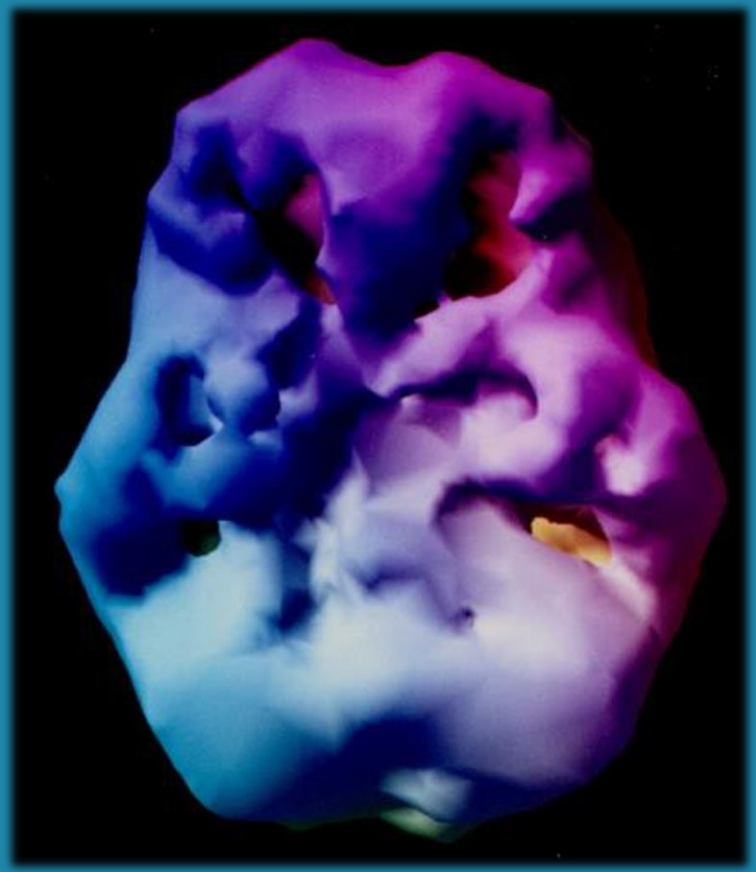
After Treatment

Courtesy Amen Clinics, Inc. www.AmenClinics.com

LP - Conc. Without and With Adderall



Normal

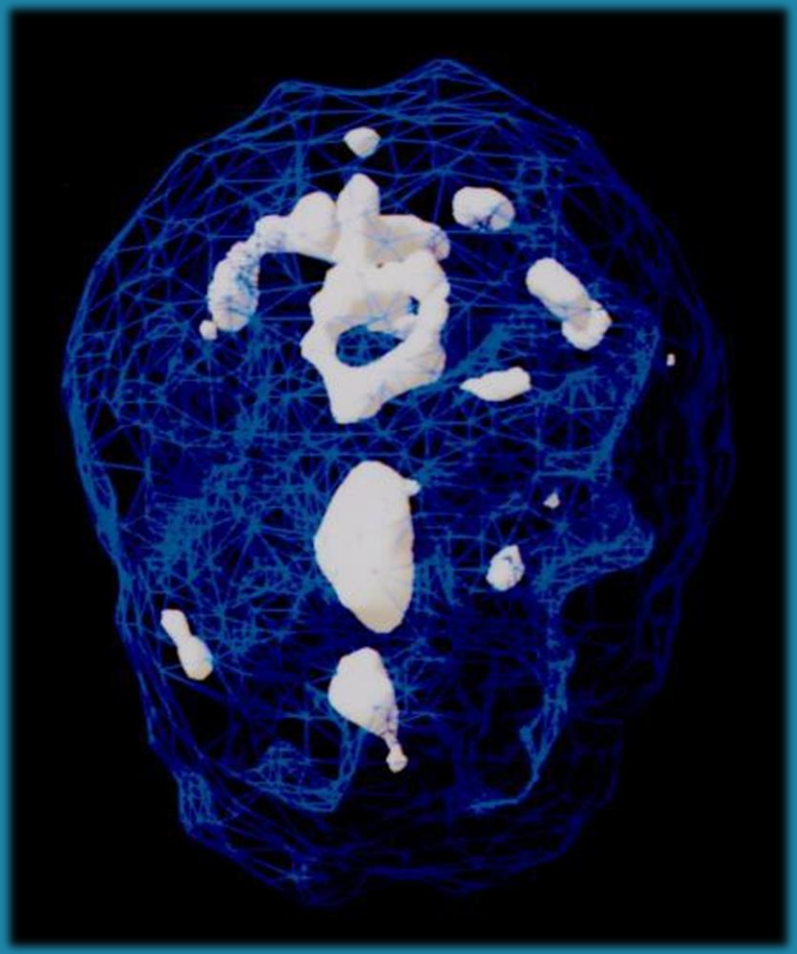


No Meds

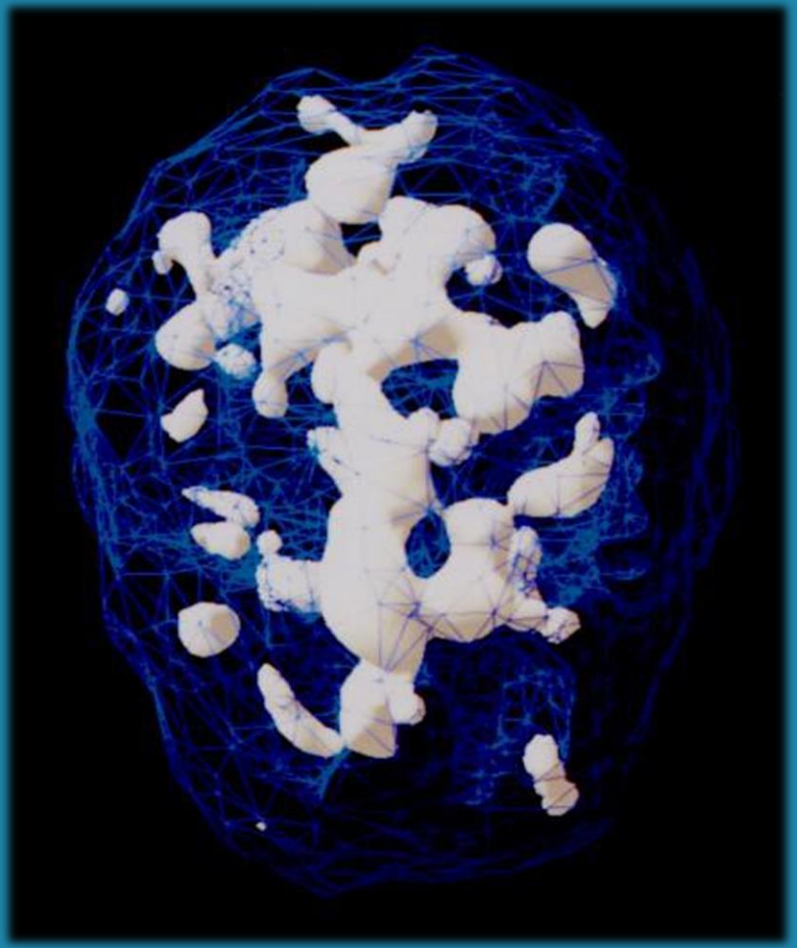
Adderall 120mg

Courtesy Amen Clinics, Inc. www.AmenClinics.com

LP - Conc. Without and With Adderall



No Meds

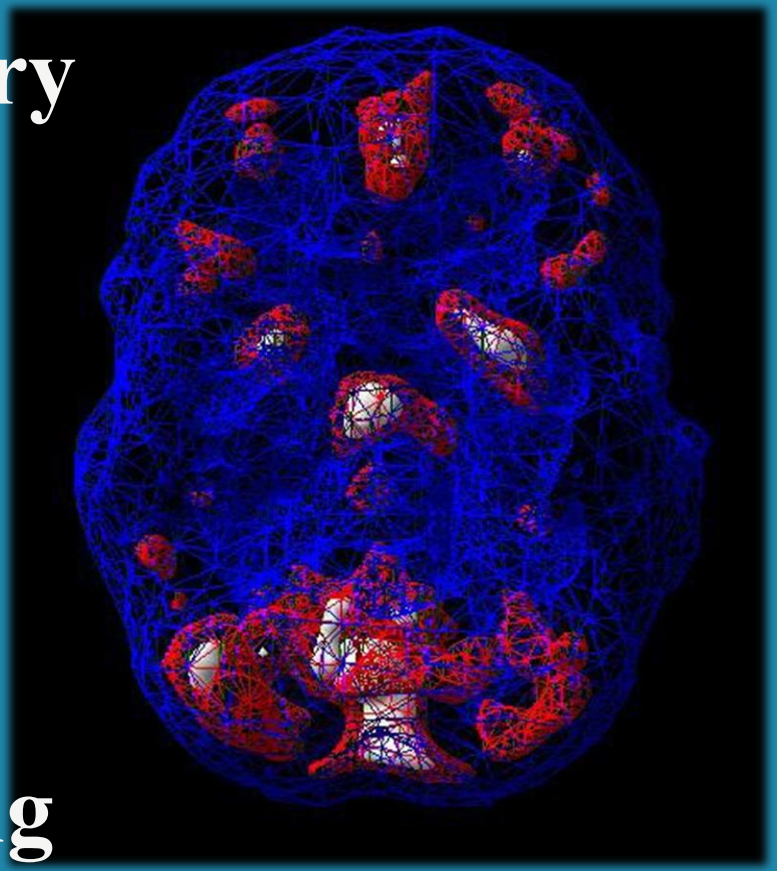


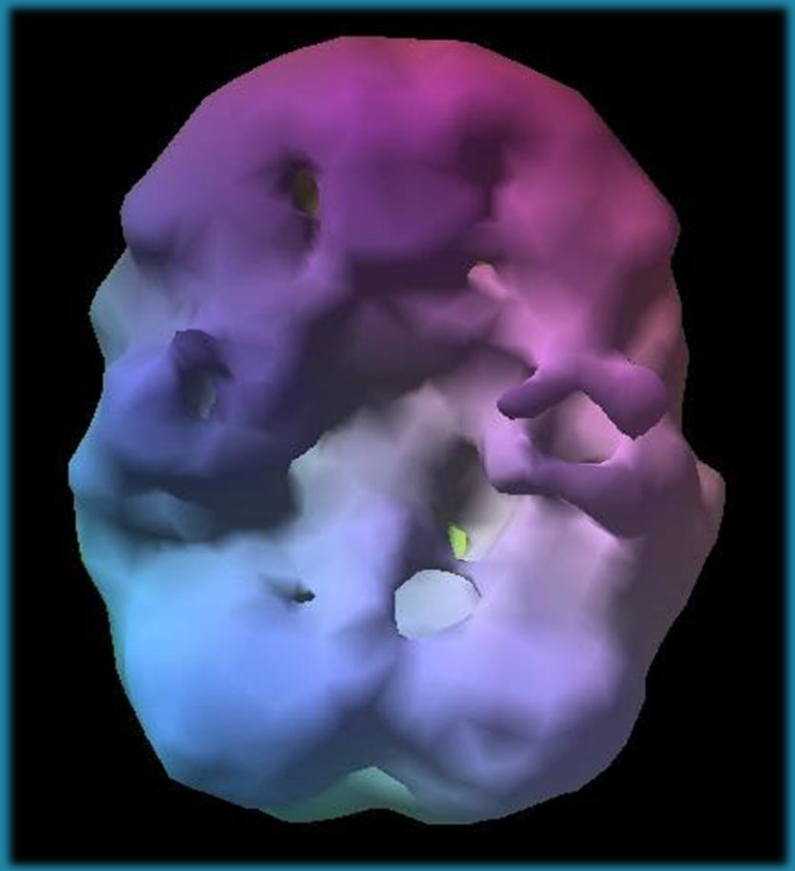
Adderall 120mg

Courtesy Amen Clinics, Inc. www.AmenClinics.com

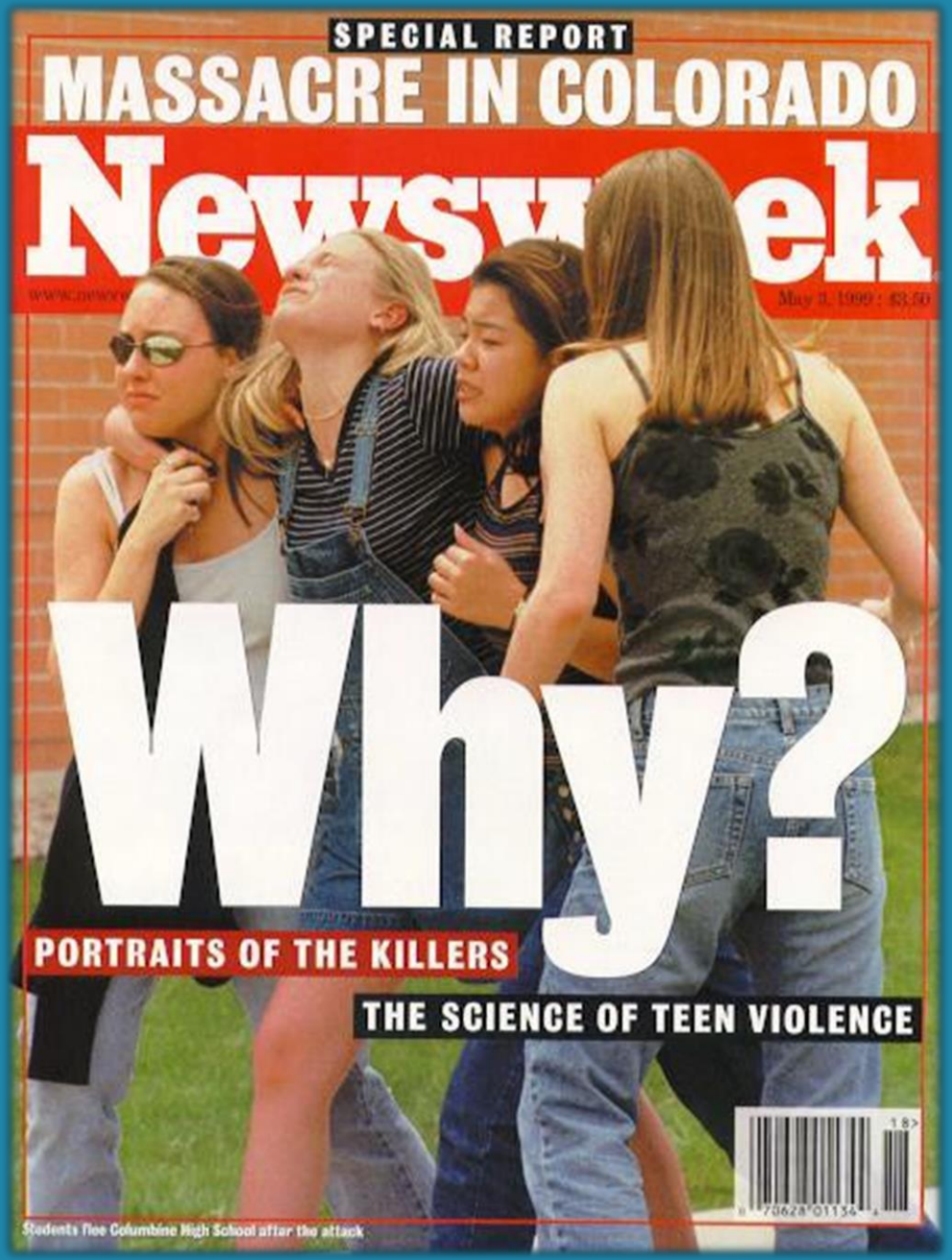
Jason Walker

- Brain injury
- Obsession
- Jealousy
- Rape
- Kidnapping



