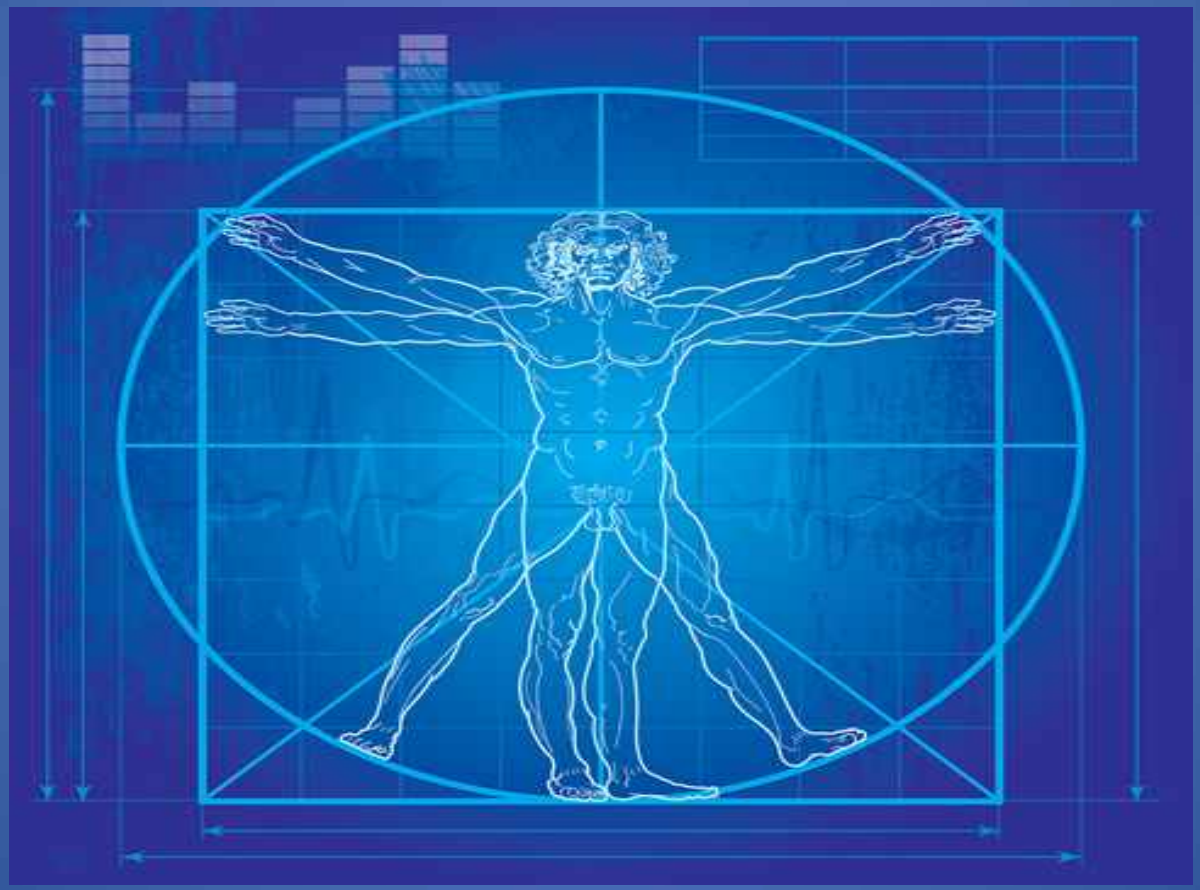
Part I

MMI Sept 2020 – Virtual Covid -19
The Essentials of Neuro-immuno-endo-psychopharmacology and Neuroimaging:

A Modern Neuroscience Approach to Understanding and treating the Child and Adult Brain in Clinical Practice



Part I

Elizabeth A. Stuller, M.D.

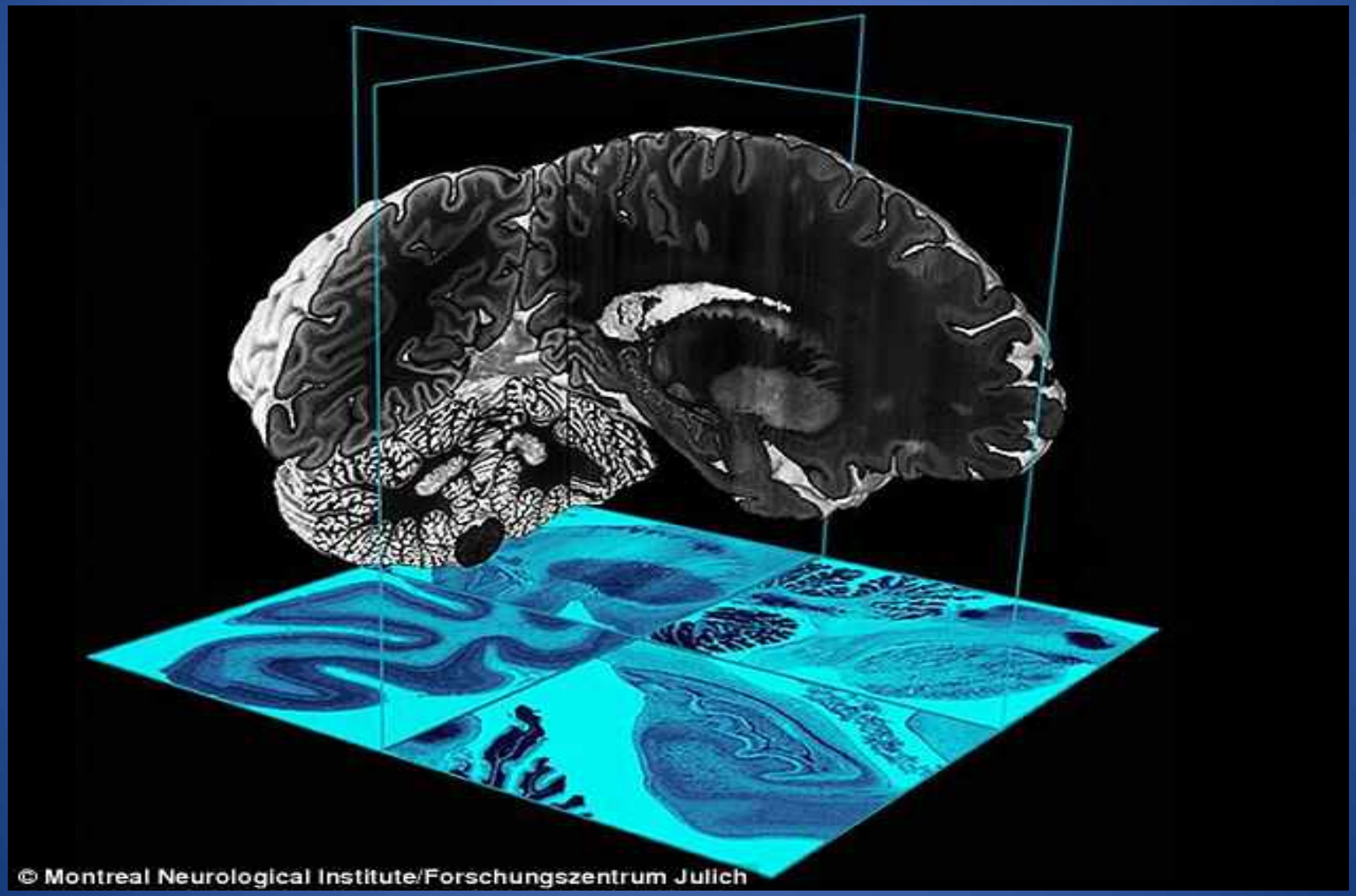
ABPN Board Certified in Adult and Addiction Psychiatry