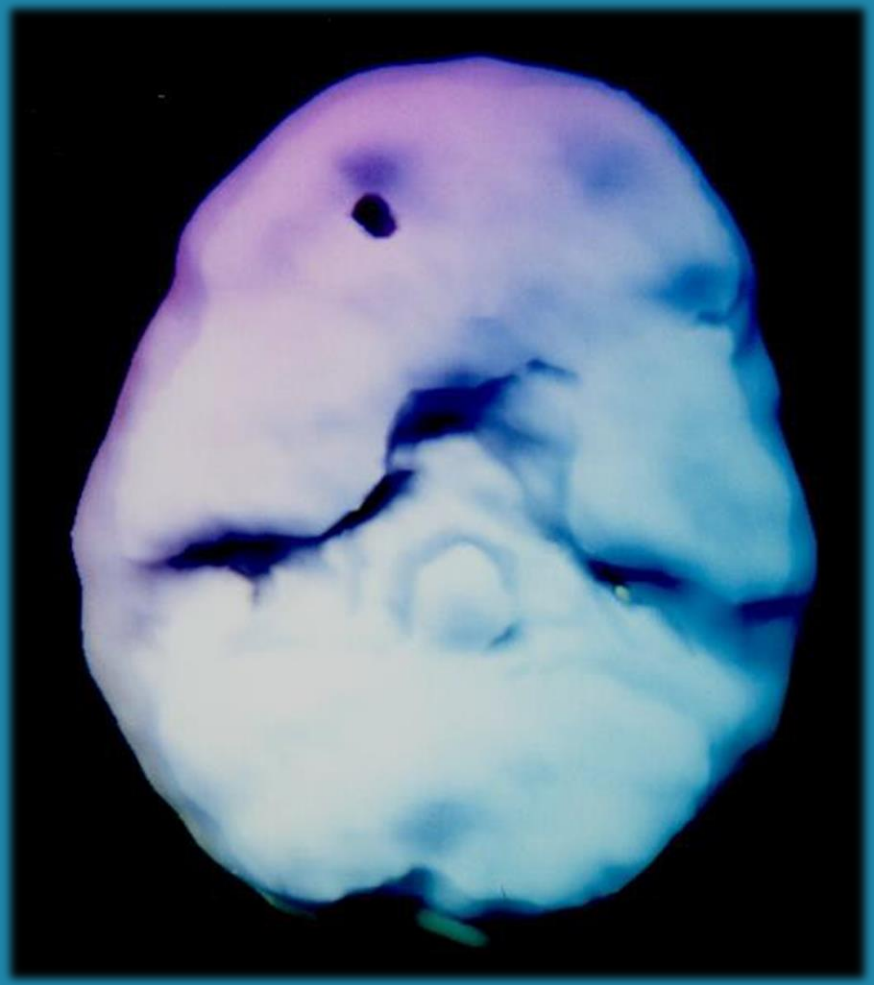


Courtesy Amen Clinics, Inc. www.AmenClinics.com

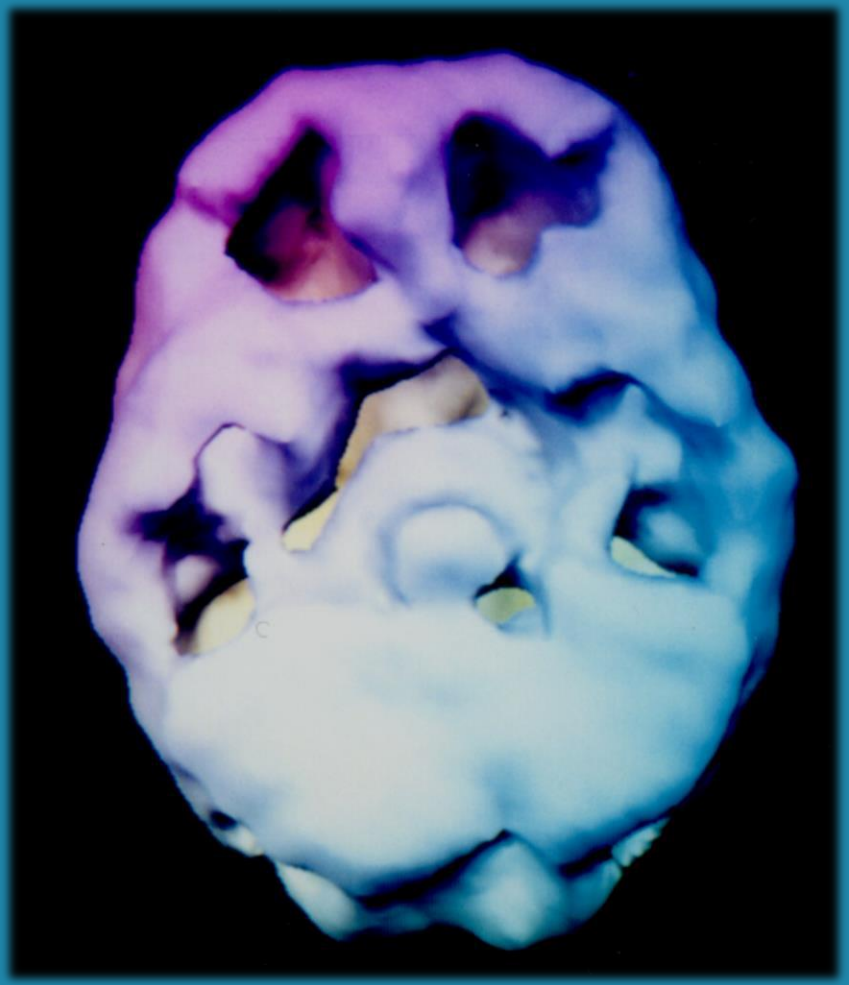


Courtesy Amen Clinics, Inc. www.AmenClinics.com

Normal

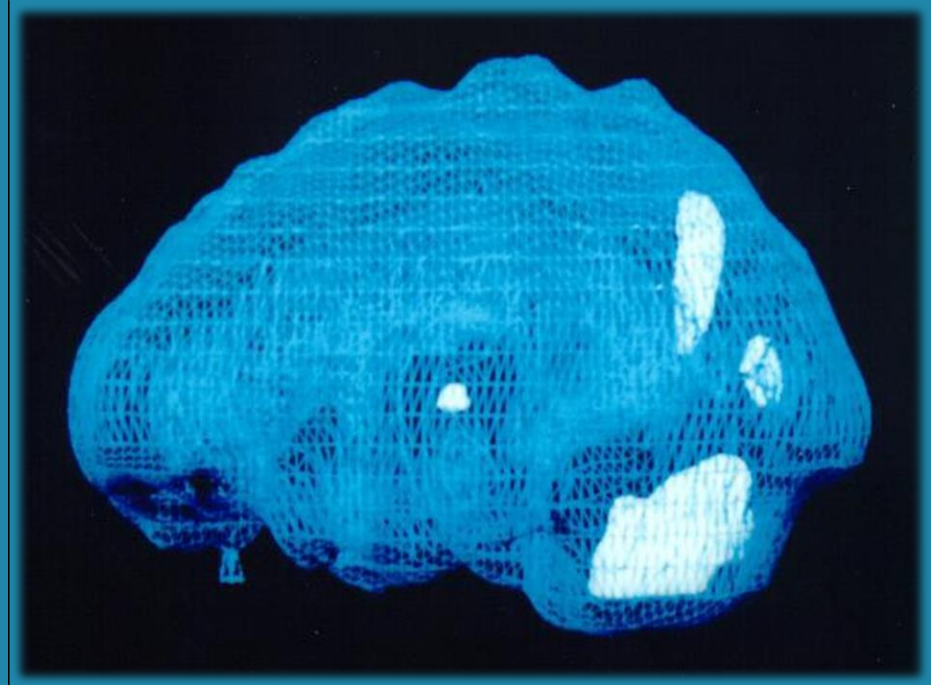


Violent Juvenile

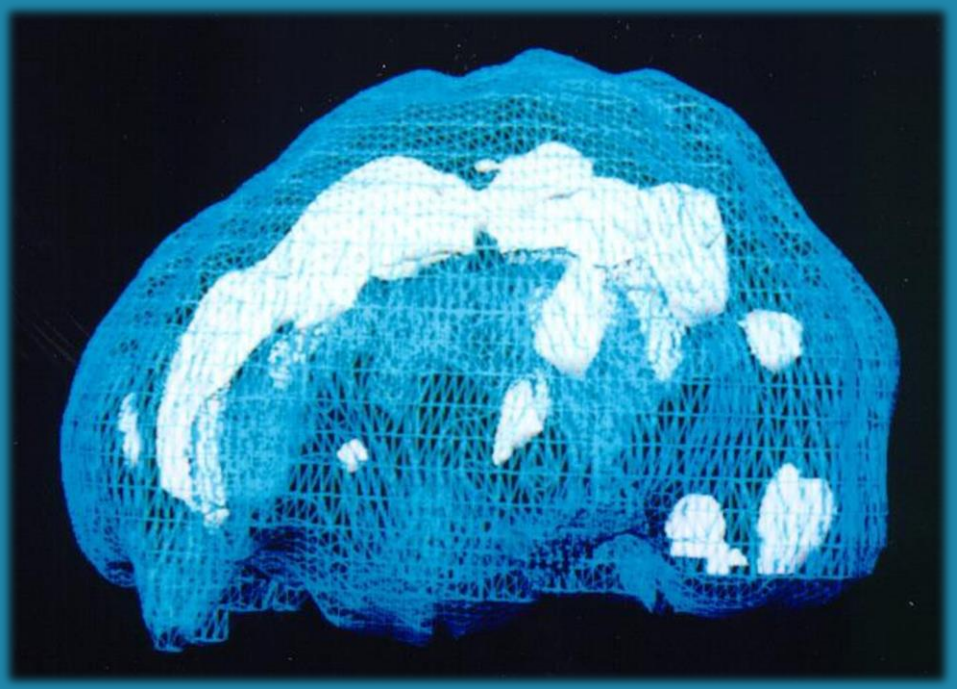


Courtesy Amen Clinics, Inc. www.AmenClinics.com

Normal



Violent Juvenile

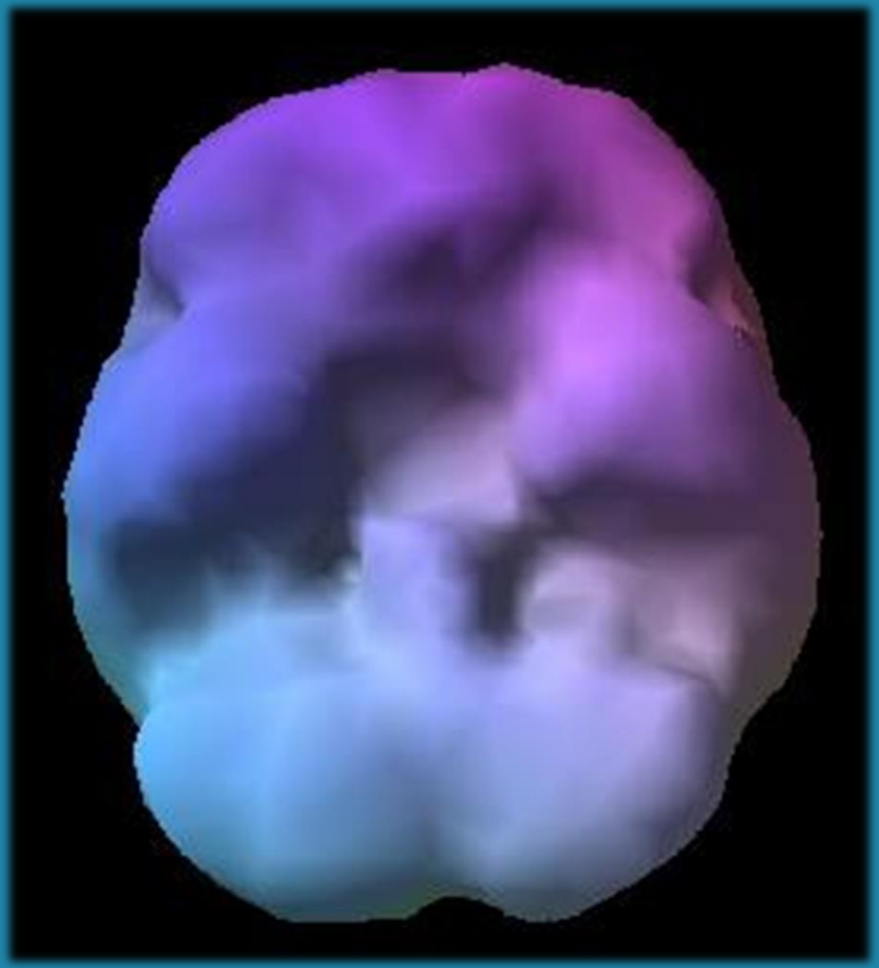


Courtesy Amen Clinics, Inc. www.AmenClinics.com

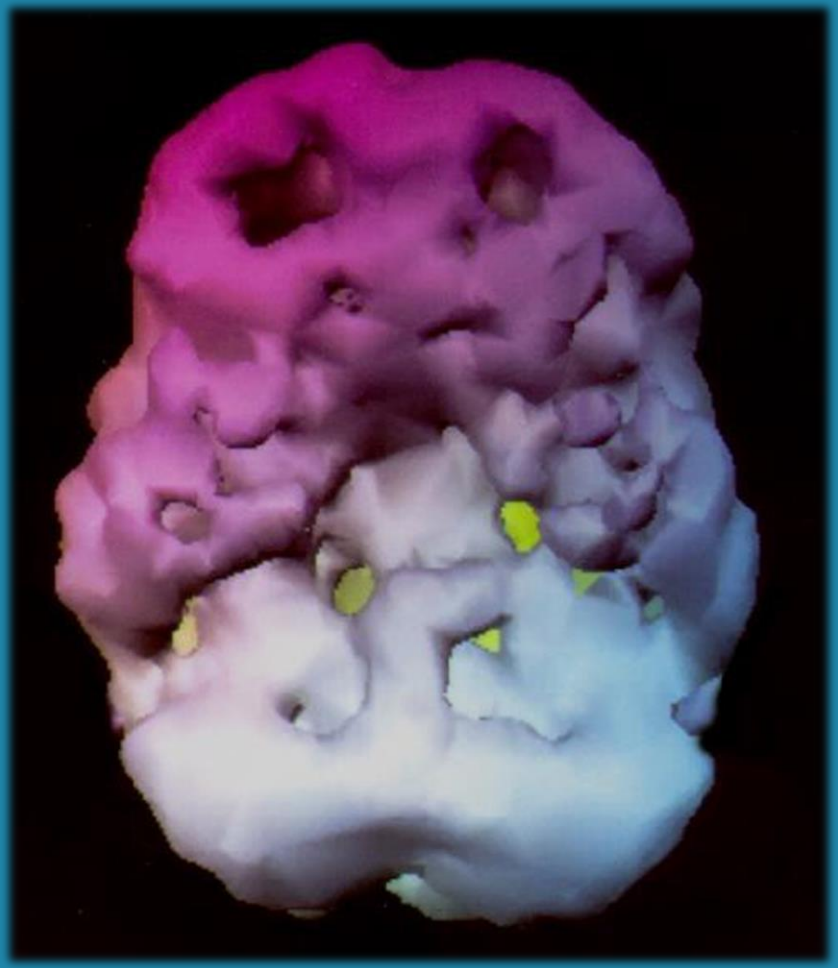
Rape
Left Hemisphere/Brain Injury

Courtesy Amen Clinics, Inc. www.AmenClinics.com

WHAT DOES HIS SOUL LIKE?



Healthy Brain

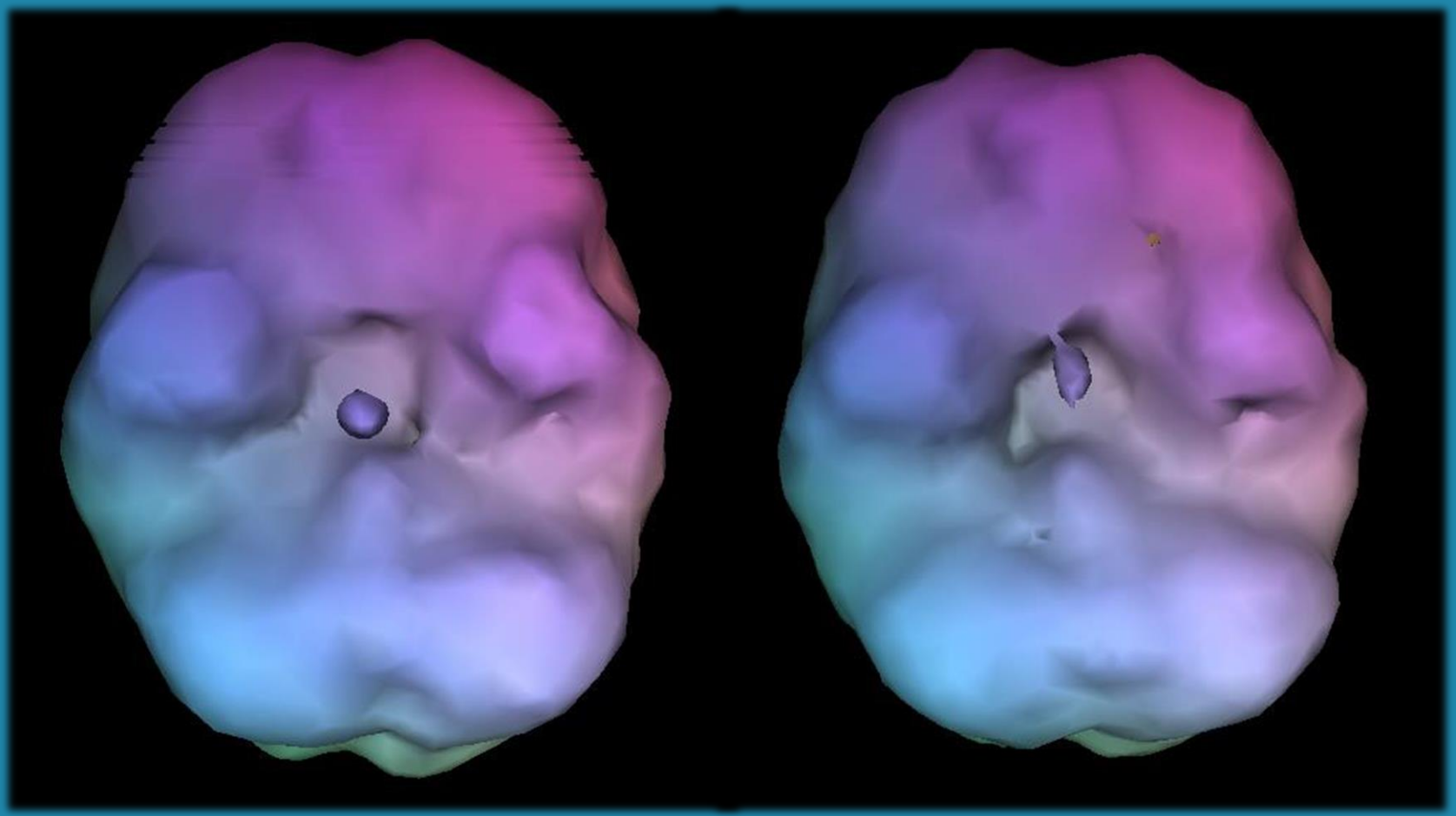


Kip Kinkel

Courtesy Amen Clinics, Inc. www.AmenClinics.com

Mild Decreased LTL

Healthy

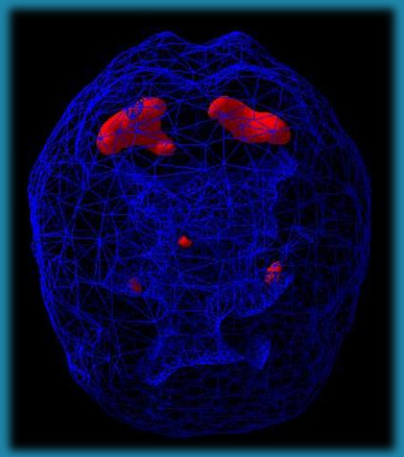


Baseline

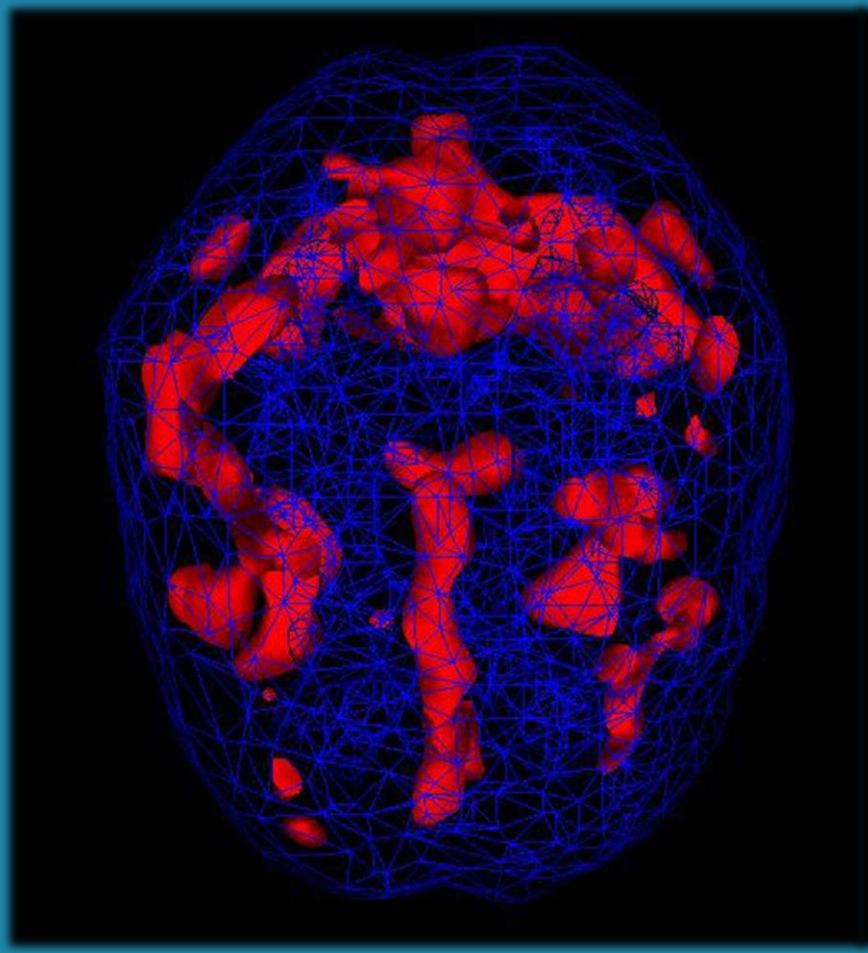
Concentration

Courtesy Amen Clinics, Inc. www.AmenClinics.com

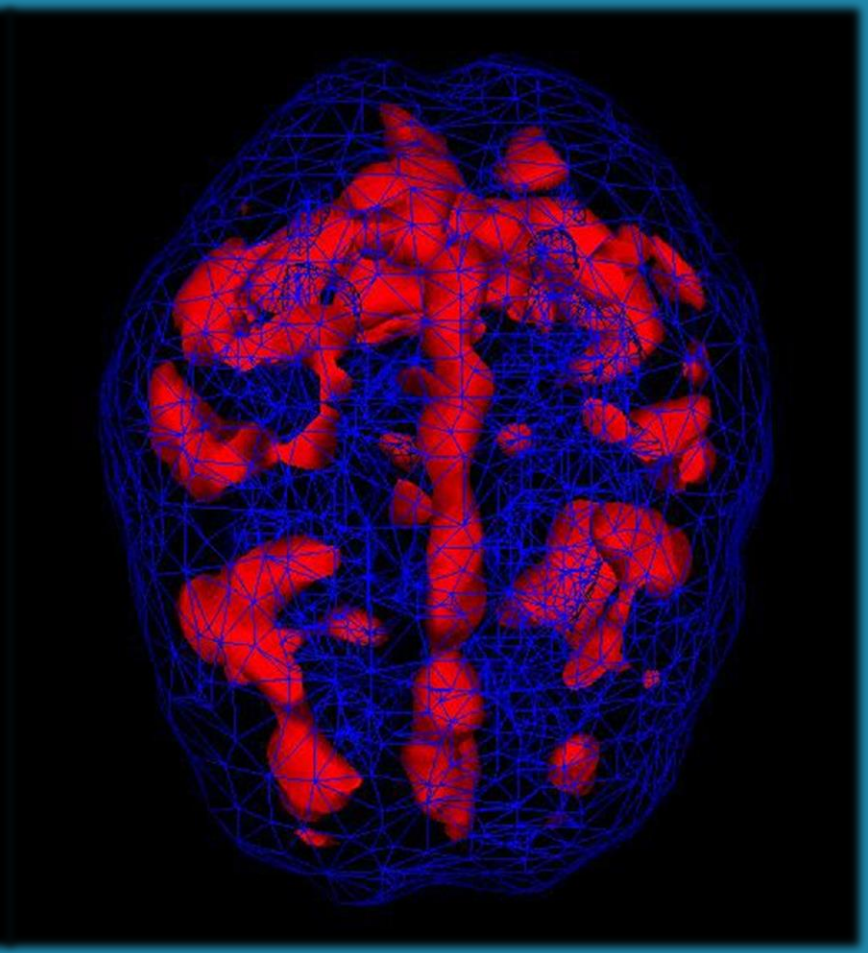
Ring of Fire



Healthy



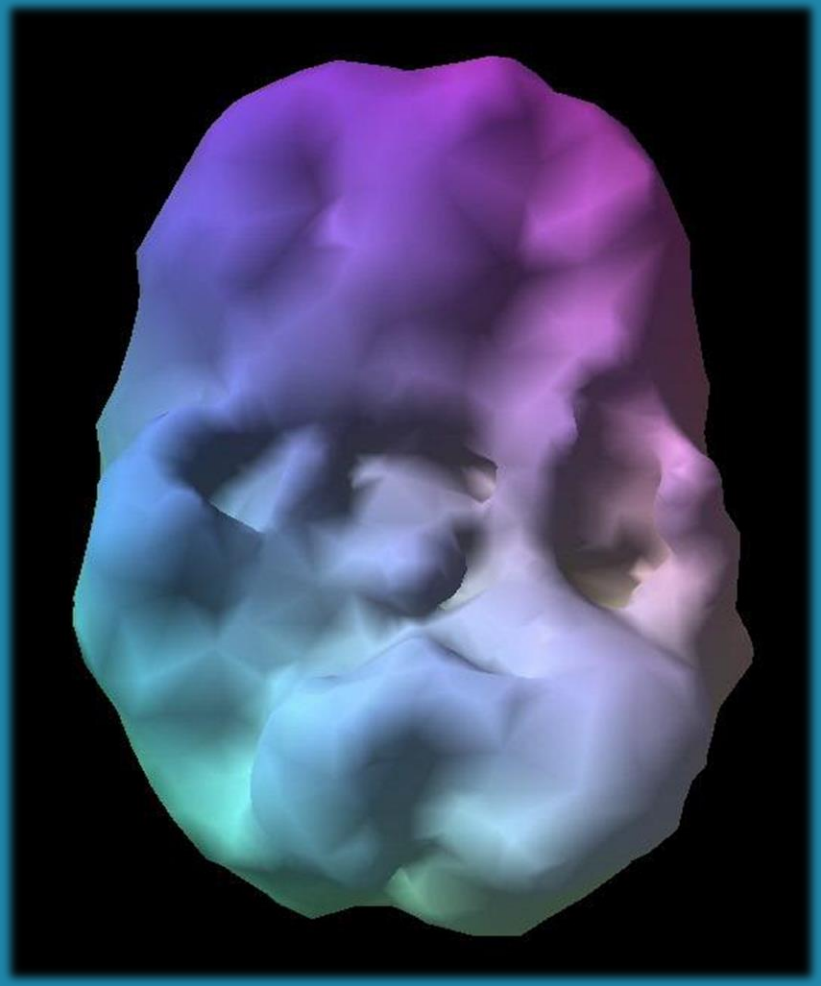
Baseline

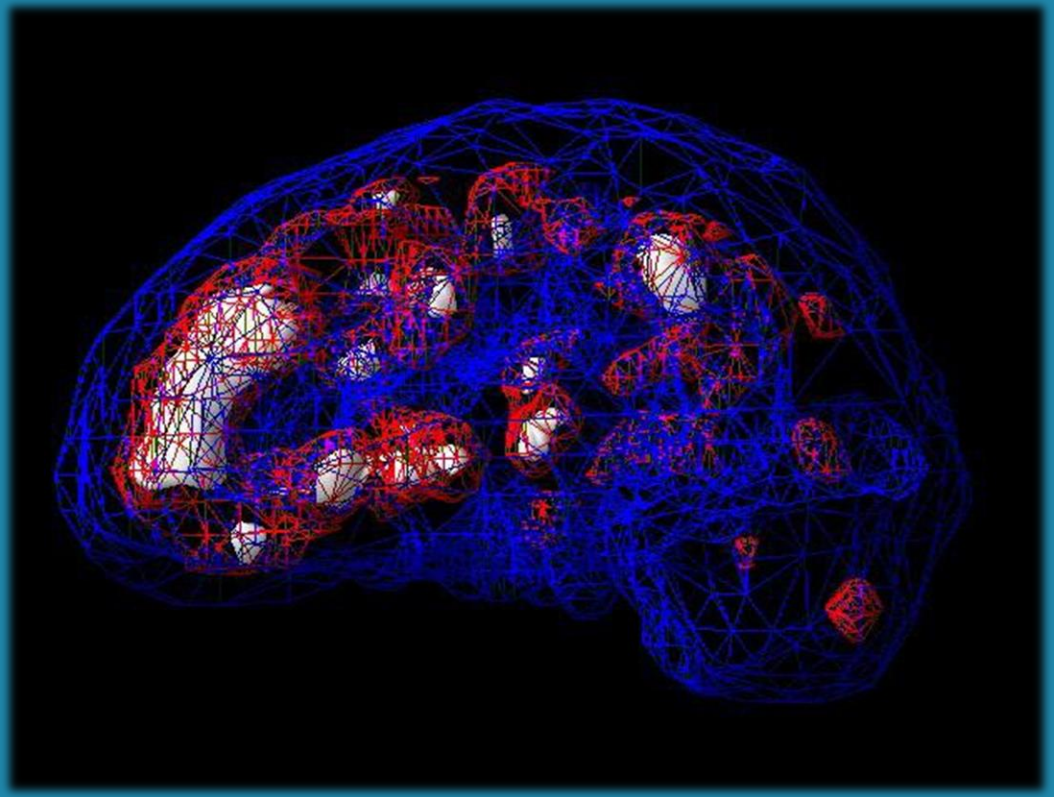


Concentration

Courtesy Amen Clinics, Inc. www.AmenClinics.com

Trauma Induced Temporal Lobe Epilepsy and OCD





Courtesy Amen Clinics, Inc. www.AmenClinics.com

Research Sample – Toxic Exposure

- Rea, 2003, 30 patients with toxic mold exposure
  - 86% had abnormal low activity
- Kao, 1994, 18 children with viral encephalitis

(a) SPECT abnormal more often than CT/MR in acute phase and provided better location.

(b) Acute encephalitis locally increased rCBF

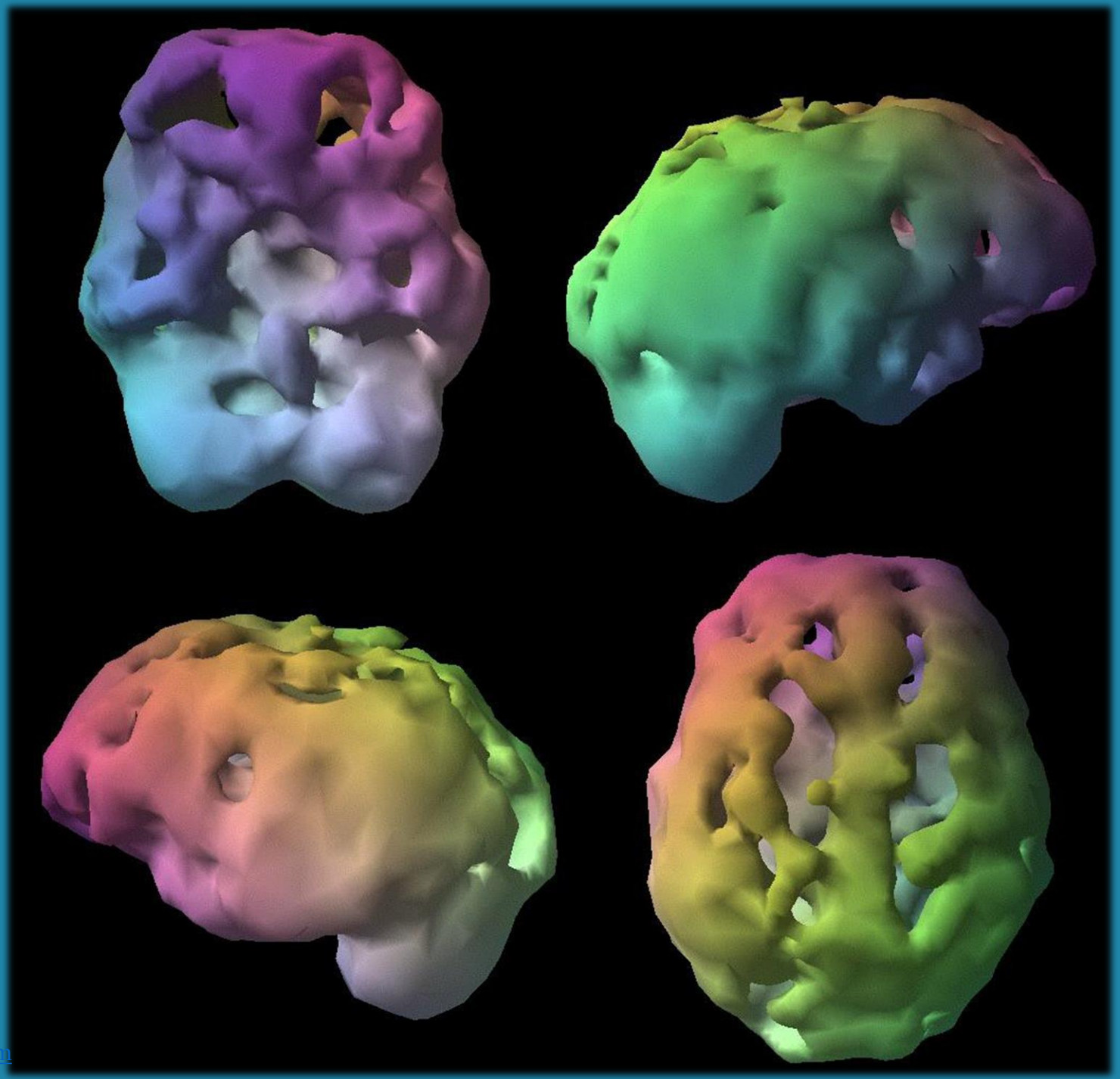
(c) After acute episodes, SPECT returns to normal in most

(d) Normal SPECT in subacute phase usually indicates a good outcome after a year.

Research Sample – Toxic Exposure

- Kao, 1998, 10 patients with CO poisoning
  - Overall decreased perfusion
- Vera, 1999, 26 children with cancer chemotherapy
  - Pattern of decreased perfusion noted
- Callender, 1993, 33 patients - environmental toxins
  - 94% had abnormal SPECT scans with most frequent areas of abnormality being temporal lobes (67.7%), frontal lobes (61.3%), basal ganglia (45.2%), thalamus (29.0%), and parietal lobes (12.9%)

Toxic Exposure



Courtesy Amen Clinics, Inc. www.AmenClinics.com

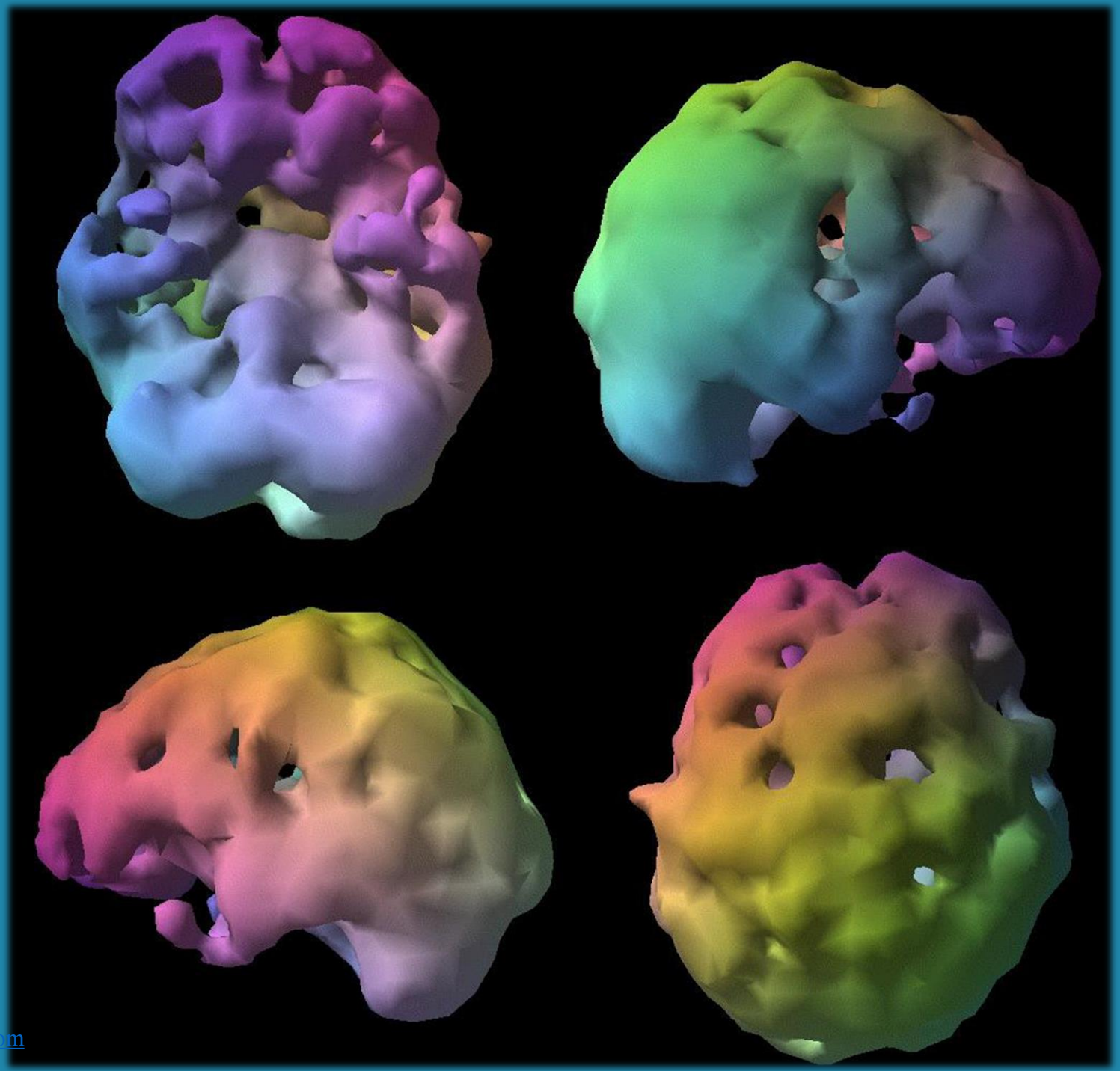
Research Sample – Substance Abuse

- Andinoff, 2006, 35 cocaine vs. 37 normals
  - Decreased bilateral orbital frontal PFC
- Kucuk, 2000, 10 teenagers with inhalant abuse
  - Serious decreased overall activity
- Okada, 1999, 16 solvent abusers
  - Overall decreased activity
- Botelho, 2006, 17 heroin addicts
  - Overall decreases especially in PFC

Research Sample – Substance Abuse

- Tungving, 1986, 9 THC smokers
  - Decreased overall perfusion
- Noel, 2002, 20 alcoholics
  - Decreased medial PFC predicts increased relapse
- Pezawas, 2002, 21 opiod dependent
  - Overall decreased activity compared to normals
- Pallavicini, 2002, 60 drug abusers, abstinent 28 days
  - Abnormally decreased in 60% of patients
- Harris, 1999, 22 abstinent alcoholics and controls
  - Decreased cerebellum in abstinent alcoholics, increased aging