FAPA, FASAM

The Brain – The Final Frontier


THE
BRAIN
INITIATIVE
NIH
National Institutes of Health

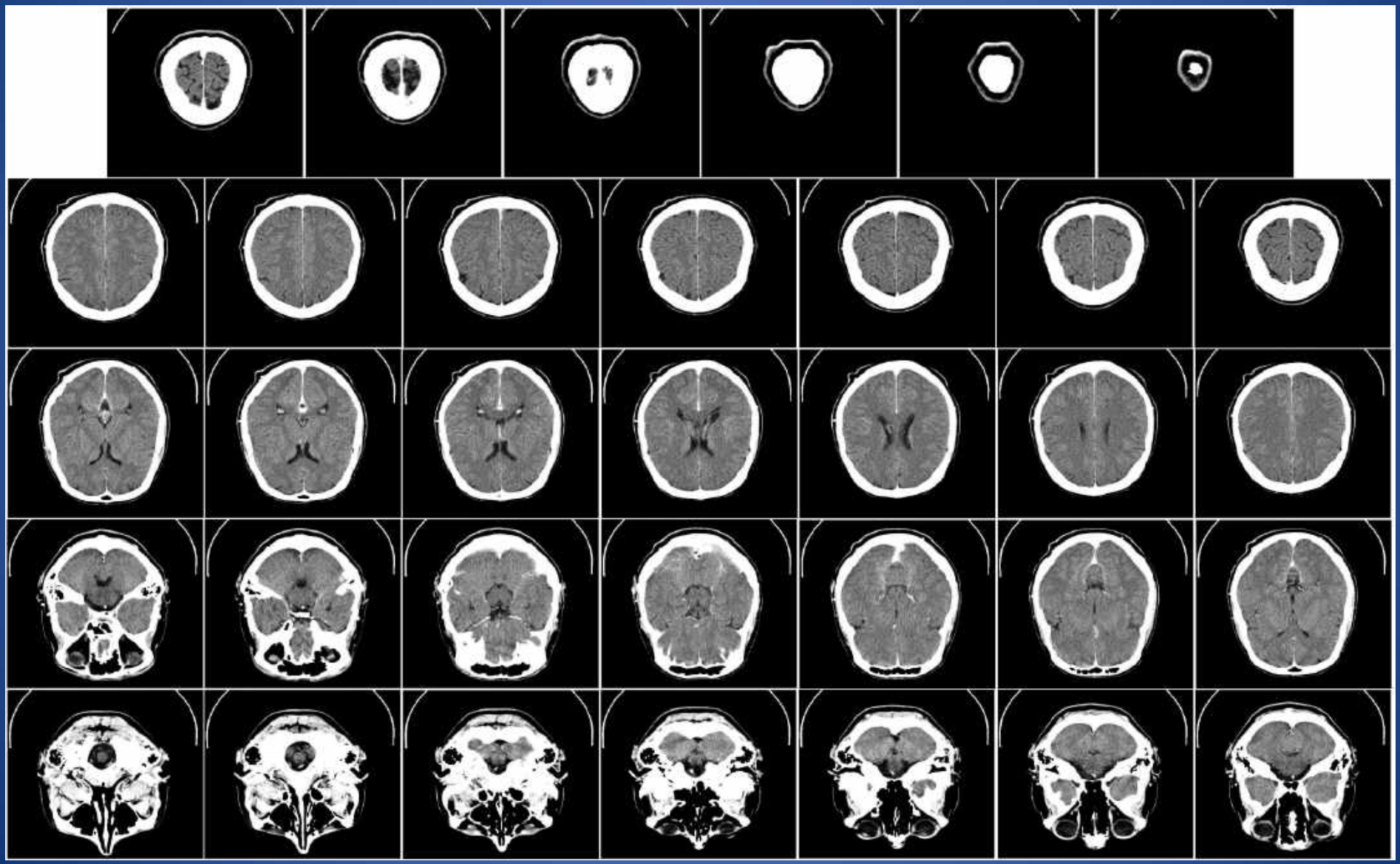
Advancements in Neuroimaging



X-Ray

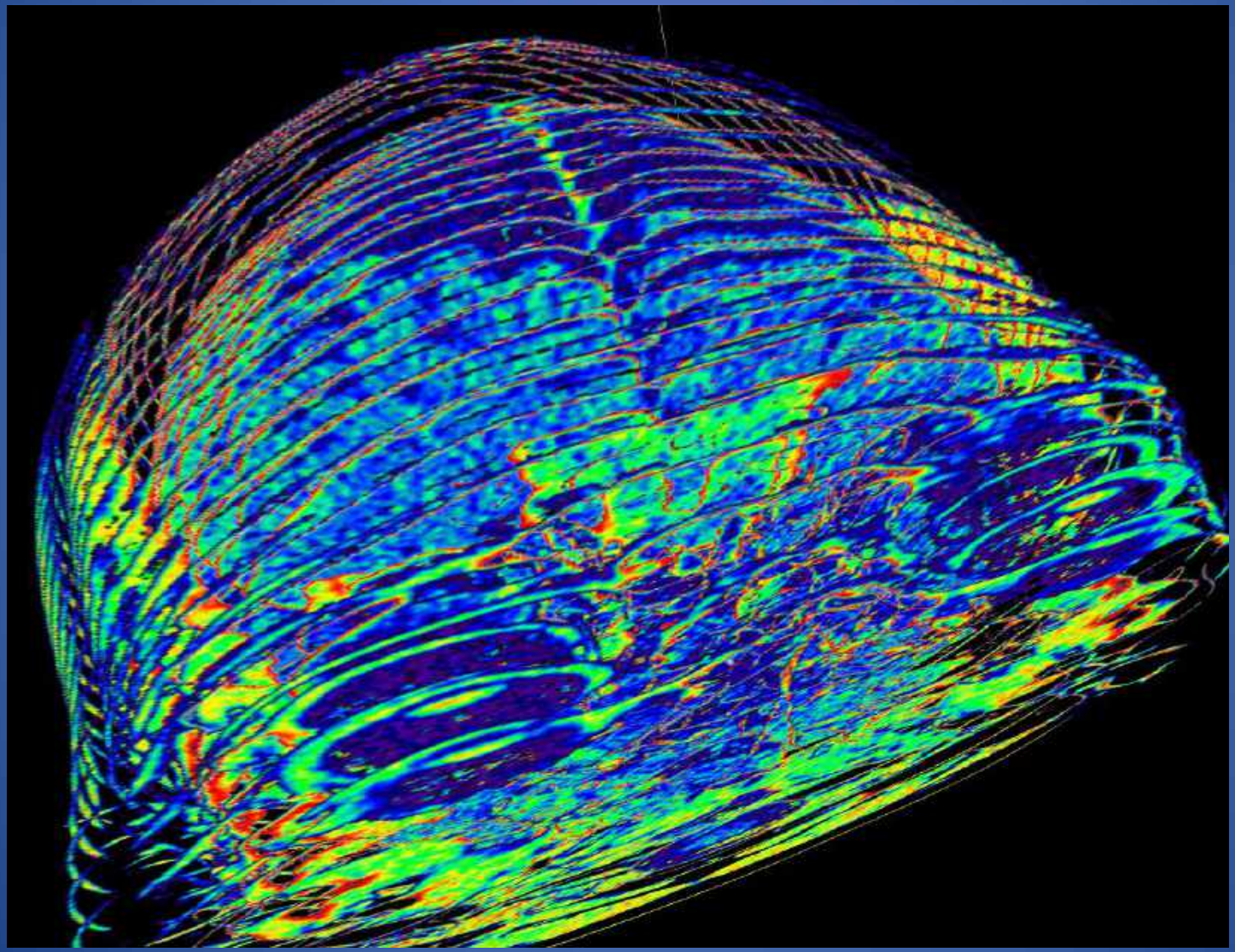