Substance Abuse



Courtesy Amen Clinics, Inc. www.AmenClinics.com

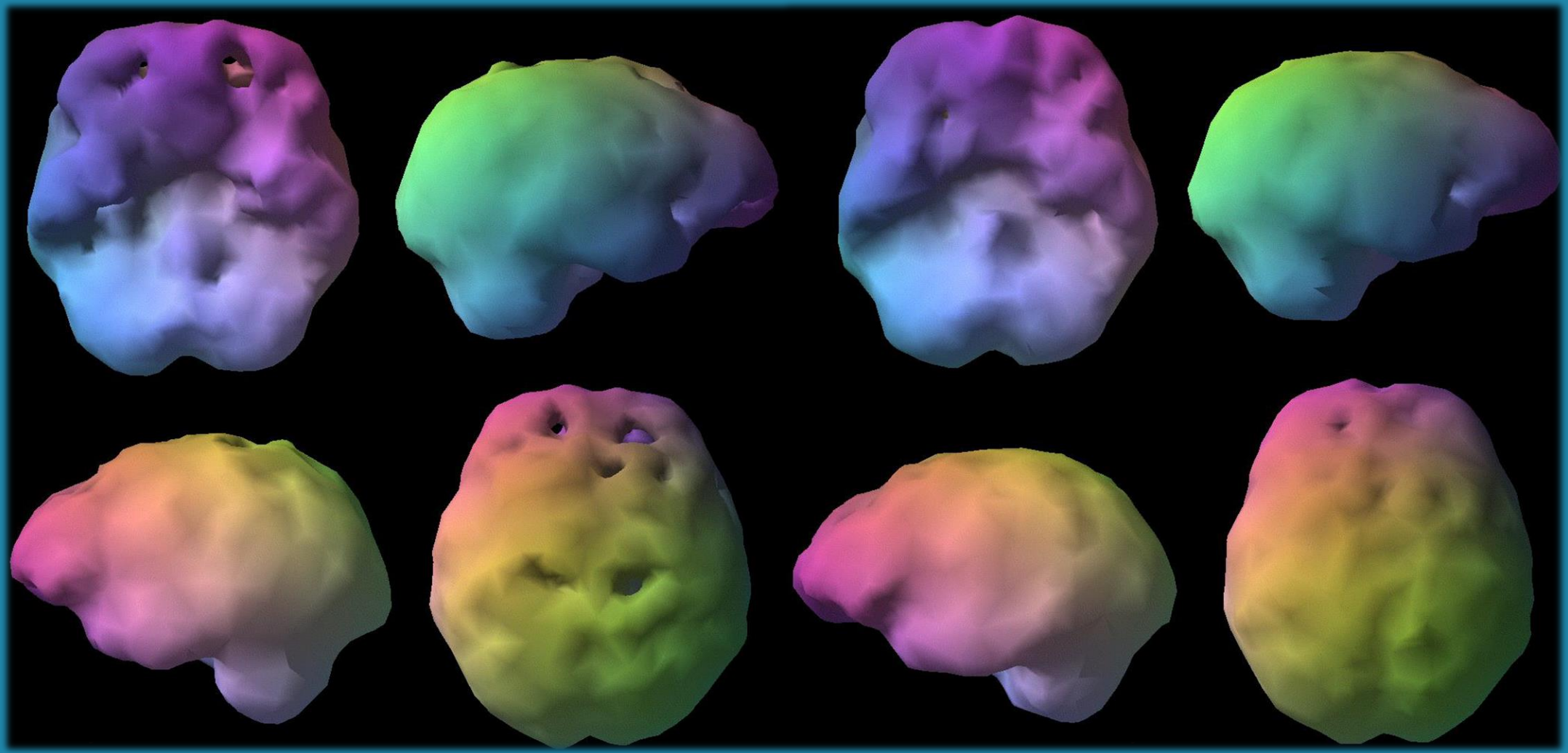
Research Sample – Treatment Response

- 107 studies, 2695 patients
- Shi, 2003, 320 patients with brain injury and HBOT
  - HBOT increased SPECT and treatment response
- Cho, 2007, 34 children with ADHD, Ritalin + vs. –
  - SPECT correctly classified 88%, responders lower AC
- Lee, 2005, 23 ADHD, Ritalin improved i/o PFC
- Matthew, 1996, 10 SAD patients and light therapy
  - Increases in responders in PFC and AC

Research Sample – Treatment Response

- Amen, 2006, 6 police officers and EMDR
  - Decreased right lateral temporal lobe and increased L DLPFC
- Shimizu, 2006, 51 Alzheimer's with donezepil
  - Increased frontal lobes
- Vangu, 2003, 15 patients before and after ECT
  - Increases in PFC/temporal lobes in treatment responders
- Hoehn-Saric, 1991, 6 patients with OCD
  - Prozac decreases hyperfrontality in OCD

Treatment Response



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 – SSR***
- **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***

Courtesy Amen Clinics, Inc. www.AmenClinics.com

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 donepezil***
- **Kanetaka 2008 (n91) –** ***Alzheimer's PFC perfusion predicts positive response to donepezil***
- **Jobst 1997 (n391) –** ***Predict Alzheimer's 89% sensitivity, 80% specific, 83% accurate, with CT 80% sensitive, 93% specific, and 89% accurate***

Courtesy Amen Clinics, Inc. www.AmenClinics.com

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 & FTLD 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*

Answering Important Questions

SCIENTIFIC EVIDENCE?

>2800 articles housed on website about SPECT in clinical psychiatric practice

HAS DR. AMEN'S TEAM PUBLISHED RESEARCH

>50 peer reviewed articles

CAN'T DOCTORS TELL CLINICALLY?

How can you tell without looking? Large outcome studies say most psychiatric treatments are not better than placebo

EXPENSE?

Consider cost of having an ineffectively treated psychiatric disorder

RADIATION DOSE WITH SCANS?

Exposure is less than most CT scans, which are routinely ordered when needed

WILL IT IMPROVE OUTCOMES?

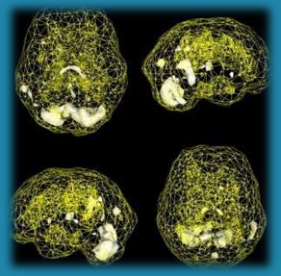
ACI sees complex patients who failed 3 providers and 6 medicines, after 6 months >75% show improvement across all measures, 85% improved QOL

DOES ACI MAKES DIAGNOSES ONLY FROM SCANS?

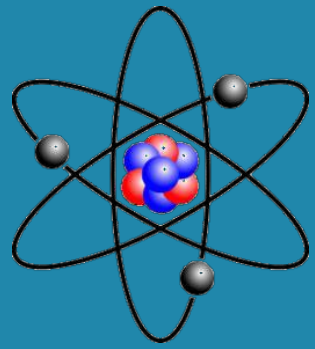
No, we use scans in the context of full bio / psycho / social / spiritual evaluations

WILL SCANS GIVE A FINAL DIAGNOSIS

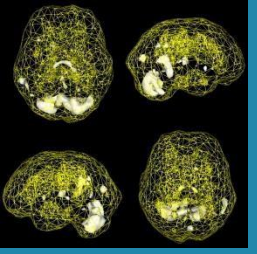
They don't. You have to talk to people. Scans give the underlying physiology of what you are treating to better guide treatment plan



Brain SPECT Imaging Made Ridiculously Simple

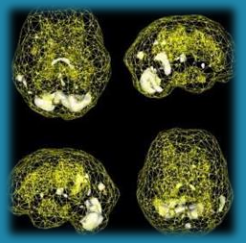


- How SPECT works
- Nuclear physics made simple
- SPECT performed, processed and rendered
- Review of SPECT cameras and imaging agents
- Reading SPECT
- How scans can fool you if you are not careful



How SPECT Works

- In nuclear imaging, radioisotopes are used
- They act like tracers or light beams, such as a flare at sea to track a lost boat
- Radioisotopes are unstable atoms that emit gamma rays or photons that can be measured by gamma cameras

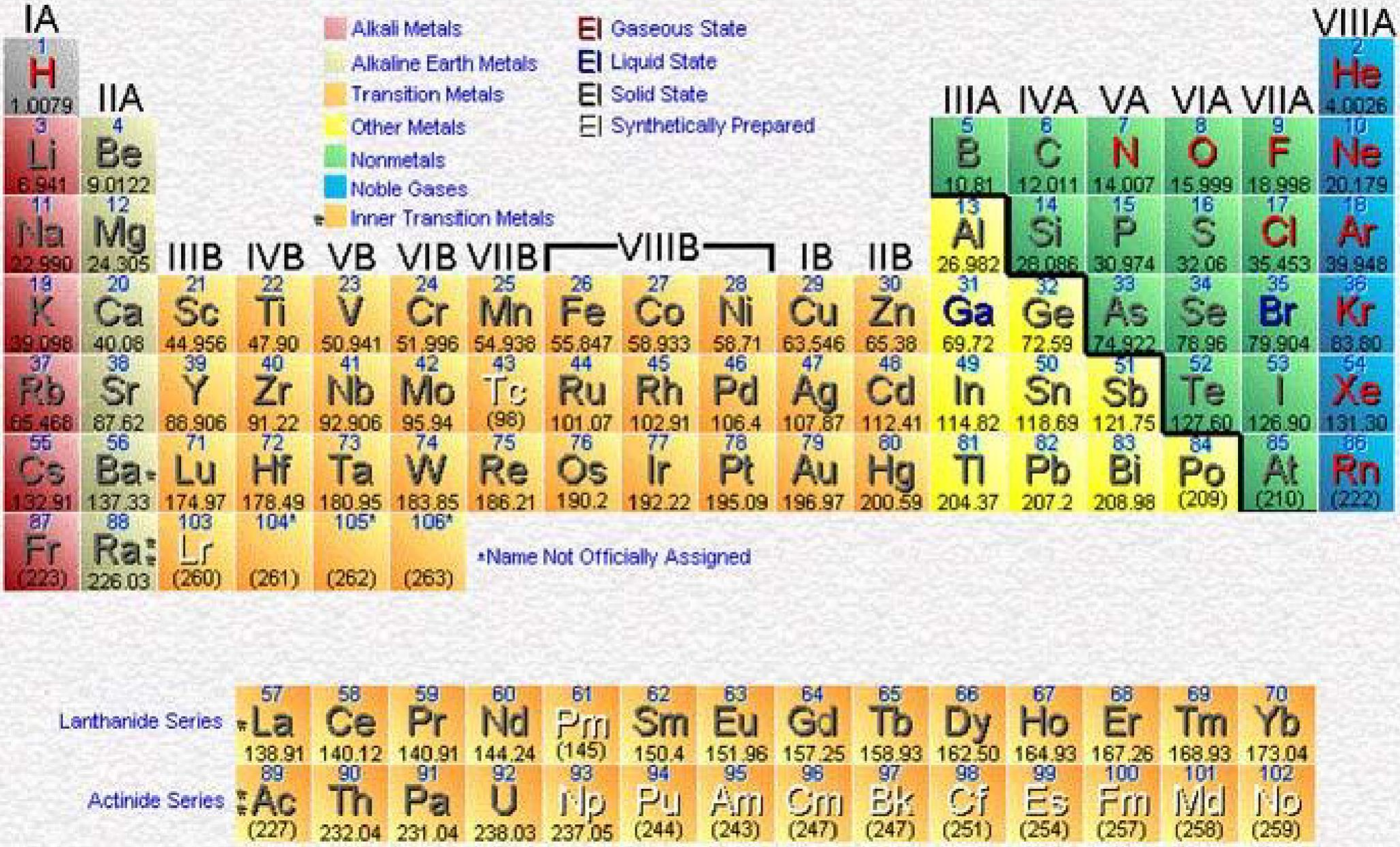


How SPECT Works

- These radioisotopes are attached to medications (radiopharmaceuticals RP) that are easily taken up by certain organs, such as the brain or heart
- The RP can be injected, swallowed or inhaled
- A camera detector takes a picture of where RP has gone, giving images of living tissue activity

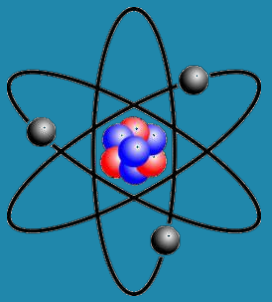
Courtesy Amen Clinics, Inc. www.AmenClinics.com

Periodic Table of the Elements



Technetium

- Technetium has 22 reported isotopes, mass number ranging from 90-111
- Tc 99 (43 protons, 56 neutrons)



- Half-life = 6.01 hours
- Need a full 24 hours between scans

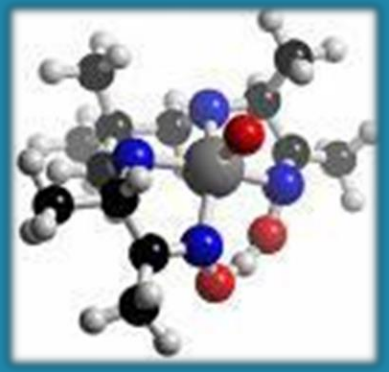
Units of Radioactivity

Becquerel (Bq)

- 1 Bq = one radioactive decay per second

Curie (Ci)

- 1 Ci = 3.7×10^{10} radioactive decays per second
- Typical patient dose is 20-25 millicuries of Tc



SPECT Radiopharmaceuticals

- Currently, two clinically available tracers
- Ceretec (HMPAO, Exametazime)
- Neurolite (ECD, Bicysate)
- Both have advantages and disadvantages.

HMPAO Ceretec

- 80% taken up in a first pass extraction
- Peak uptake within several minutes of injection
- Taken up through blood-brain barrier (BBB), converted to another shape that cannot cross back over BBB
- Remains fixed in brain for several hours
- Measures regional cerebral blood flow

HMPAO Ceretec

Advantages

- Seems to provide more stable imaging over time
- Main tracer uptake is in the cerebellum, which contains half of the brain's neurons
- Amen Clinics database is made up almost exclusively of HMPAO scans

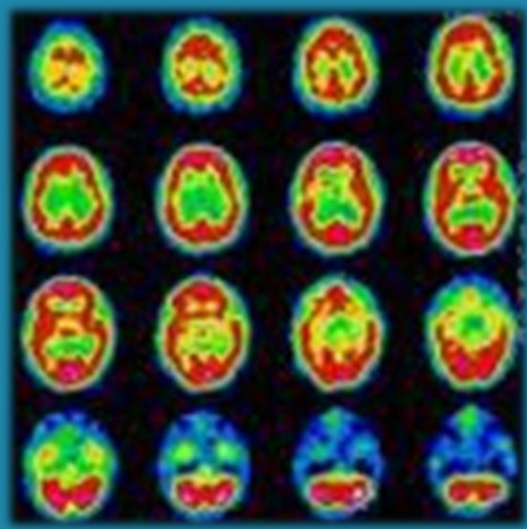
Disadvantages

- It can be taken up outside of the brain and cause artifacts that need to be understood and dealt with

Courtesy Amen Clinics, Inc. www.AmenClinics.com

ECD Neurolite

- Enters brain tissue through BBB
- Also converted to a form which cannot pass back through the BBB



Courtesy Amen Clinics, Inc. www.AmenClinics.com

ECD Neurolite

Advantages

- Major advantage is that there is no extra-axial uptake, such as in the tear ducts or parotid glands, and artifact is less of a problem.

Disadvantage

- In our experience, ECD underperfuses the temporal lobes, which needs adjustment in comparing it to HMPAO scans
- ECD does not seem as stable over time, and its most intense uptake is in the occipital lobes, as opposed to the cerebellum

Other Tracers and Agents

- Xenon 133 gas, blood flow tracer
- DaTscan for DA receptors
- Iodine 123 amphetamine (IMP)
  - Iodine-123-QNB, an acetylcholine muscarinic antagonist, for Alzheimer's disease
  - Iodine-123-Iodine labeled ligands IBZM and IBZP for imaging dopamine system in Parkinson's disease
  - Iodine-123 labeled ligands for imaging the benzodiazapine and the serotonin receptors

Safety of SPECT

- Brain SPECT imaging is a safe procedure
- Radiation from Tc-99m HMPAO is 0.7 rem (Roentgen equivalent man) per 20 mCi dose
- Similar to bone scan or head CT
- 43% of the average annual background radiation in the U.S.
- OSHA gives 5 rem a year as a safe exposure

Safety of SPECT

Devous, past president of SNM, writes:

SPECT and PET have no more risk than MRI-based procedures… Indeed, there are no data that have ever demonstrated any harm to humans by radiation exposure at diagnostic imaging levels. In fact, current data support the presence of radiation hormesis: that low levels of radiation exposure induce beneficial effects of cellular repair and immune system enhancement… Therefore it should be concluded that neither SPECT nor PET brain imaging procedures are associated with any particular risk over activities of daily living and certainly should not be considered to be any more "risky" than MRI or any of its associated functional imaging derivatives

The Gamma Camera

Gamma camera collects photons emitted from patient, enabling scientists to reconstruct a picture of where the gamma rays originated and determine how a particular organ or system is functioning.

Courtesy Amen Clinics, Inc. www.AmenClinics.com

The Gamma Camera

- Components making up the gamma camera are:
  - Collimator
  - Detector crystal
  - Photomultiplier tube array
  - Position logic circuits
  - Data analysis computer

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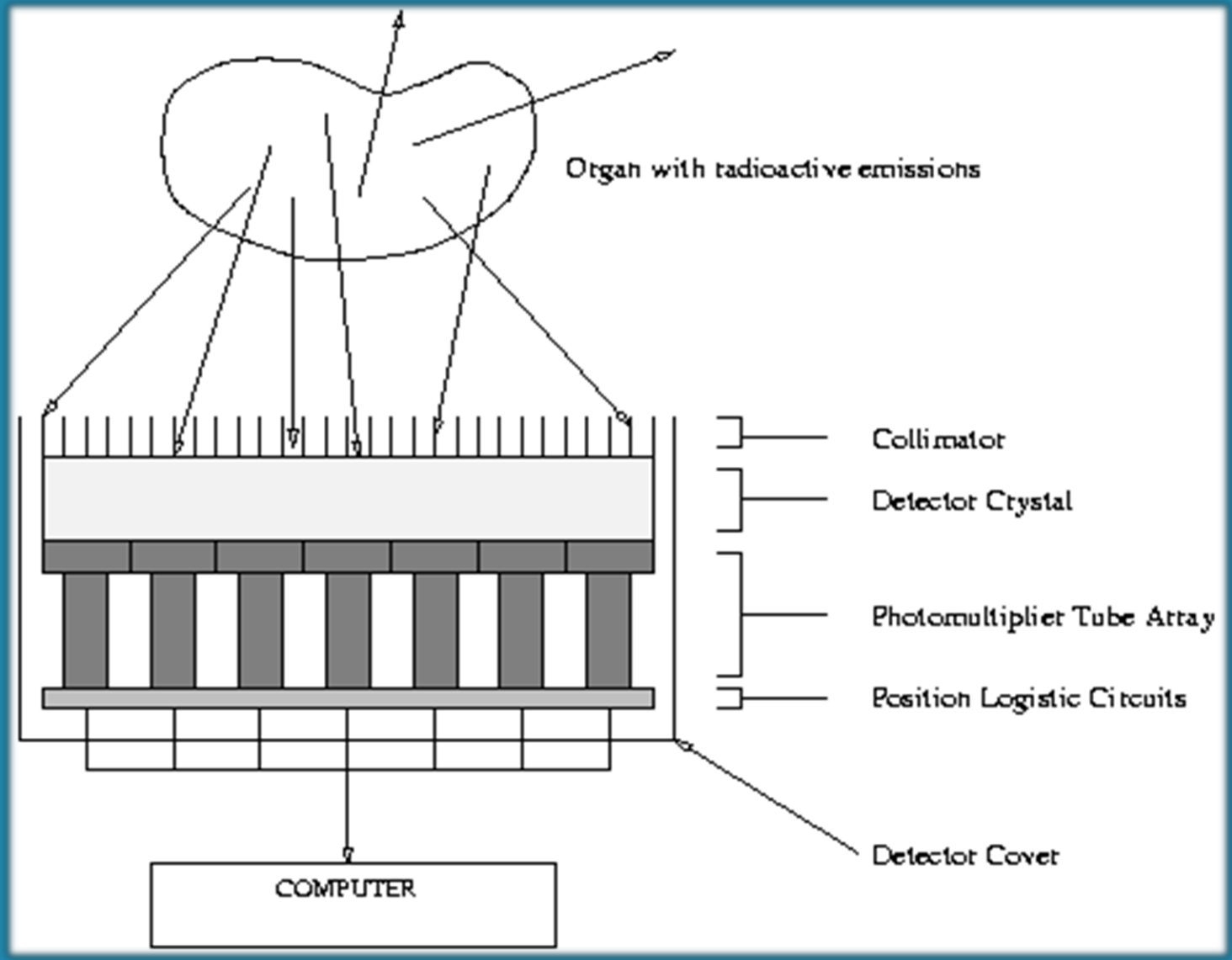
The Gamma Camera