Black and White TV

Brain CT Scan

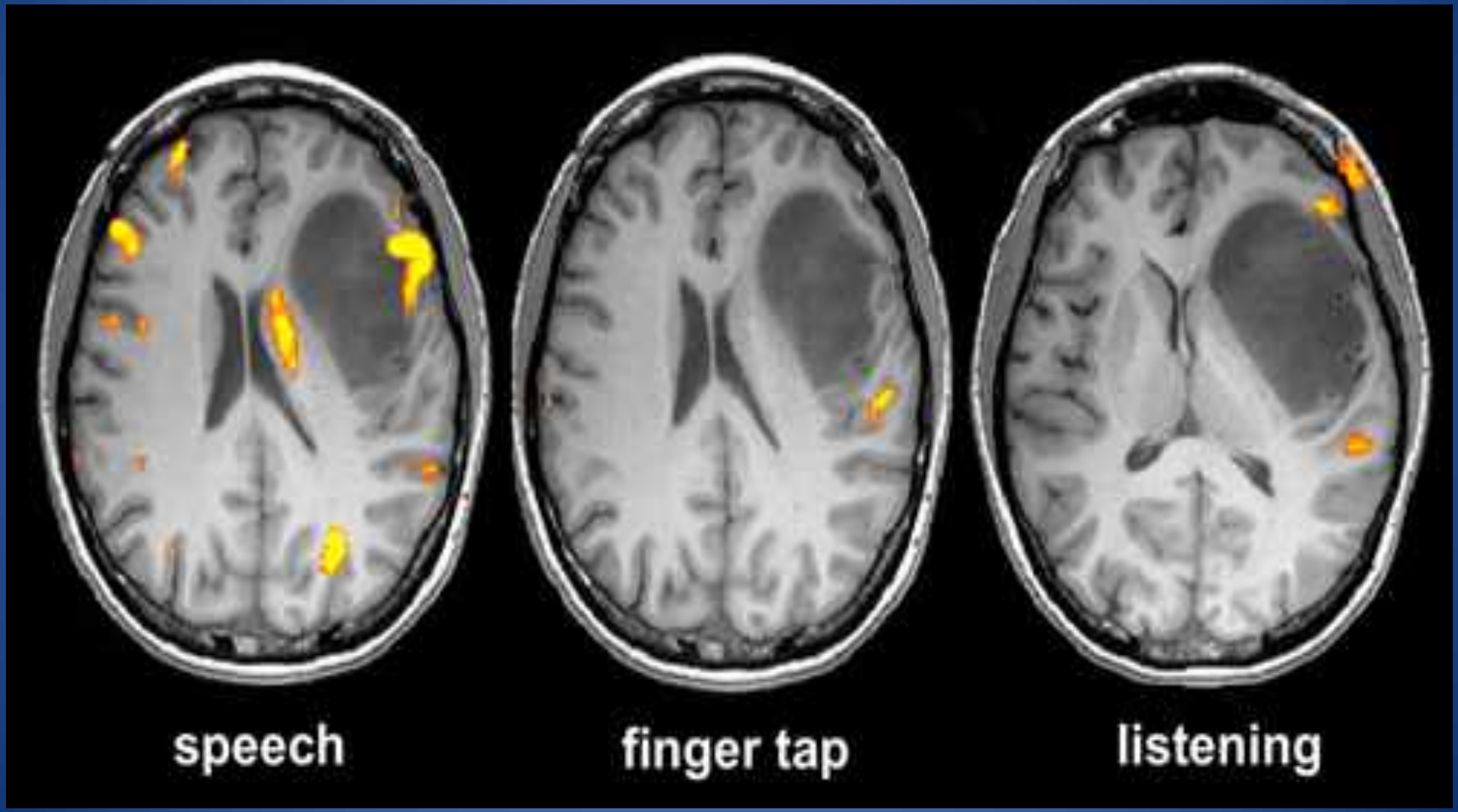


Brain MRI

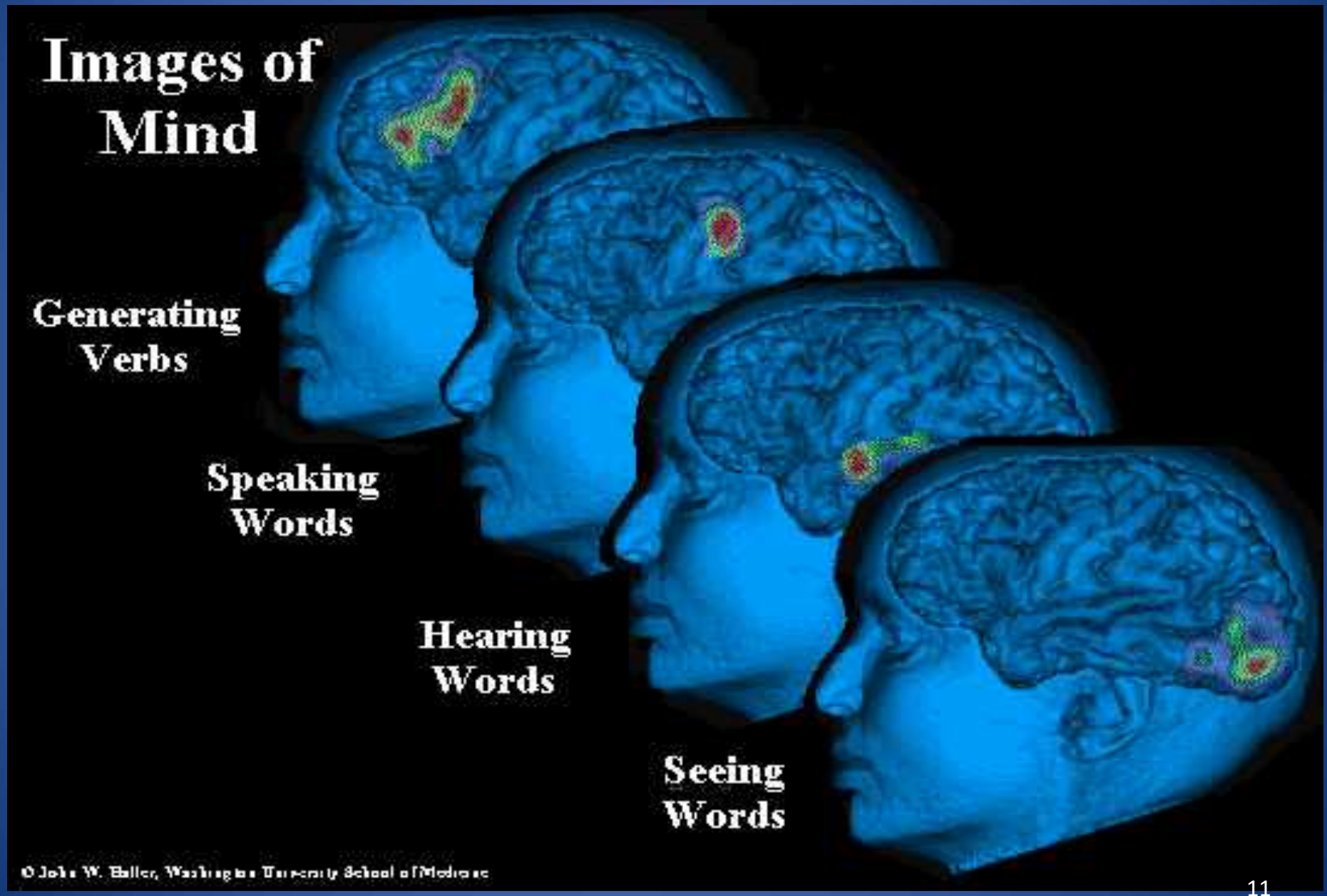
Brain CT



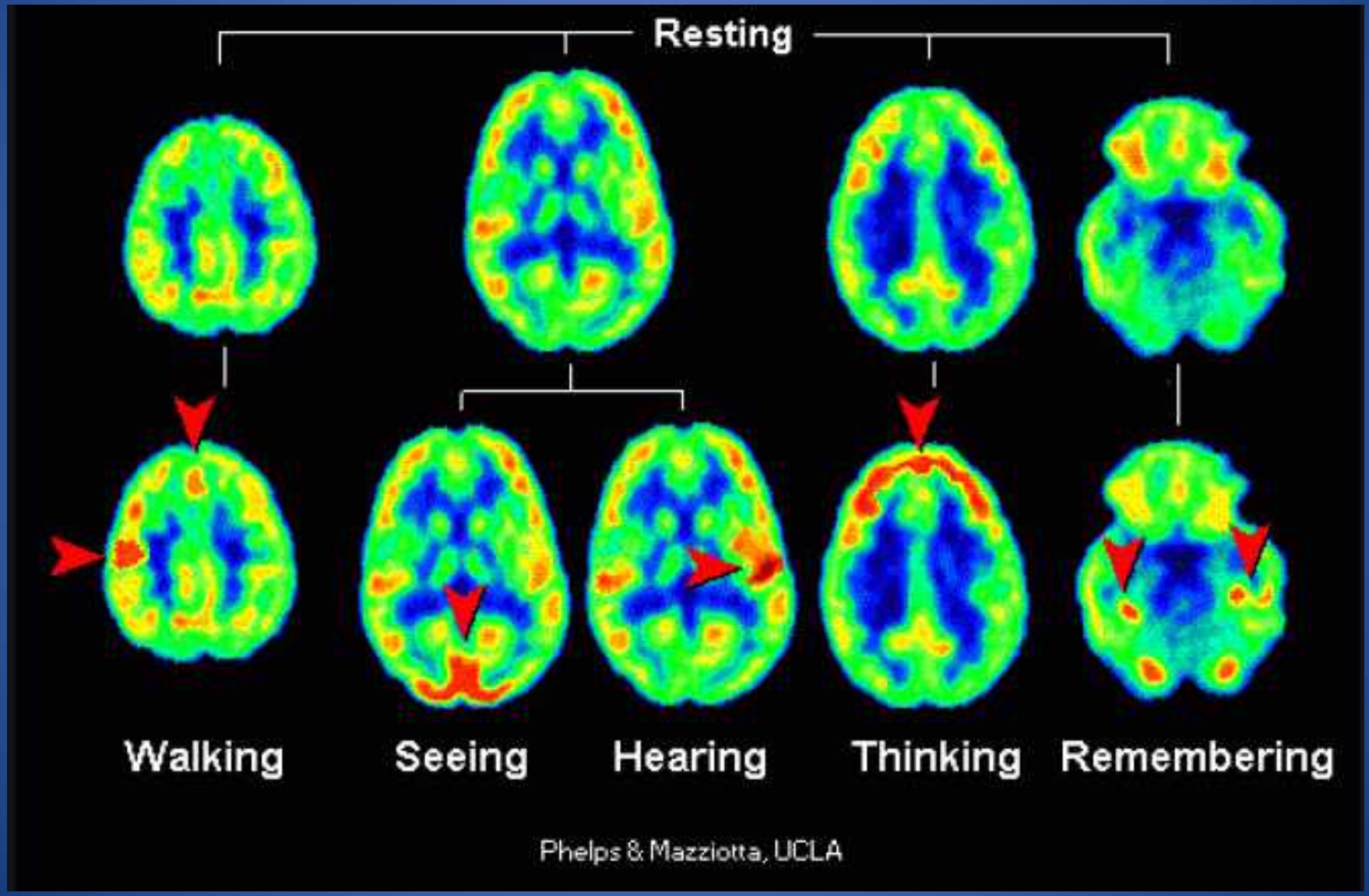