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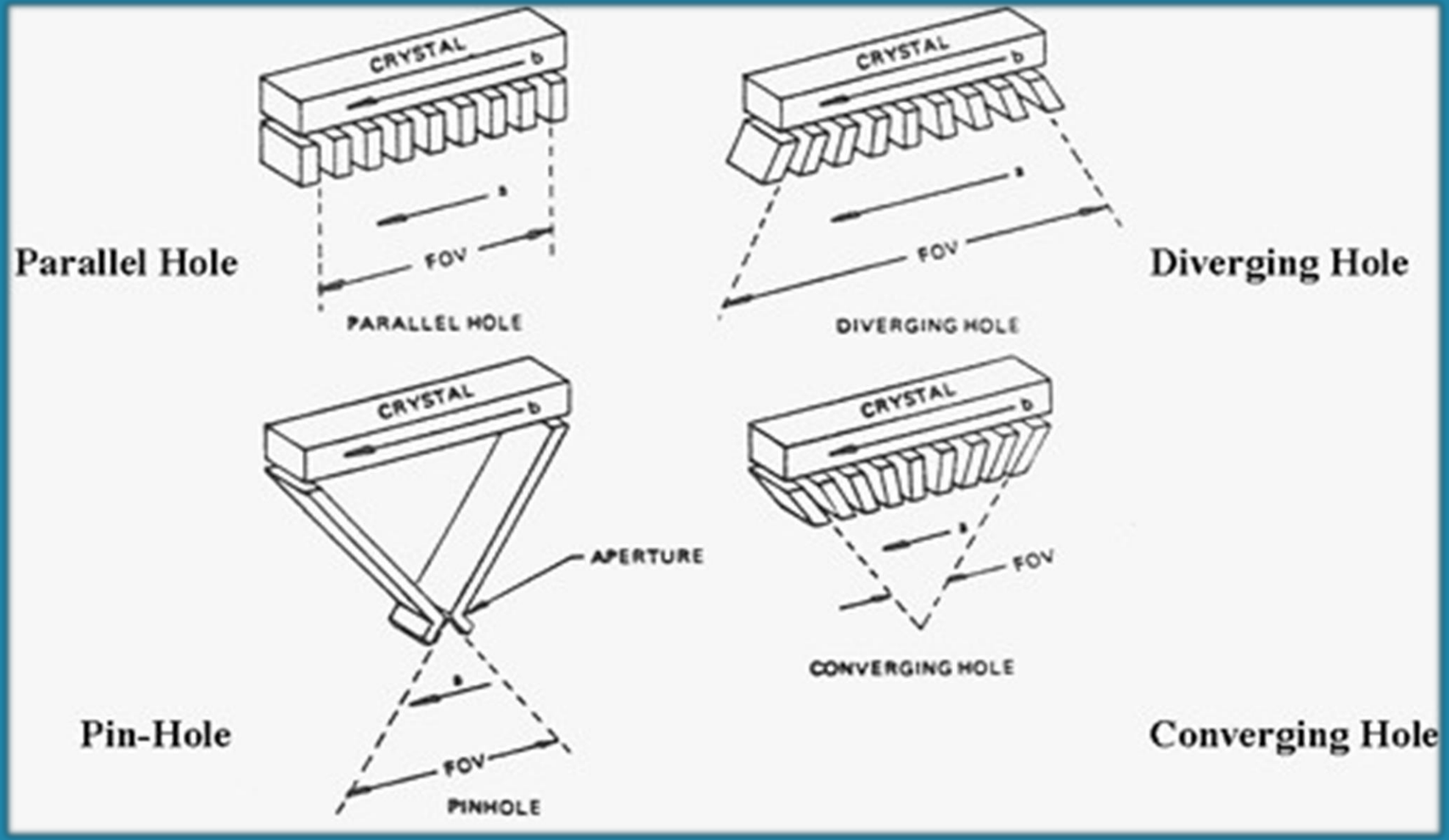
Collimator

- The first object emitted gamma photon encounters after exiting the body is the collimator
- Pattern of holes through gamma ray absorbing material, usually lead or tungsten, that allows the projection of the gamma ray image onto the detector crystal

Collimator – Parallel vs. Fan Beam



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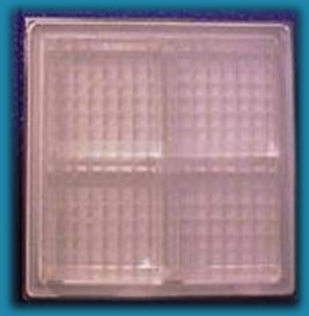
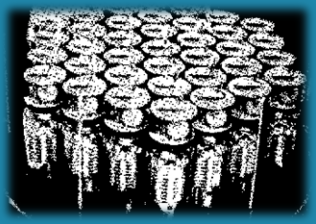
Detector Crystal



- Detect photons
- Sodium iodide [NaI] detector crystal optimal
- Typically 3/8" thick
- Photon interacts with crystal causing the release of electrons which in turn interact with the crystal lattice to produce light
- Process known as scintillation.

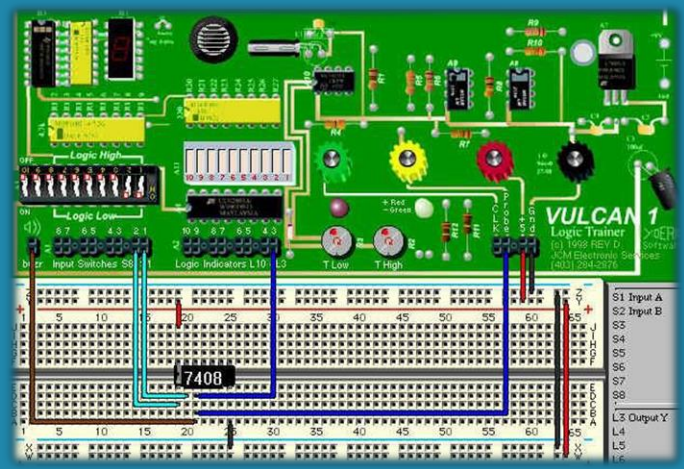
Photomultiplier Tubes PMT



- Only very small amount of light given off from scintillation detector, so PMT tubes attached to the back of crystal.
- PMT tubes detect and amplify the electrons and converts them into an electrical pulse.
- Each gamma camera has several photomultiplier tubes arranged in a geometrical array. The typical camera has 37 to 91 PMT's.

Position Logic Circuit

- Immediately follow the PMT tube array
- Receive the electrical impulses from the tubes
- Allows the position circuits to determine where each scintillation event occurred in the detector crystal.



Data Analysis Computer

- Finally, to deal with incoming data and process it into a readable image a processing computer is used
- Computer may use various different methods to reconstruct an image

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Images

- Images acquired are digital consisting of picture elements called pixels
- Typical SPECT acquisition consists of 60 to 120 projections
- Each projection will have approximately 100,000 counts, and take about 20 seconds
- Each scan is made up of about 10 million counts or times the photons hit the crystals

Time in Camera

- **Data acquisition times for a complete SPECT scan:**
  - **Single headed camera 46-60 minutes**
  - **Dual headed camera 30 min**
  - **Triple headed camera 15 min**

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Dual Head SPECT System

- Most commonly used in a hospital setting and enjoys the largest installed base
- Performs all types of nuclear medicine studies; excellent general purpose system.

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Triple Head SPECT System

- Specialized system, optimized for brain and cardiac imaging
- Small detectors allow for "close in" positioning of detectors
- 3 heads means short acquisition/scanning times
- Largest installed base of any brain SPECT system

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Performing Brain SPECT

Courtesy Amen Clinics, Inc. www.AmenClinics.com

Pre-Arrival

- Patients instructed on day of exam to avoid:
  - caffeine and alcohol
- Stop stimulants 4 days prior to the scan
- Check with their doctor about other prescription medications
- A number of psychiatric medications have long biological half-lives

Scanning On or Off Medication

- I prefer brains off medication, but…
- Depends on the question being asked
- If someone stable on meds wants additional help, then scan them on their medications
- If meds not helpful, then take them off until washed out of body, then scan

Informed Consent

- Enclosed in handout material
- Send ahead of time
- Ensure patients know about injection and radiation exposure
- Insurance reimbursement varies by plans. Have patients check with their company to see if it is a covered benefit.

Informed Consent

Risks?

- Study does not involve a dye
- People do not have allergic reactions to the study
- Possibility exists, although very small, of a mild rash, facial redness and edema, fever and a transient increase in blood pressure
- Amount of radiation exposure from one brain SPECT study is approximately same as head CT scan
- Rarely, patients have green urine for a day or two

Pre-Injection

- **Steps to achieve consistent scan environments:**
  - **Seat patient in a quiet, dimly-lit room, eyes and ears open**
  - **No gum or candy to minimize extra-axial tracer uptake**
  - **Place intravenous access at least 5-10 minutes prior to injection to permit accommodation**
  - **Instruct the patient not to speak**
  - **Minimize interaction with the patient during and up to 15 min post-injection**
  - **Closely monitor demented patients and those with neurologic or movement disorders**

Why Two Scans?

- Best information obtained with two scans
- Various disorders affect the same regions of the brain in different ways depending on rest or concentration
- To minimize residual activity interfering with the second study, the intervening time between two studies should be no less than 24 hours
- ACI usually does concentration scan first

Baseline Study

- Patient sits quietly for about 10 minutes before injection of the radiopharmaceutical
- Patient instructed not to talk and to just allow his or her mind to wander
- After the injection patient should remain quiet for a minimum of 10 minutes

Concentration Study

- Protocol consists of a standardized concentration challenge task administered by a computer (Conner's CPT)
- Protocol lasts 15 minutes
- Tracer administered at 3 minutes into the test, allowing at least 10 minutes of concentration following injection

Scan

- Image acquisition may begin 20-30 minutes after the resting or concentration phase
- Patient needs to hold very still
- If desired, give patient a blanket, as room is often cold for health of cameras
- Goal is 10,000,000 counts per stud
- With HMPAO, imaging should be completed within 4 hr post injection if possible

Sedation

- After injection
- IV Versed (midazolam), needs to be monitored
- Short acting
- Amnestic
- Consult with an anesthesiologist or nurse anesthetist

Information Pertinent Reading the Scan

- **The following data is essential for proper interpretation of scan:**
  - **Patient history (including any past drug use or trauma)**
  - **Age, gender**
  - **Reason for the study**
  - **Current medication and when last taken**
  - **Time of start of last menstrual cycle**
  - **Any recent morphologic imaging studies (e.g. CT, MRI)**

Brain SPECT Processing

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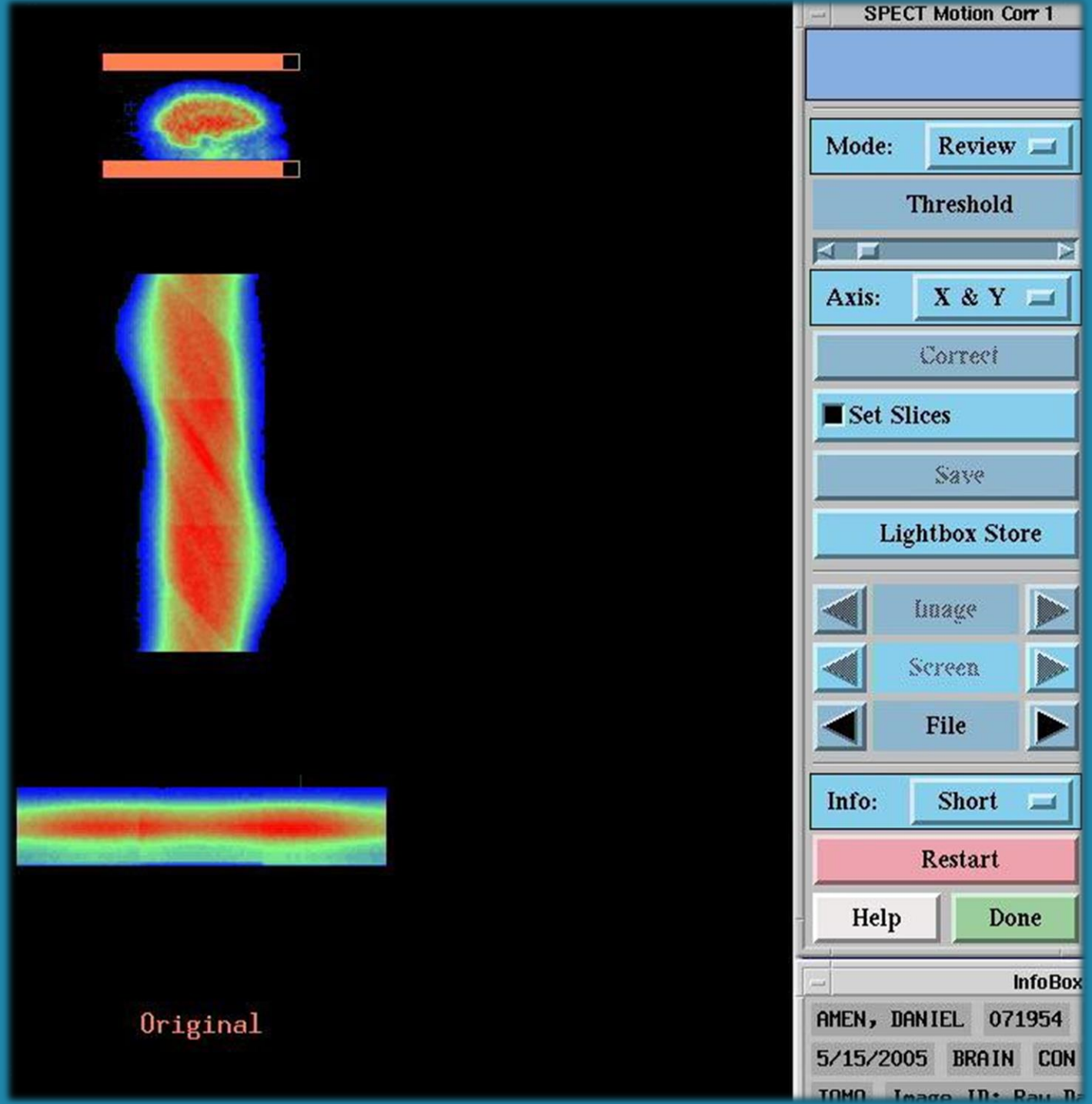
Processing Raw Data

- Once the camera captures the raw data it needs to be processed so it can be easily read
- ACI processes all of the scans in the same way to give us good consistency and reliability
- Here are the steps…

Check for Motion

- No motion….
- This can be a challenge
- Do not trust motion correction software
- Beauty of SPECT, you can scan patients for up to 6 hours if needed
- You can even sedate them, after the injection, if needed, and not affect the scan

Check for Motion



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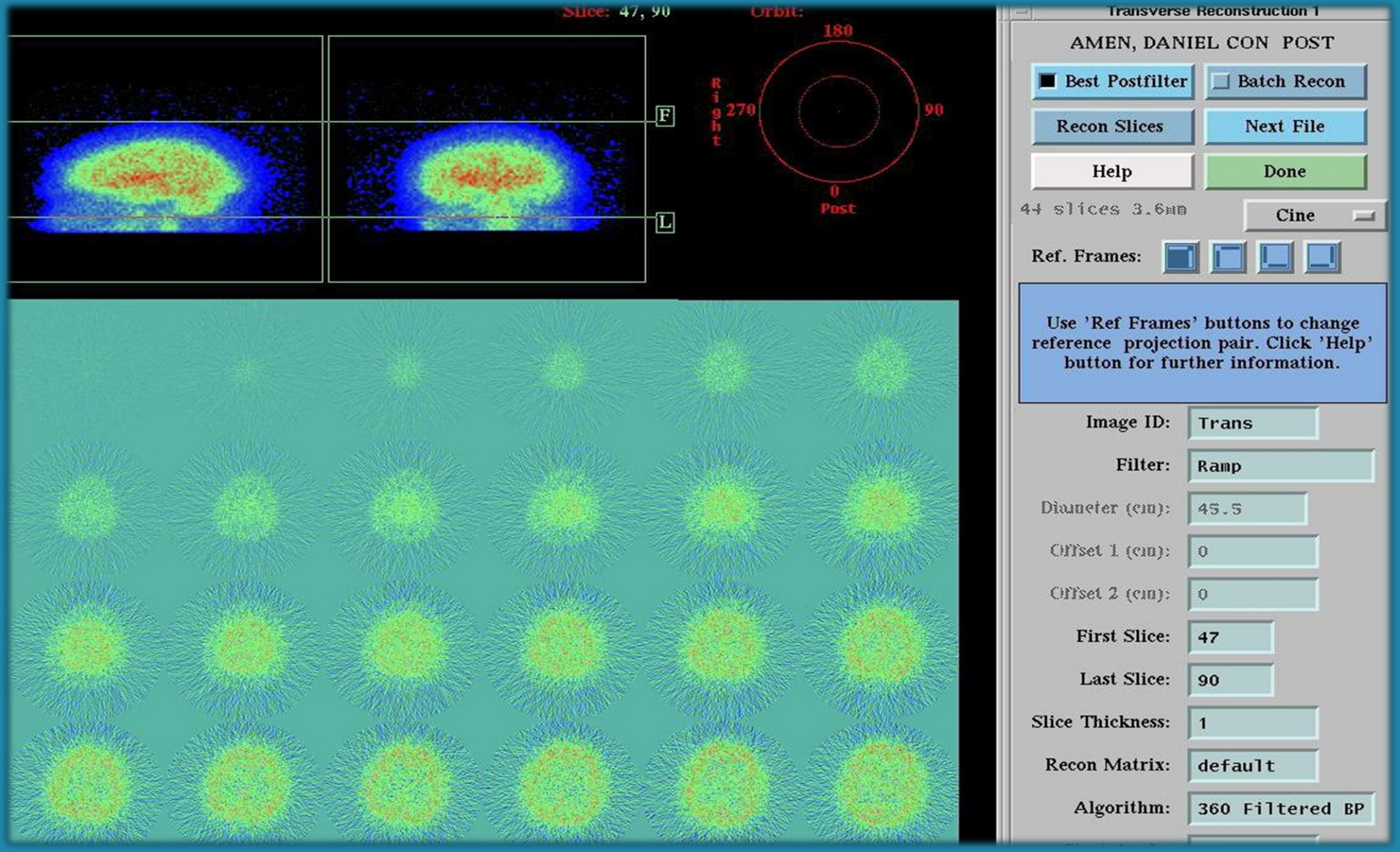
Transverse Reconstruction