Functional MRI



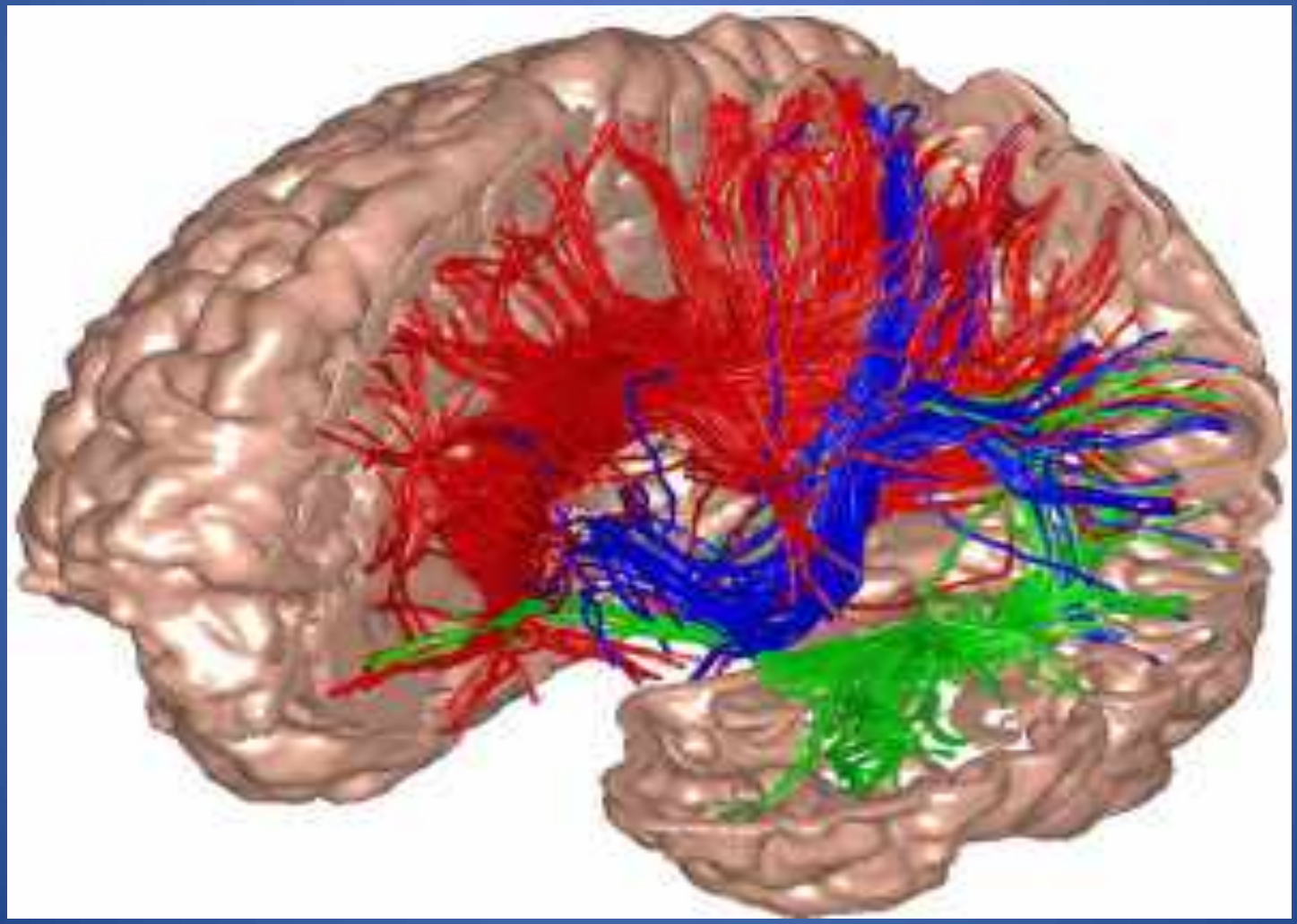
PET Imaging


Images of Mind
Generating Verbs
Speaking Words
Hearing Words
Seeing Words
© John W. Haller, Washington University School of Medicine

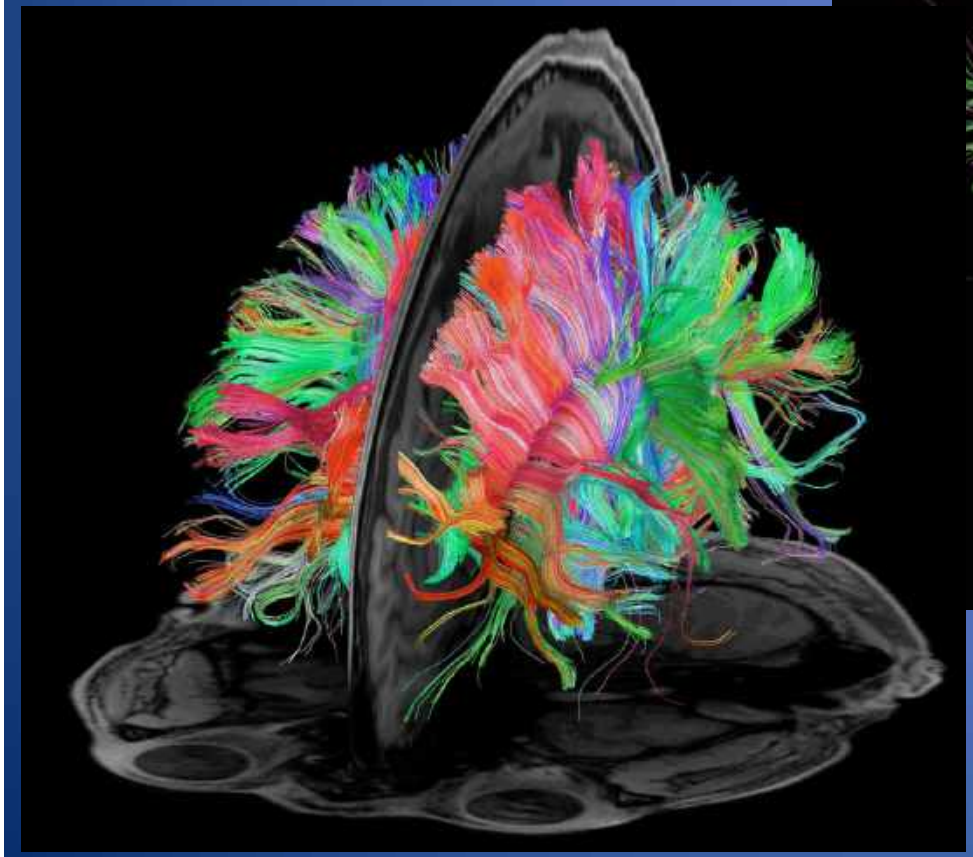
PET Imaging

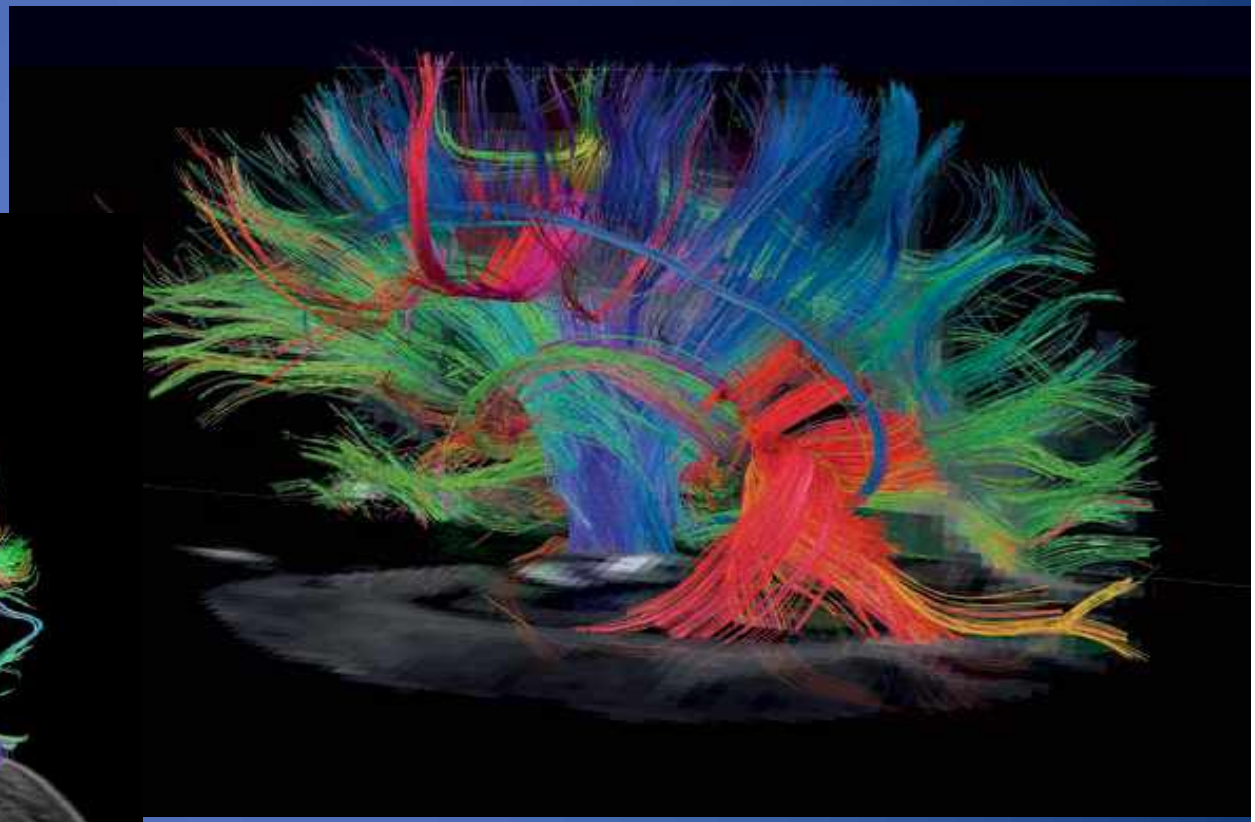

Resting
Walking
Seeing
Hearing
Thinking
Remembering