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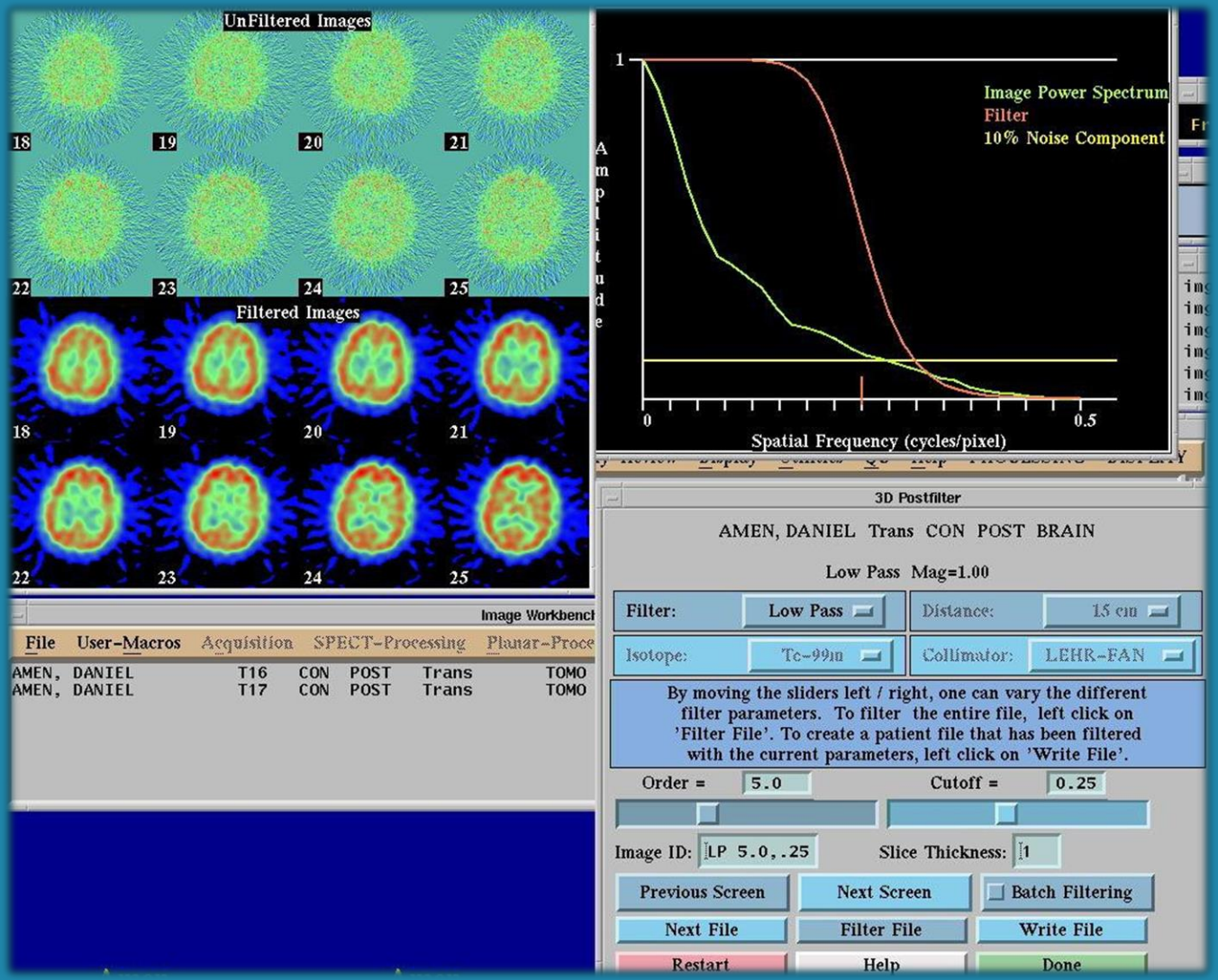
Filter Data

- Low pass filter
- Order 5.0
- Cut off 0.25
- Smoothes images making them easier to read



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Attenuation Correction

- Helps deeper tissue have similar look to surface
- Change Method, 0.110 setting

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Mask Data

- To eliminate artifact
- 0.000 setting

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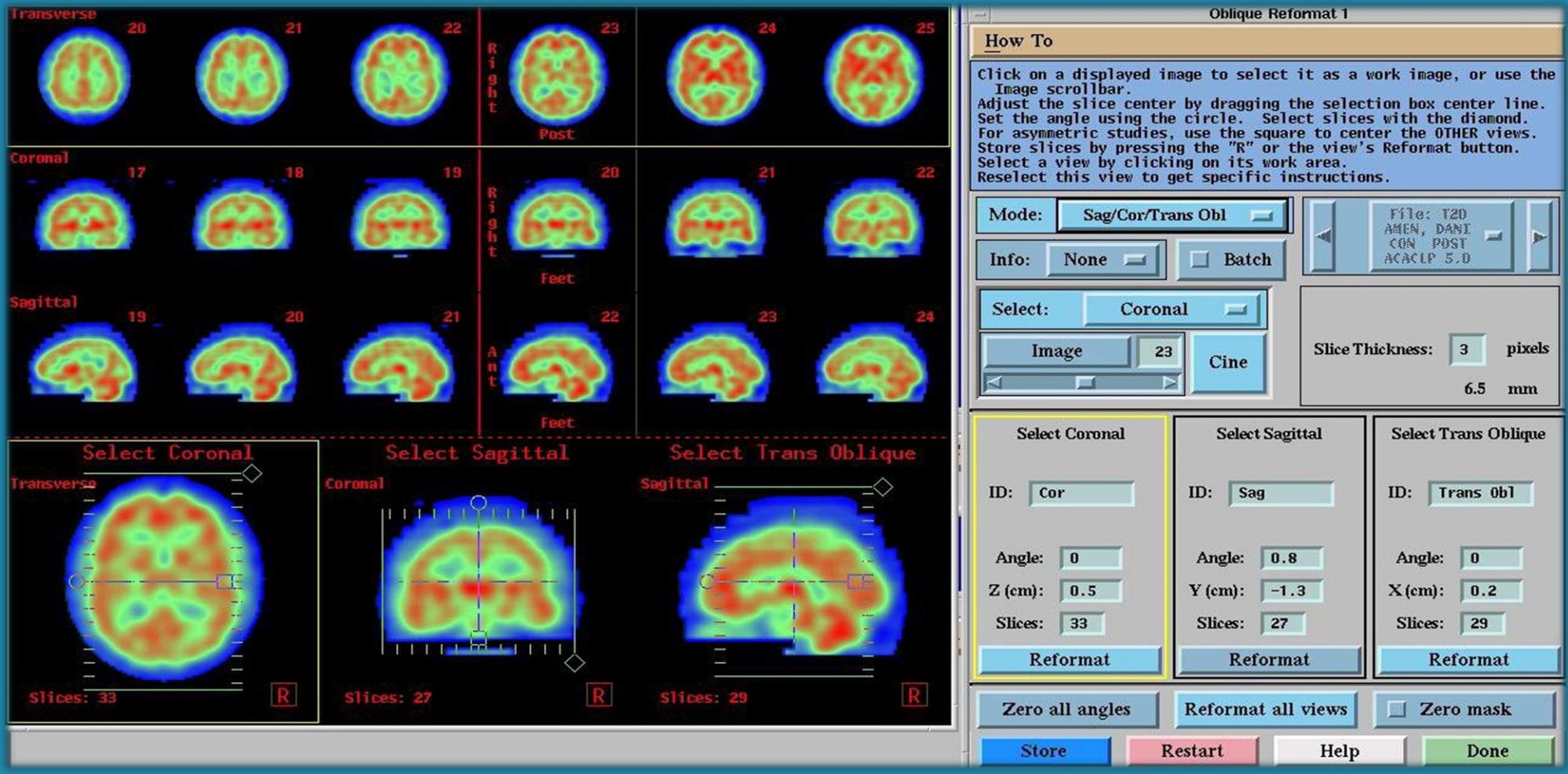
Oblique Reformat

- Spatial orientation for slices



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An Introduction to Reading Brain SPECT

Courtesy Amen Clinics, Inc. www.AmenClinics.com

rCBF – Regional Cerebral Blood Flow

- SPECT measures relative blood flow
- Most intense pixels in brain = 100%
- Least intense pixels = 0%
- All else is scaled between these 2 poles
- Most intense pixels usually in cerebellum
- Be careful with interpretation when the cerebellum is not active with HMPAO

What Is Normal? How Do We Know?

- Full, even, symmetrical activity
- With HMPAO cerebellum most active
- Often some basal ganglia or thalamic activity
- Children most active
- Females more active than males
- 59 normal SPECT studies for children & adults

Research Sample – Normal

- Chiron, 1992, 42 children
  - By age of 2 children have same relative perfusion pattern as adults, although their brains more active
- Catafu, 1996, 68 normal adults
  - Symmetrical rCBF distribution can be assumed between homologous regions, independent of age
- Yang, 1996, 52 adults
  - Significant negative correlation found between rCBF and advancing age, particularly in males

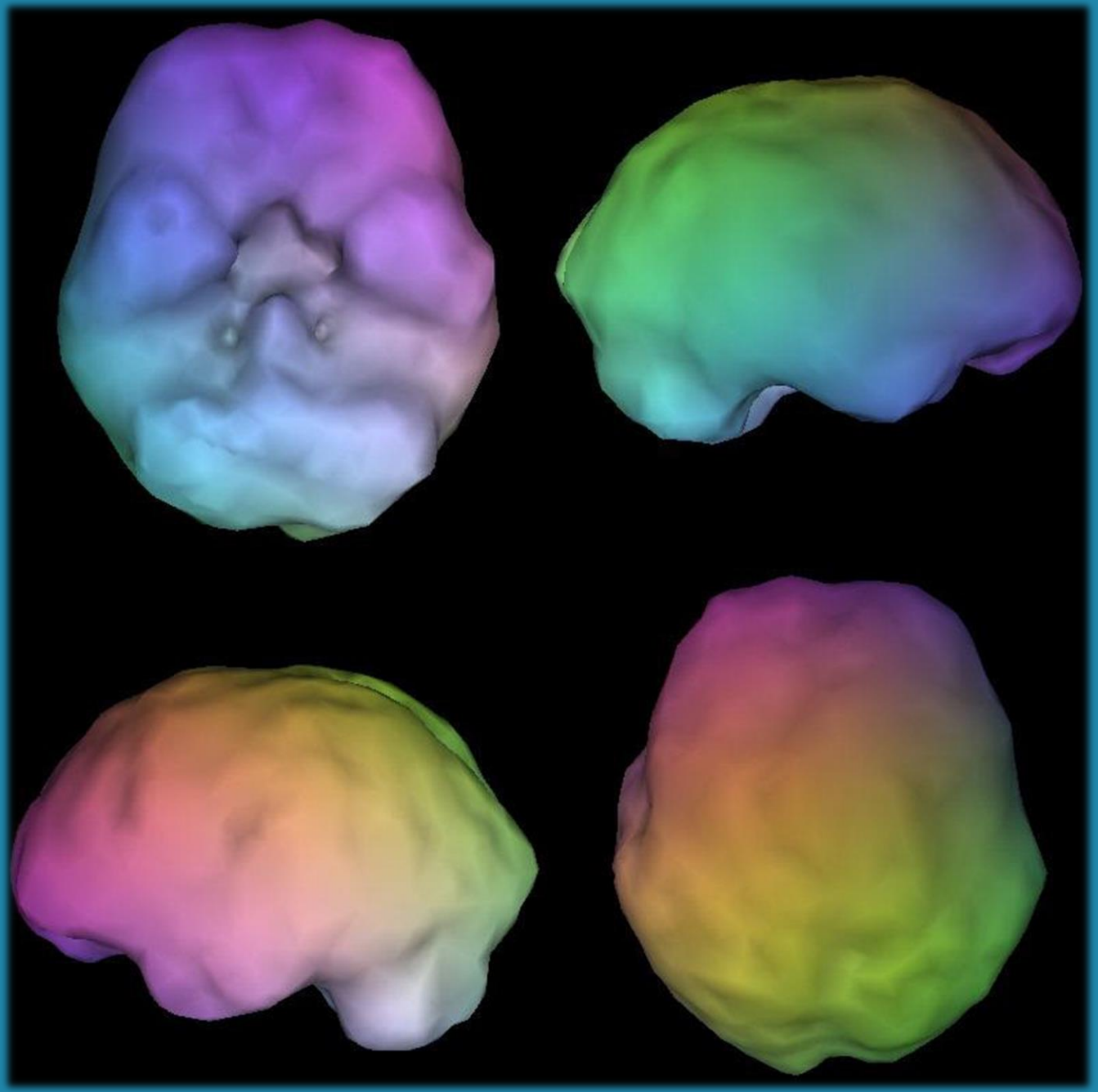
Research Sample – Normal

- **Barthel, 1997, 23 children**
  - **Systematic differences between 4 to 15-year-old children and adults regarding normal rCBF**
  - **Normal ranges should be determined separately for the age groups 4-10 and 11-15 years.**
- **Slosman, 2001, 187 adults**
  - **Significant differences between the sexes and a significant decline as a function of age**

ACI Healthy Brain Study

- No psychiatric illness
- No first degree relative with psychiatric illness
- No head injury
- No or very limited substance abuse
- Not on any medication
- Scanned 99 healthy adults

Case 1: Normal



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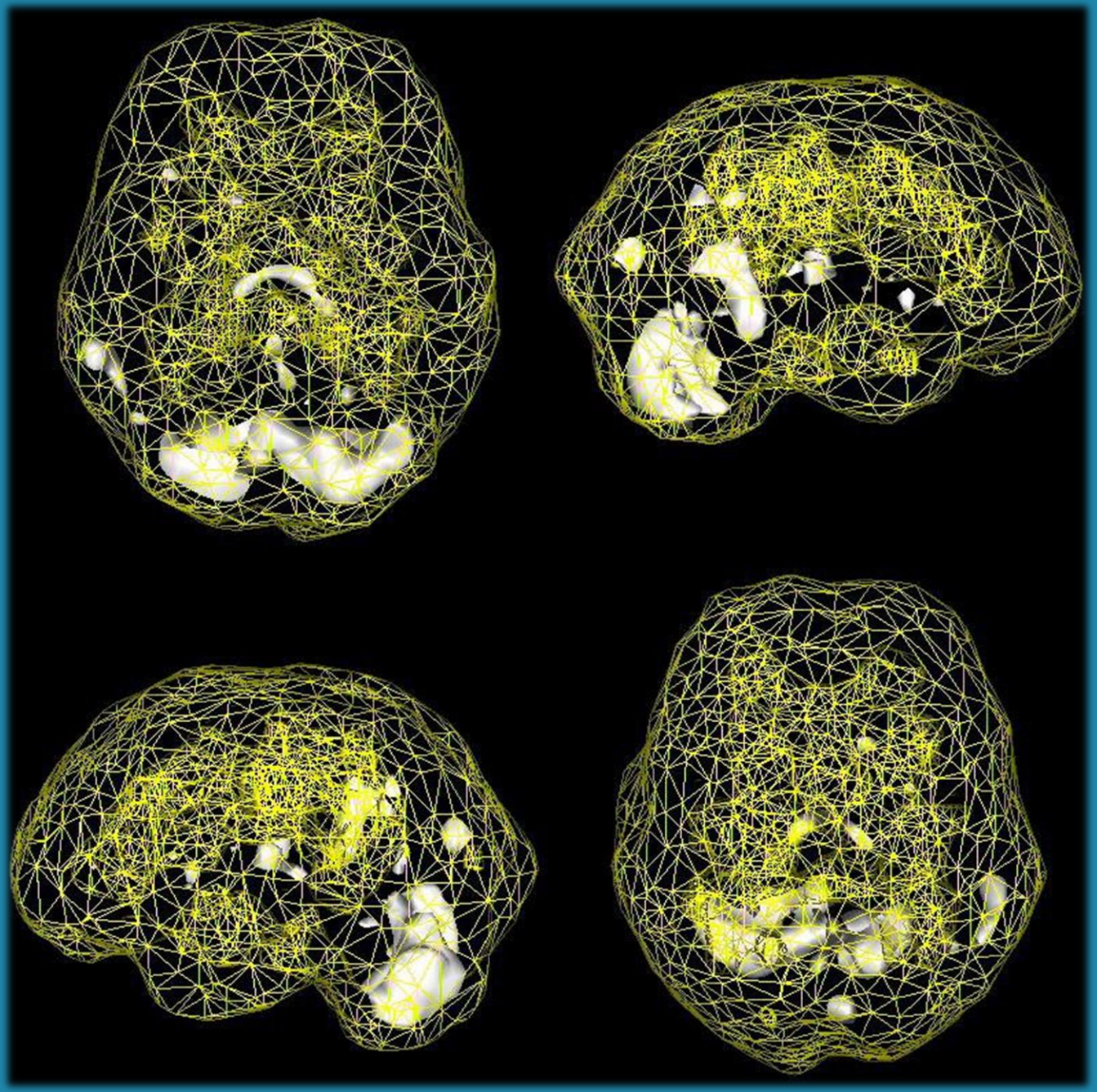
Case 1: Normal



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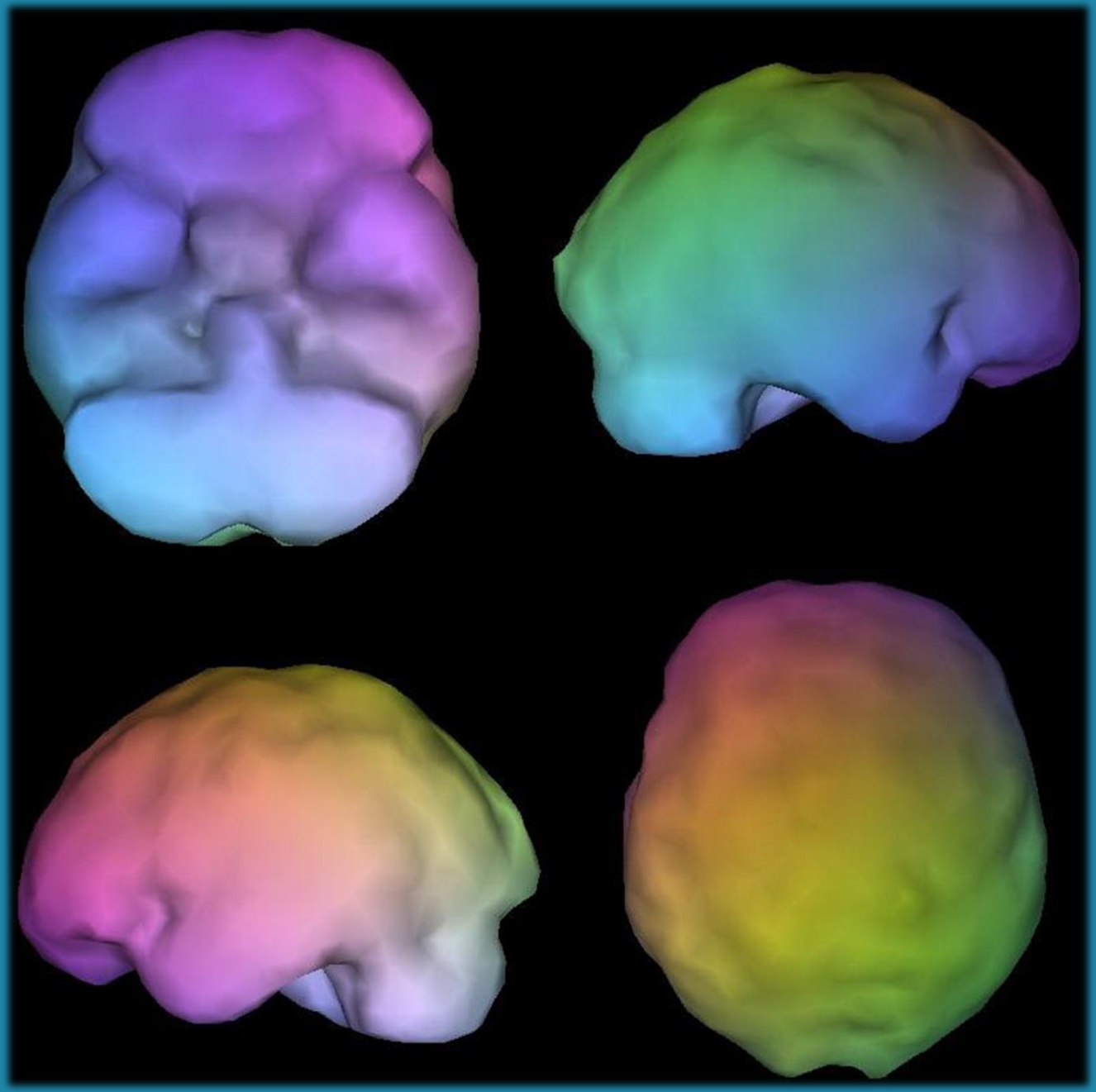
Case 2: Normal