Phelps & Mazziotta, UCLA

Tensor Diffusion Imaging



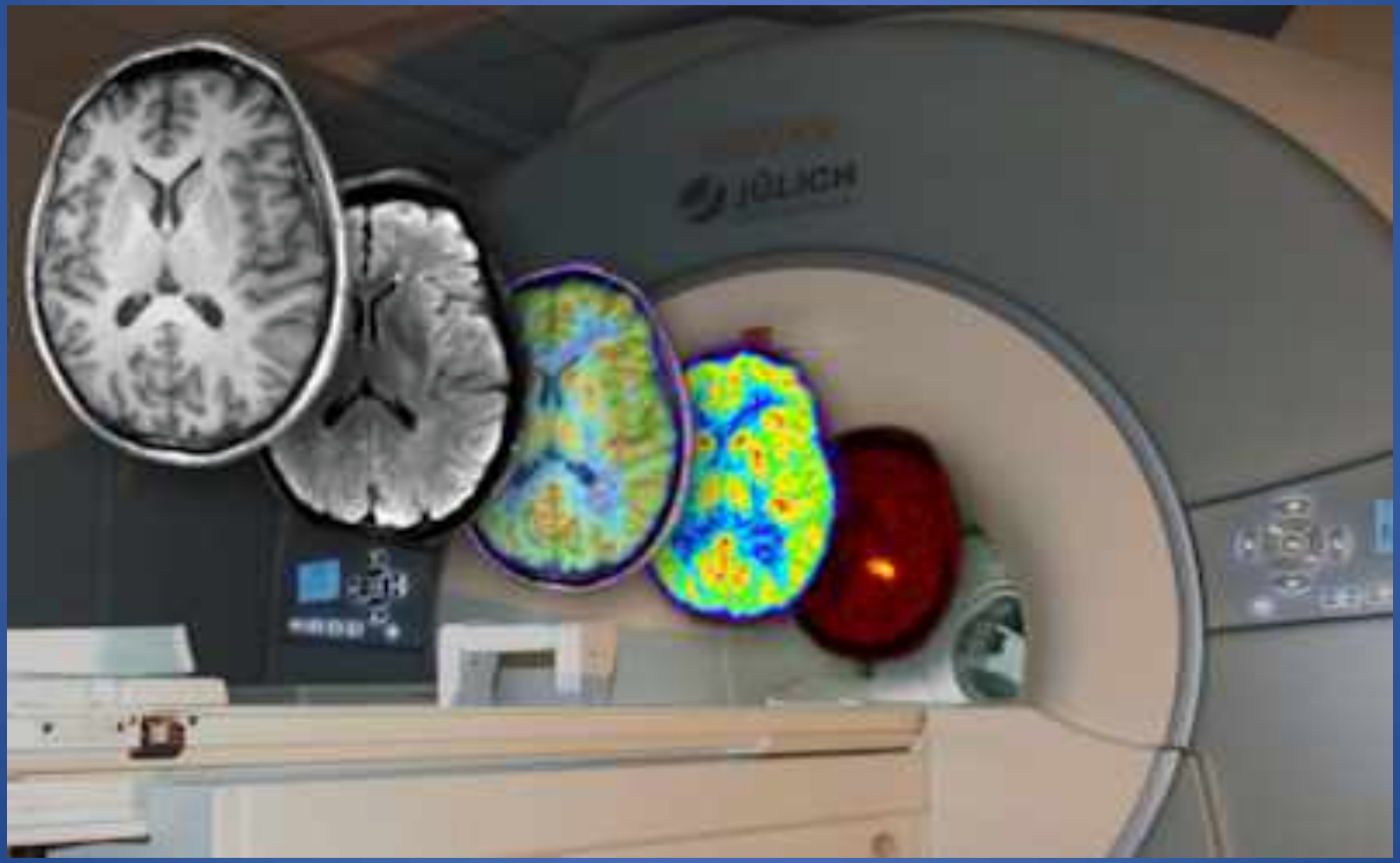
Tensor Diffusion Imaging Becoming Super Brain Assessment Tool