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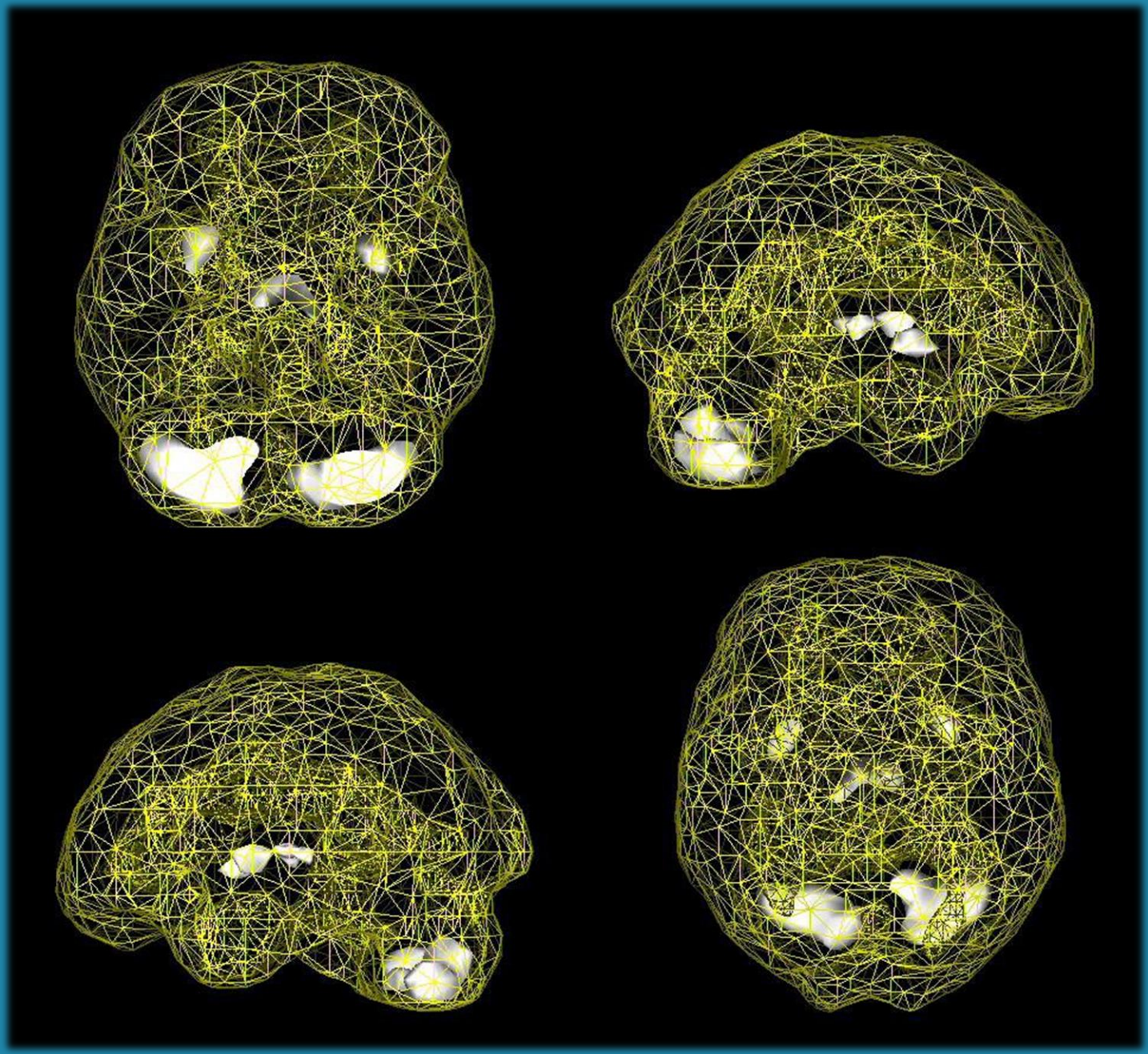
Case 2: Normal



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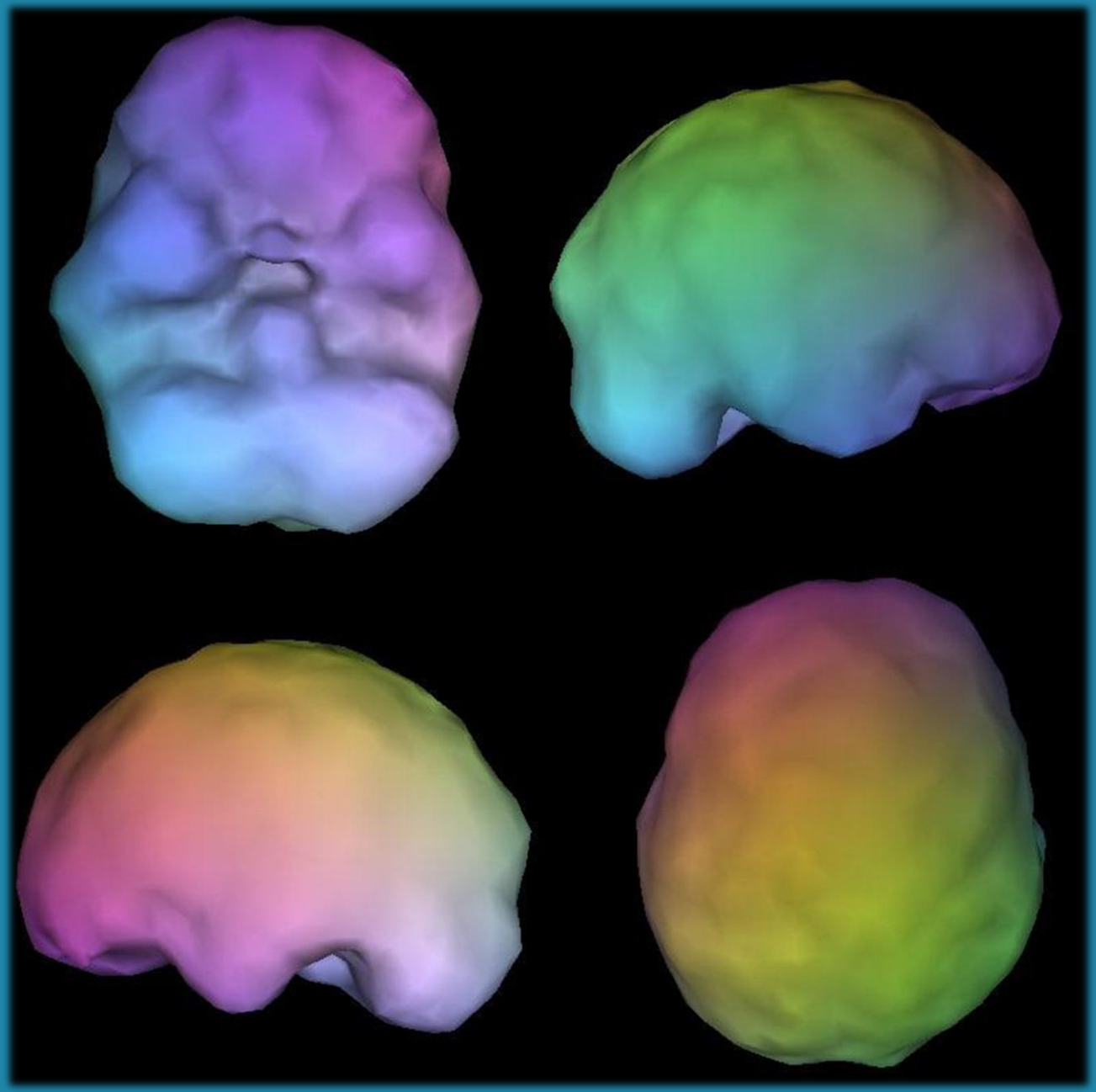
Case 3: Normal



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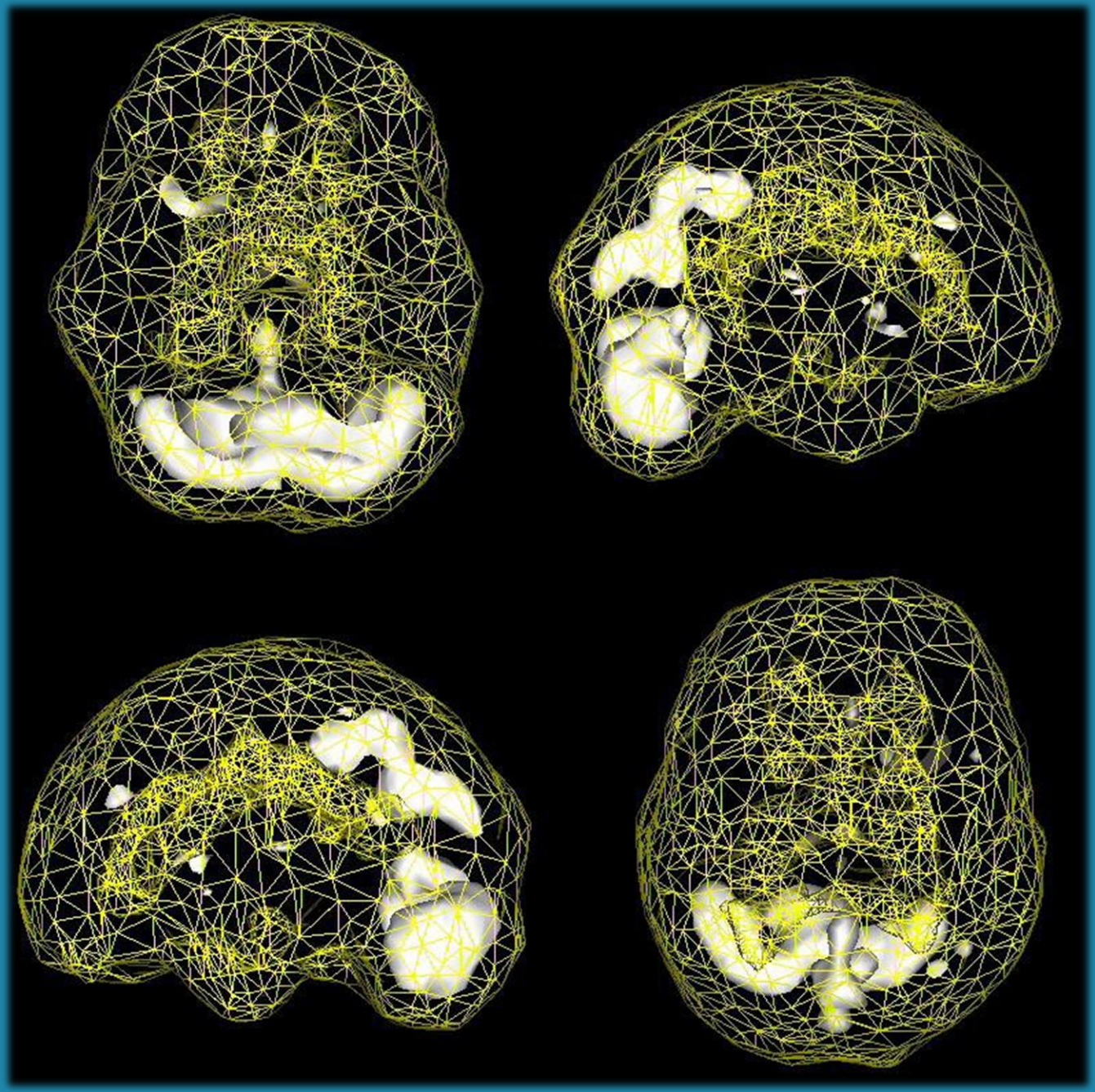
Case 3: Normal



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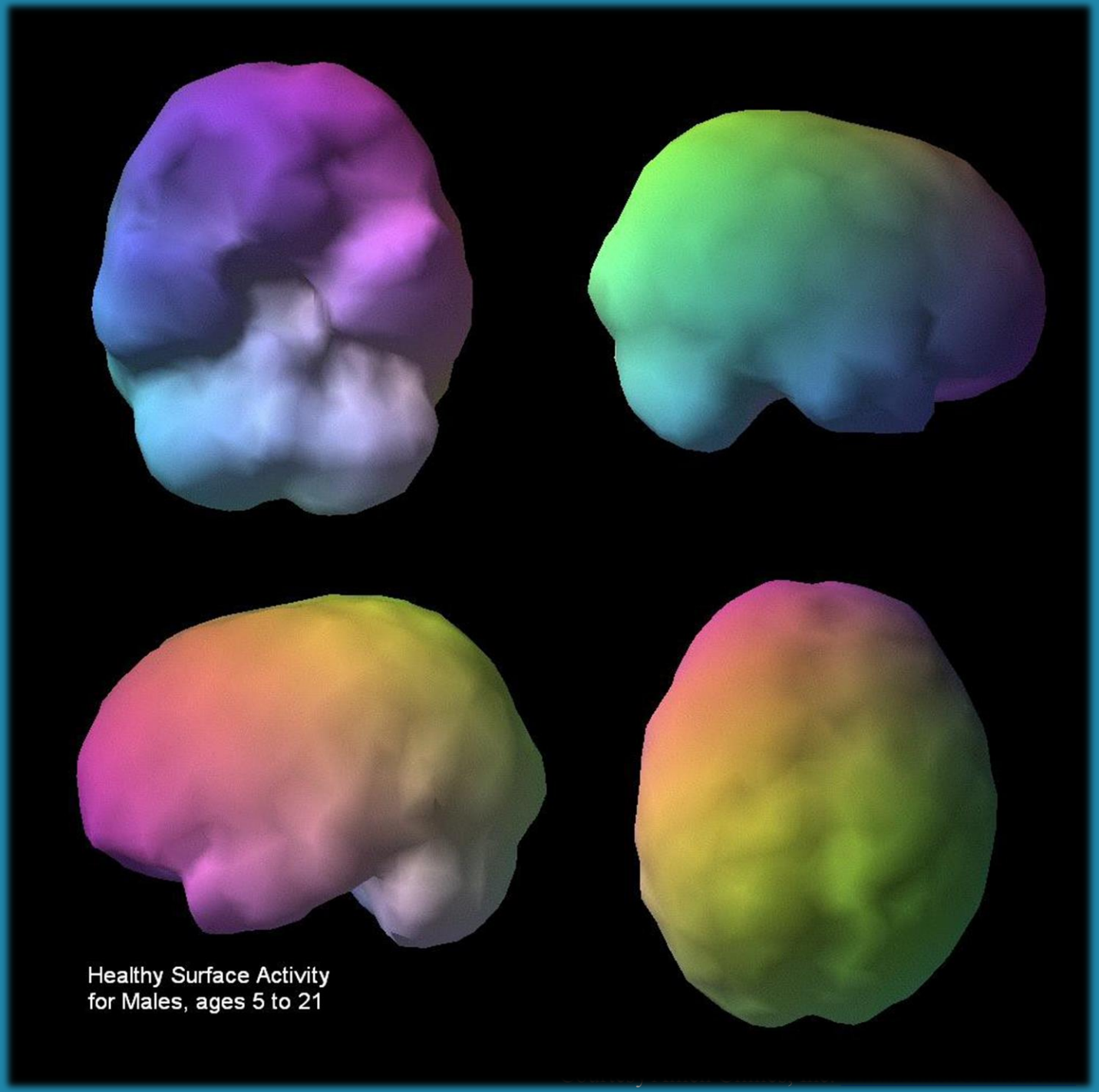
Normal Clinical Pearls

- Brain are like faces
- Age and sex matters
- See problems on SPECT years before they develop, such as Alzheimer's
- Someone might report being normal, but their scan may show they are headed for trouble

Normal Scans
Age and Gender Matched

- Surface scans show full, even, symmetrical perfusion
- Active scans vary over age and gender
- Examples that follow are from ACI's normal database for adults
- From healthiest 179 children and teens from a clinical sample

Surface Scans Males and Females



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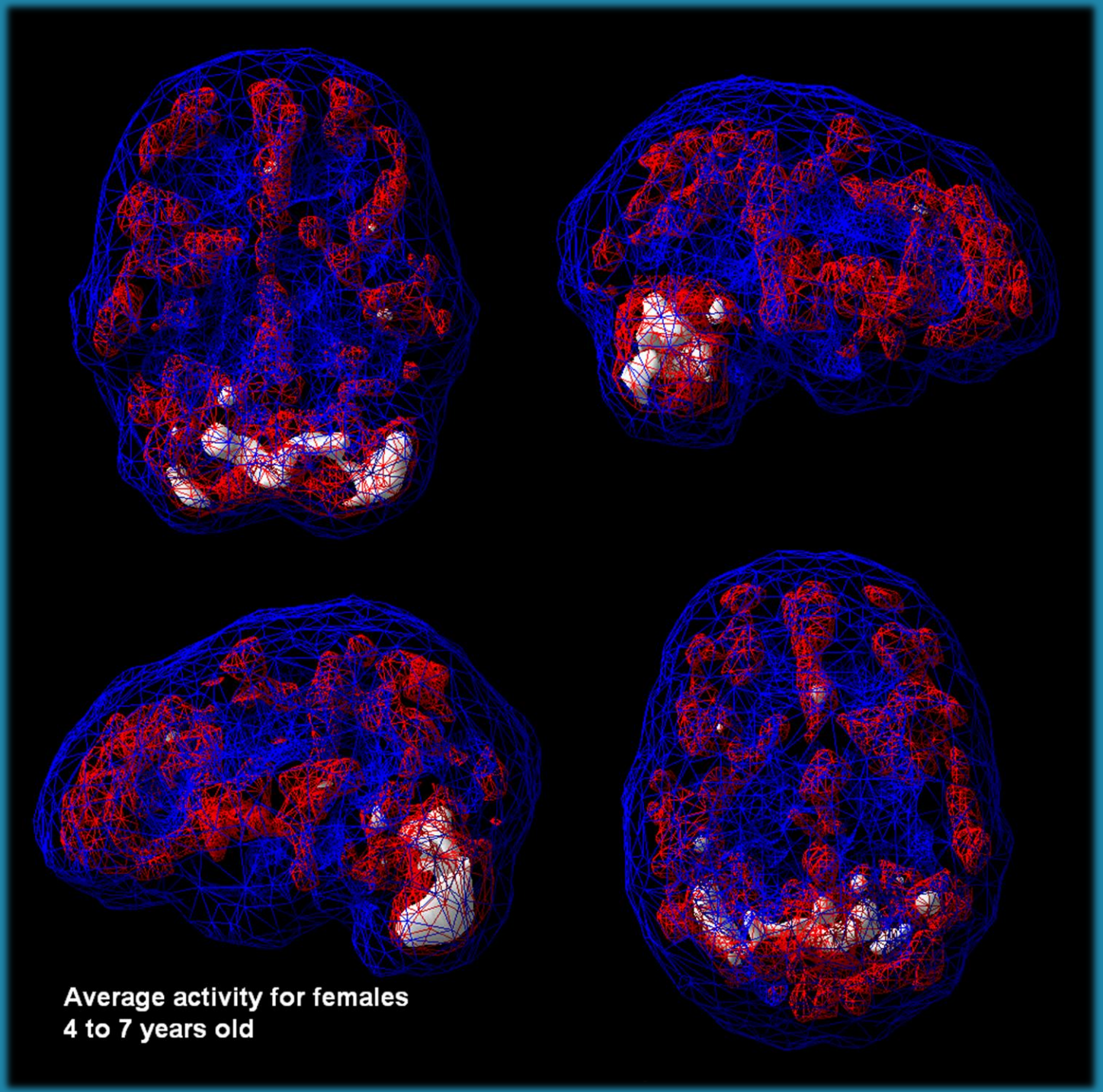
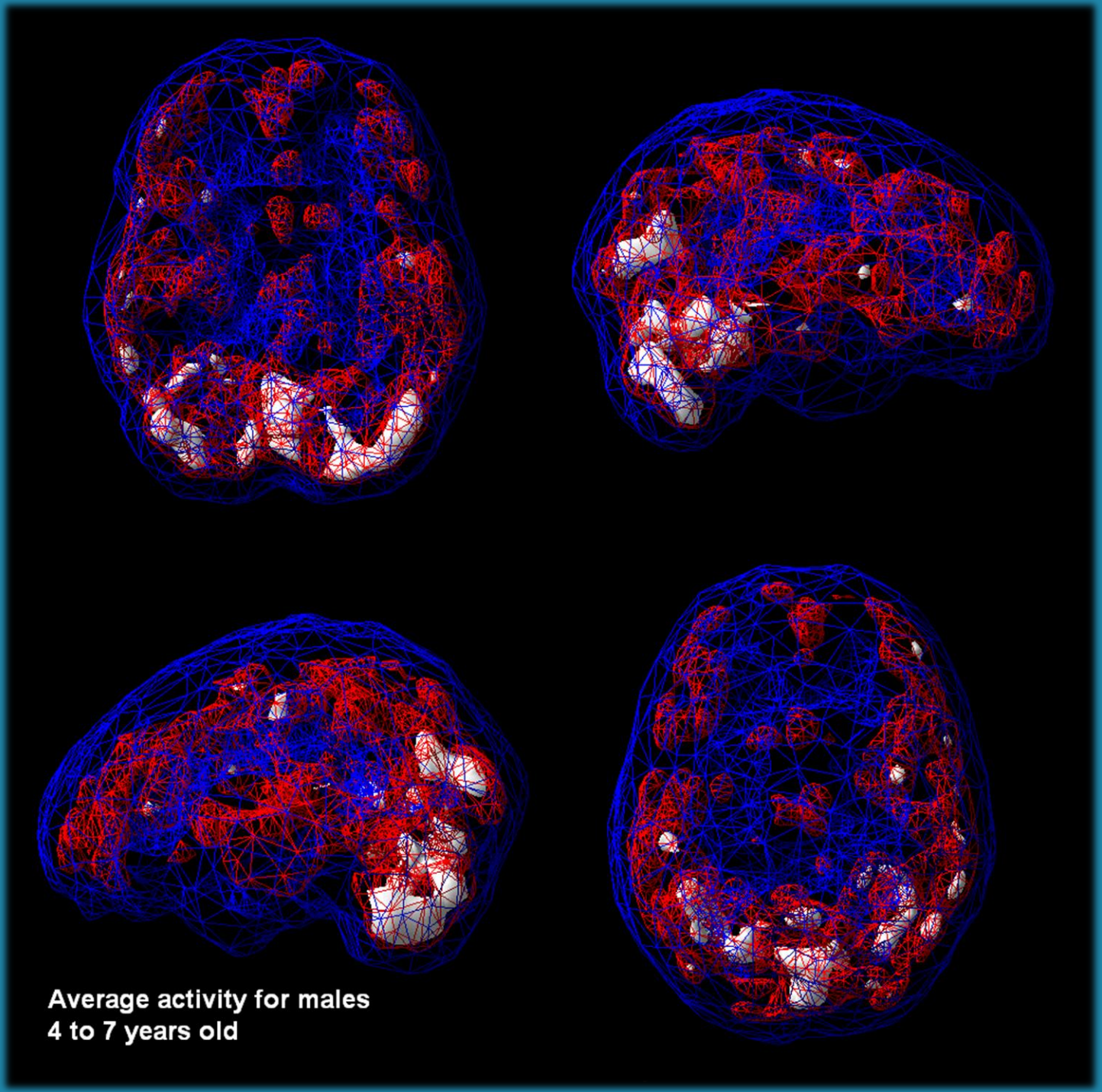
Active Scans Age 4 - 7 Females



Courtesy Amen Clinics, Inc. www.AmenClinics.com

Active Scans Age 4 - 7 Males



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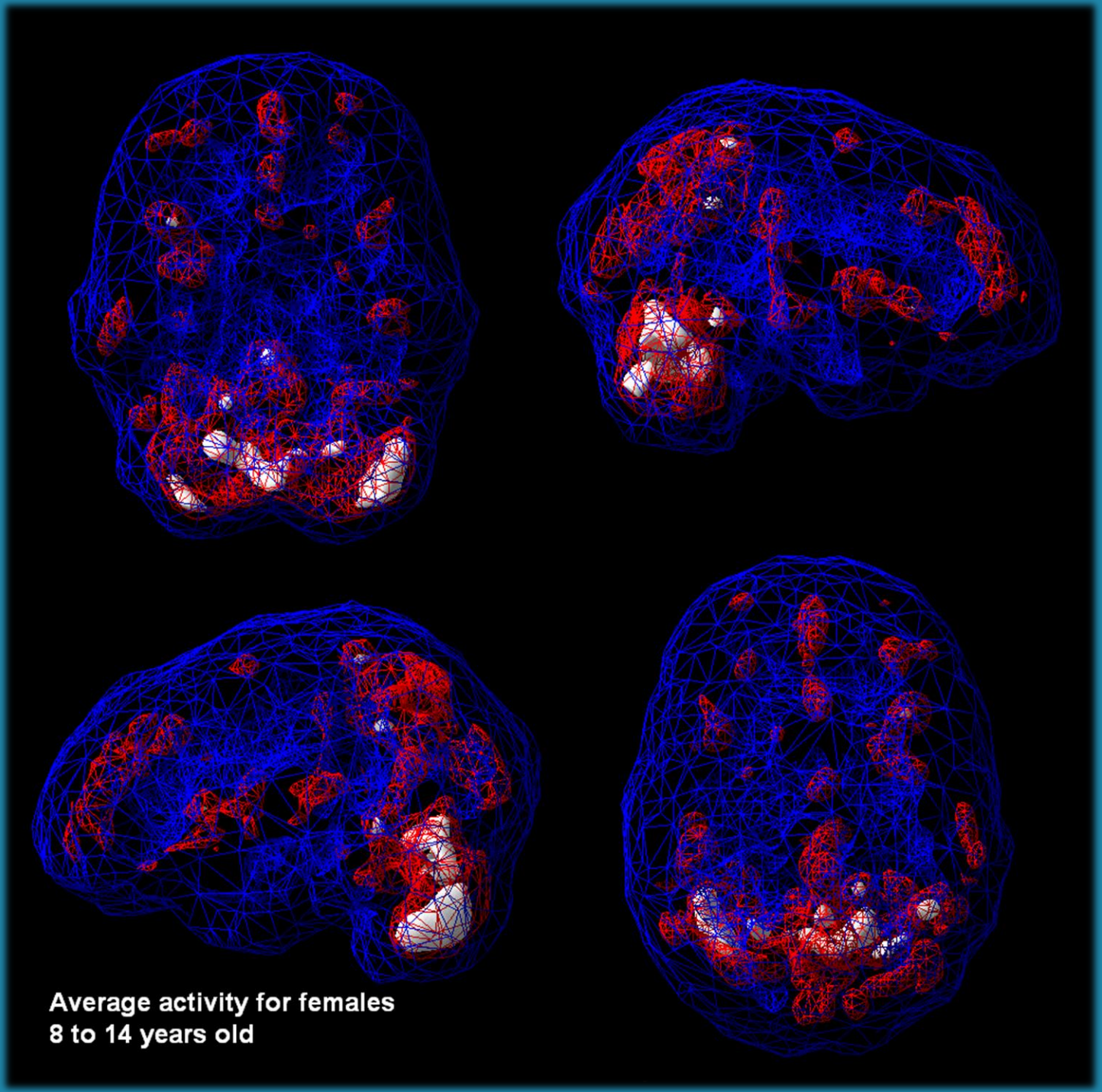
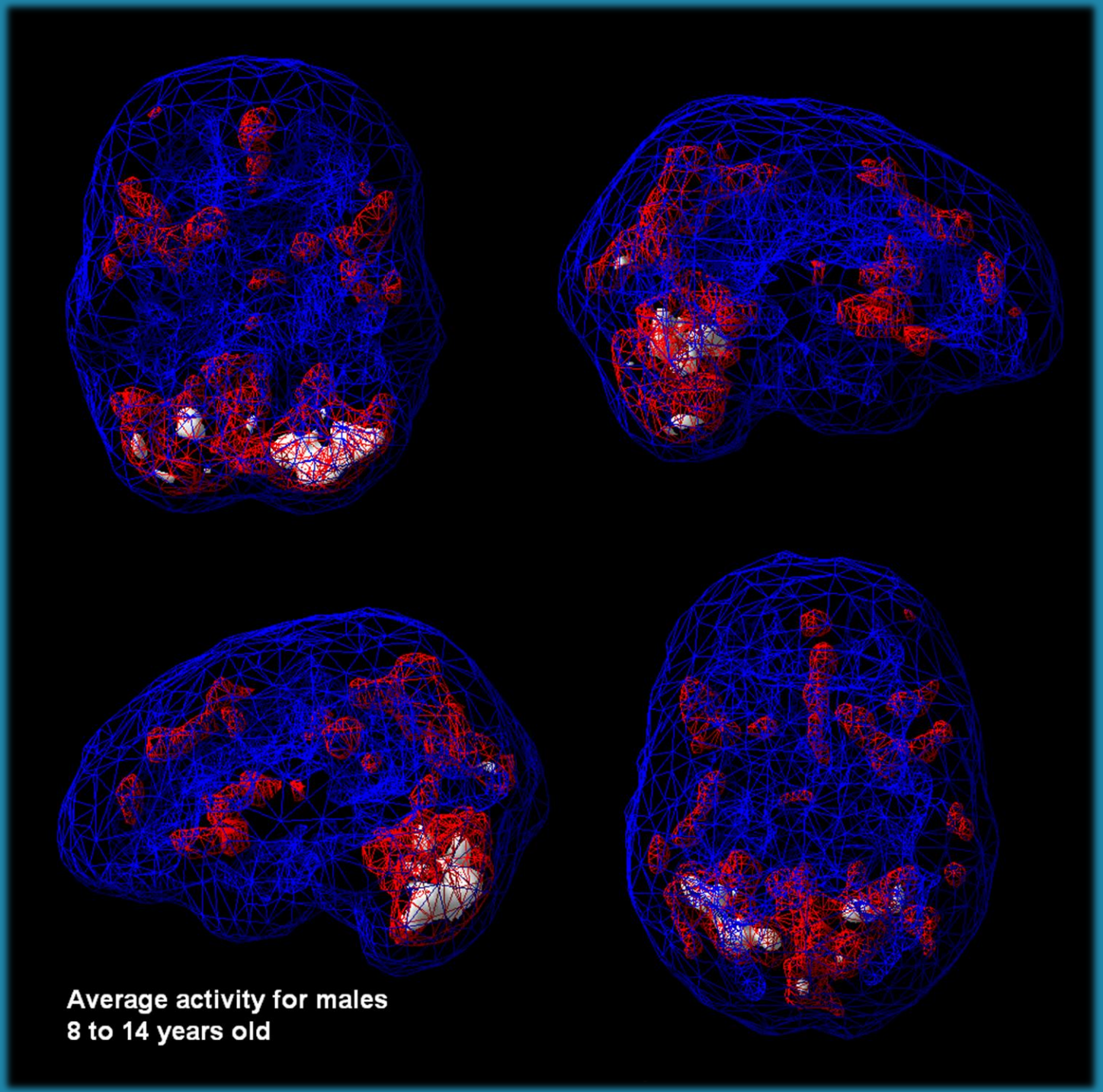
Active Scans
Age 8 - 14
Females



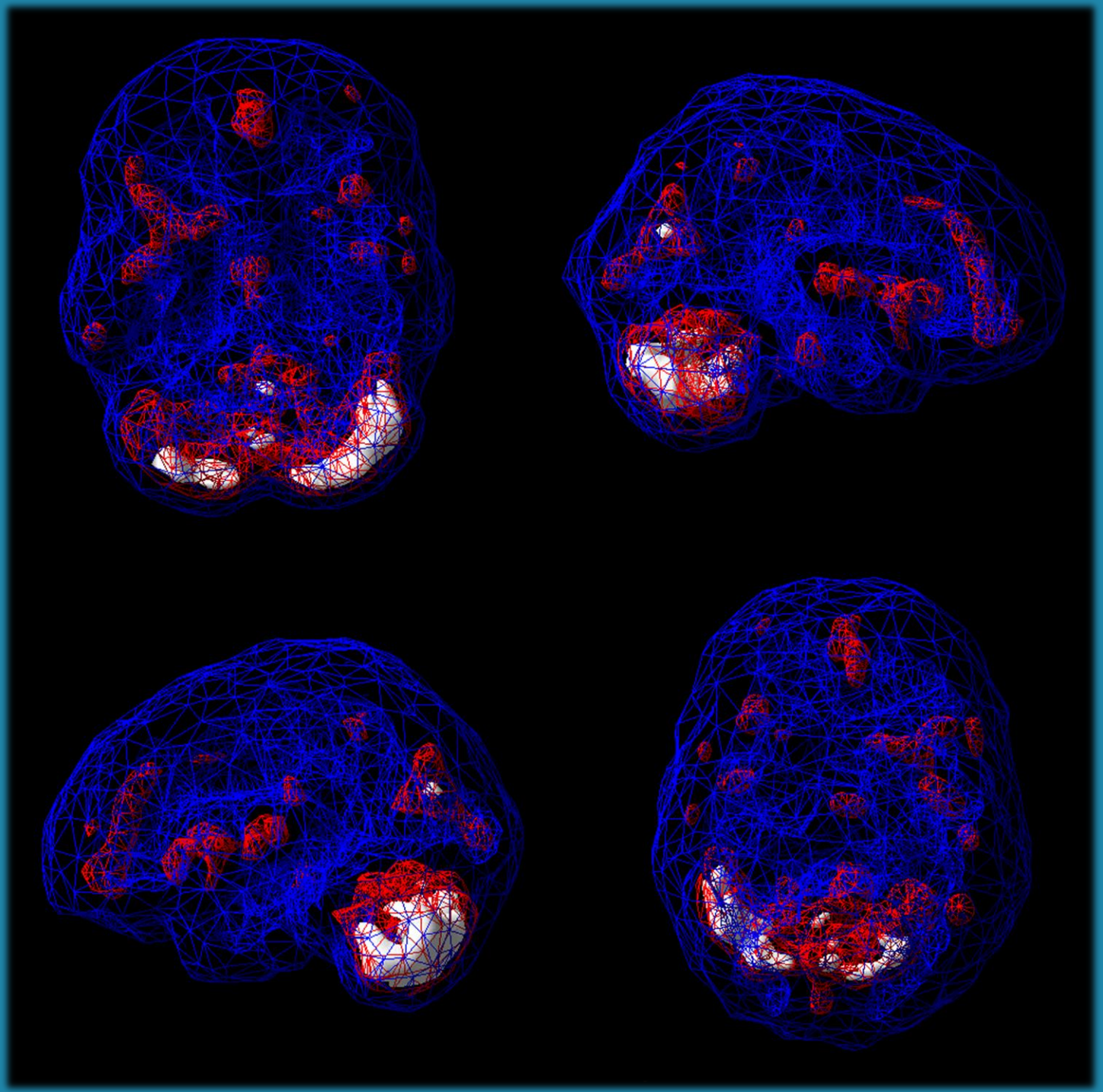
Courtesy Amen Clinics, Inc. www.AmenClinics.com

Active Scans Age 8 - 14 Males



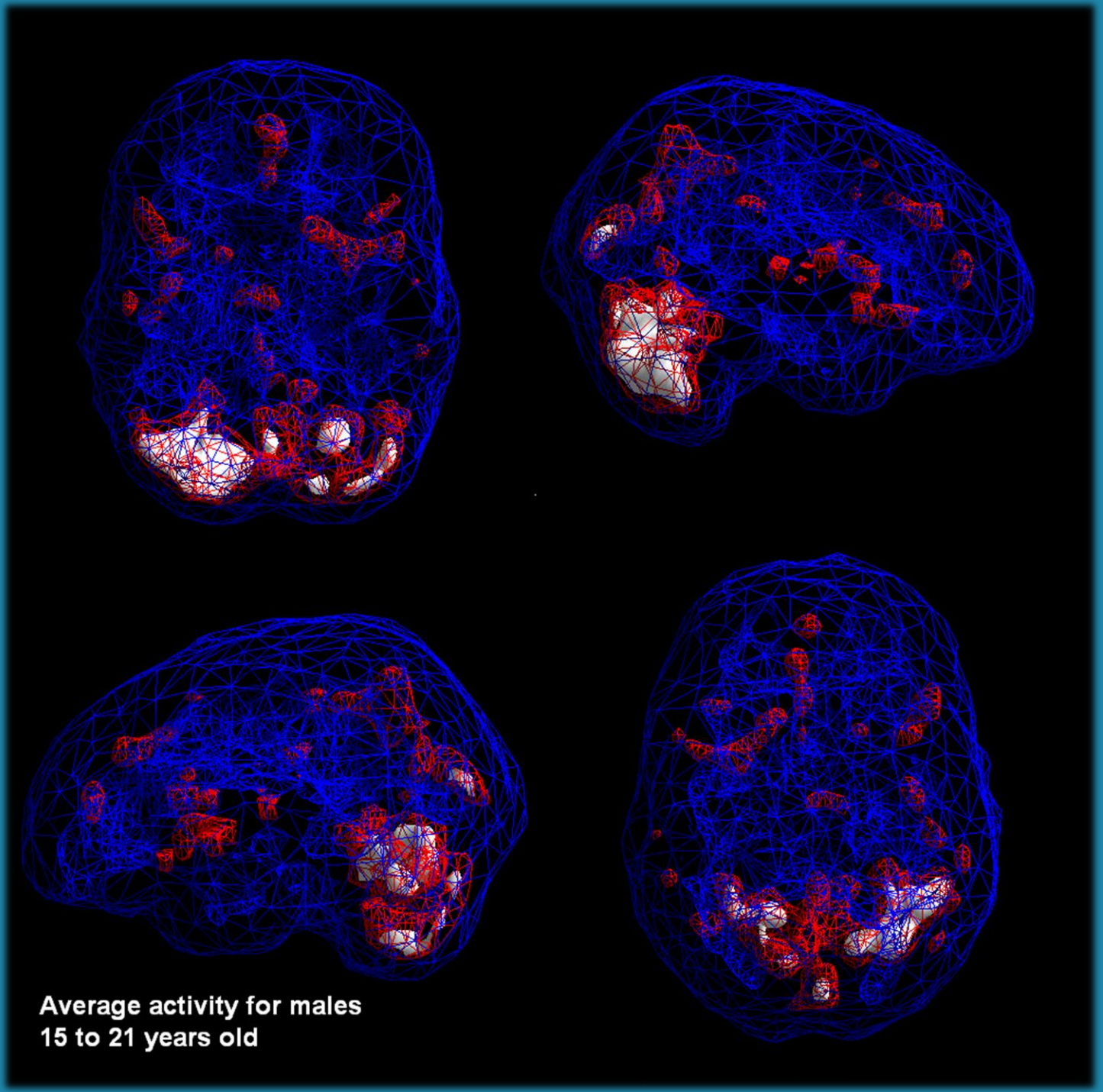
Courtesy Amen Clinics, Inc. www.AmenClinics.com

Active Scans
Age 15 - 21
Females



Courtesy Amen Clinics, Inc. www.AmenClinics.com

Active Scans Age 15 - 21 Males



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