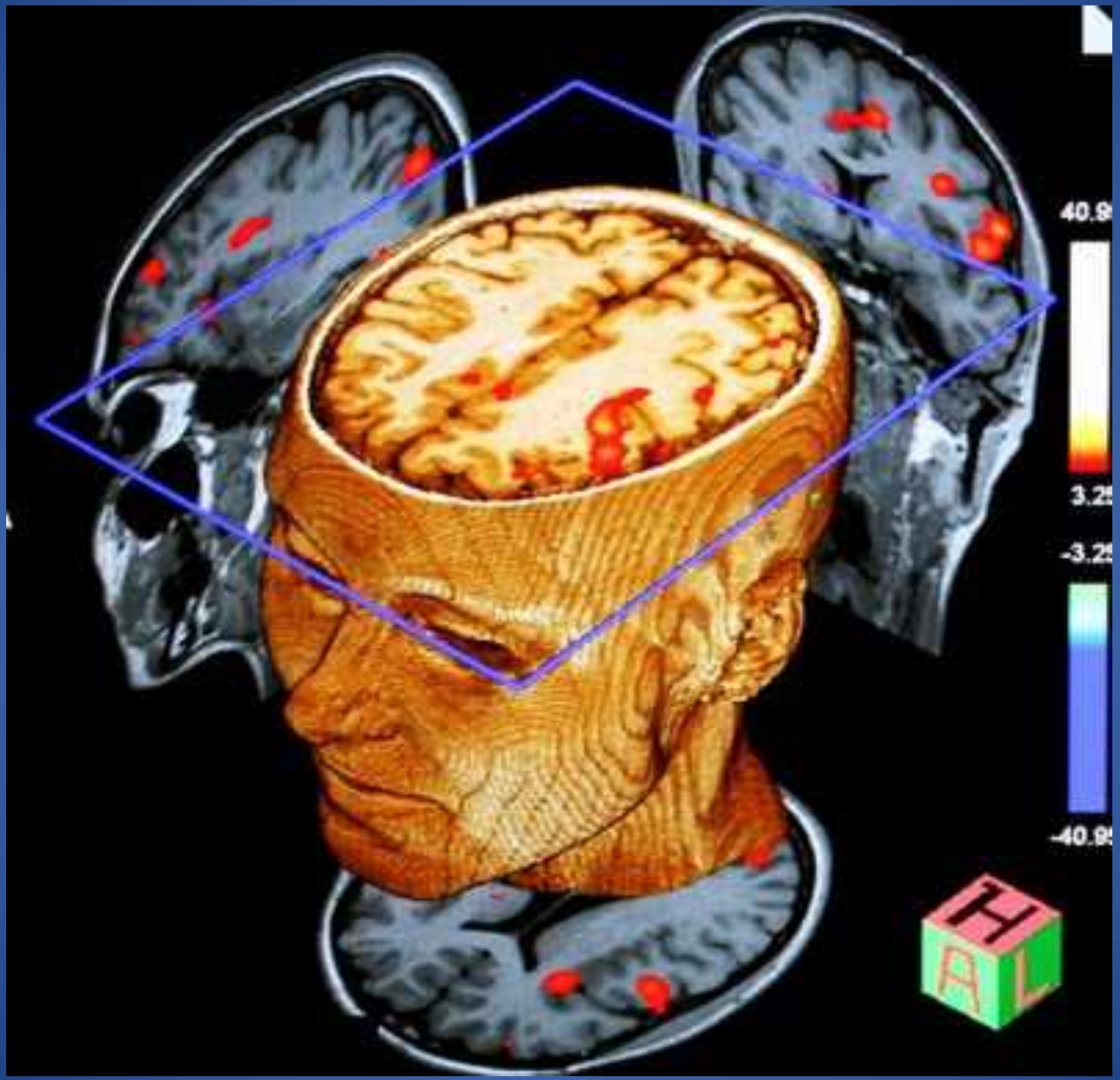


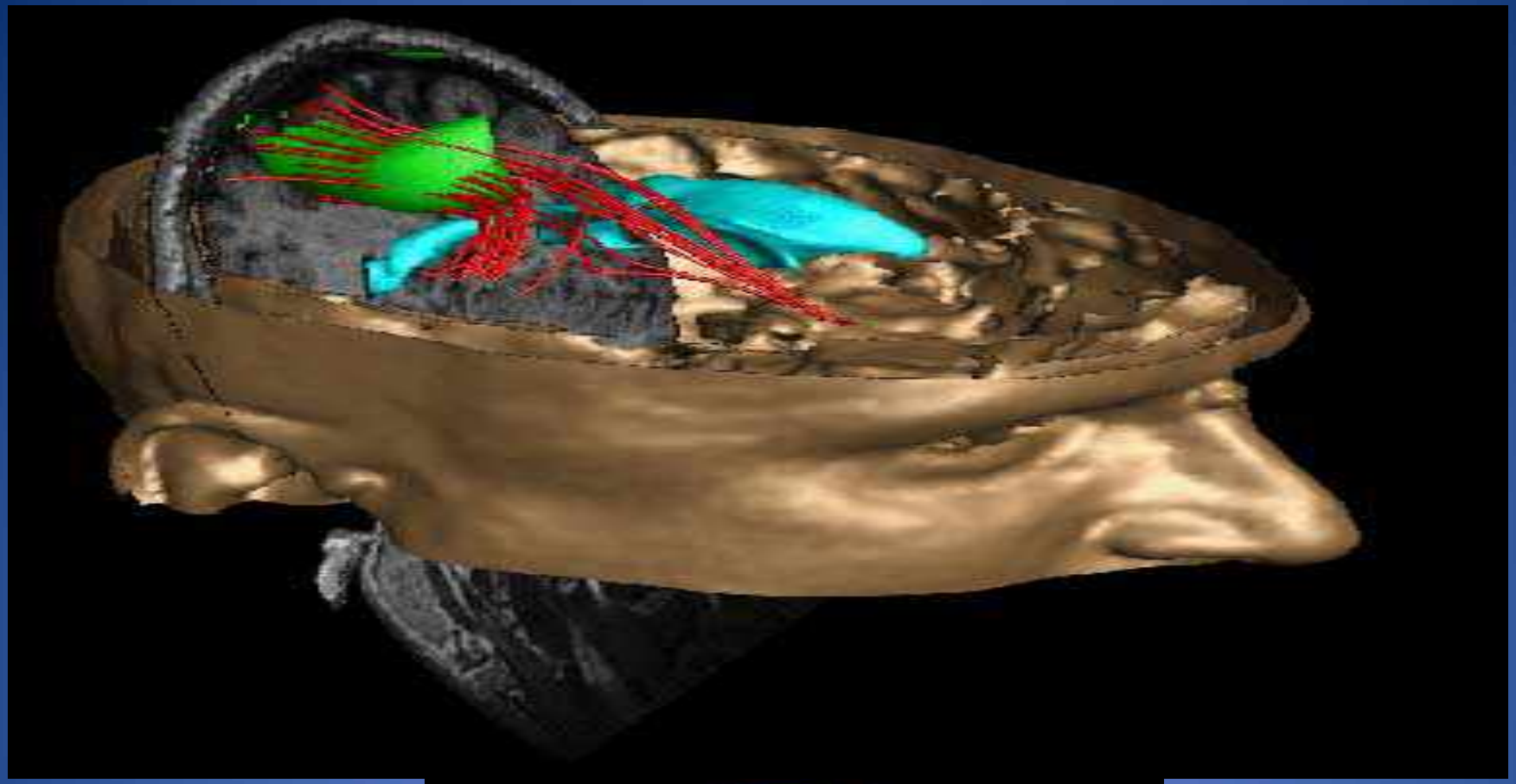
Neuroimaging and the Future of Brain Cartography

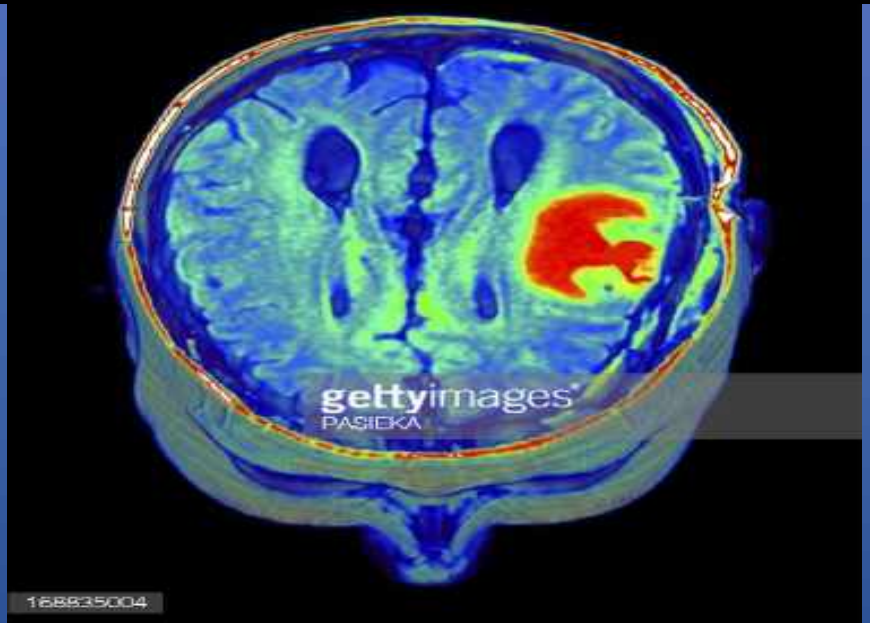
Cartography is the study and practice of making maps. Combining science, aesthetics, and technique, cartography builds on the premise that reality can be modeled in ways that communicate spatial information effectively. Wikipedia

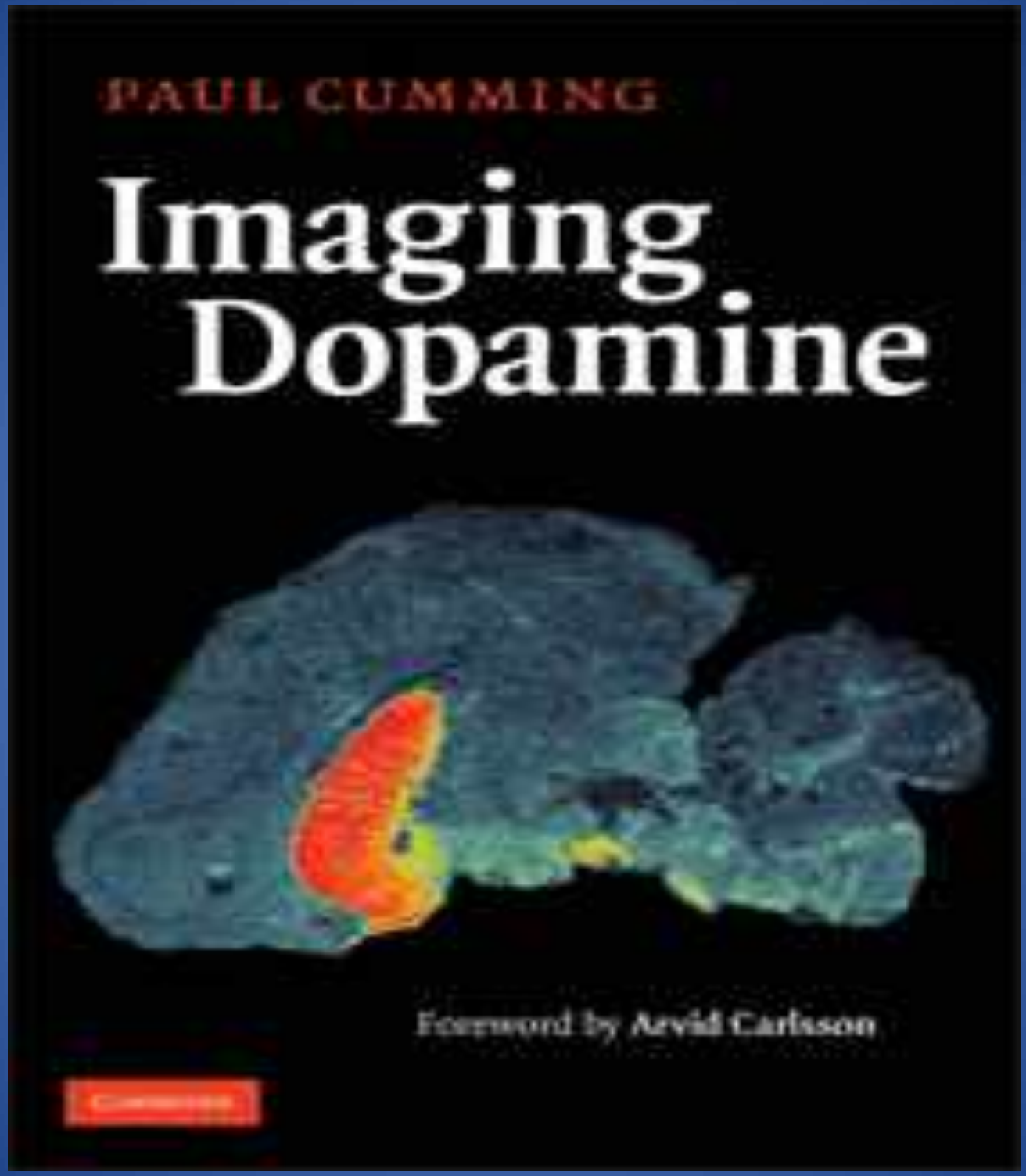


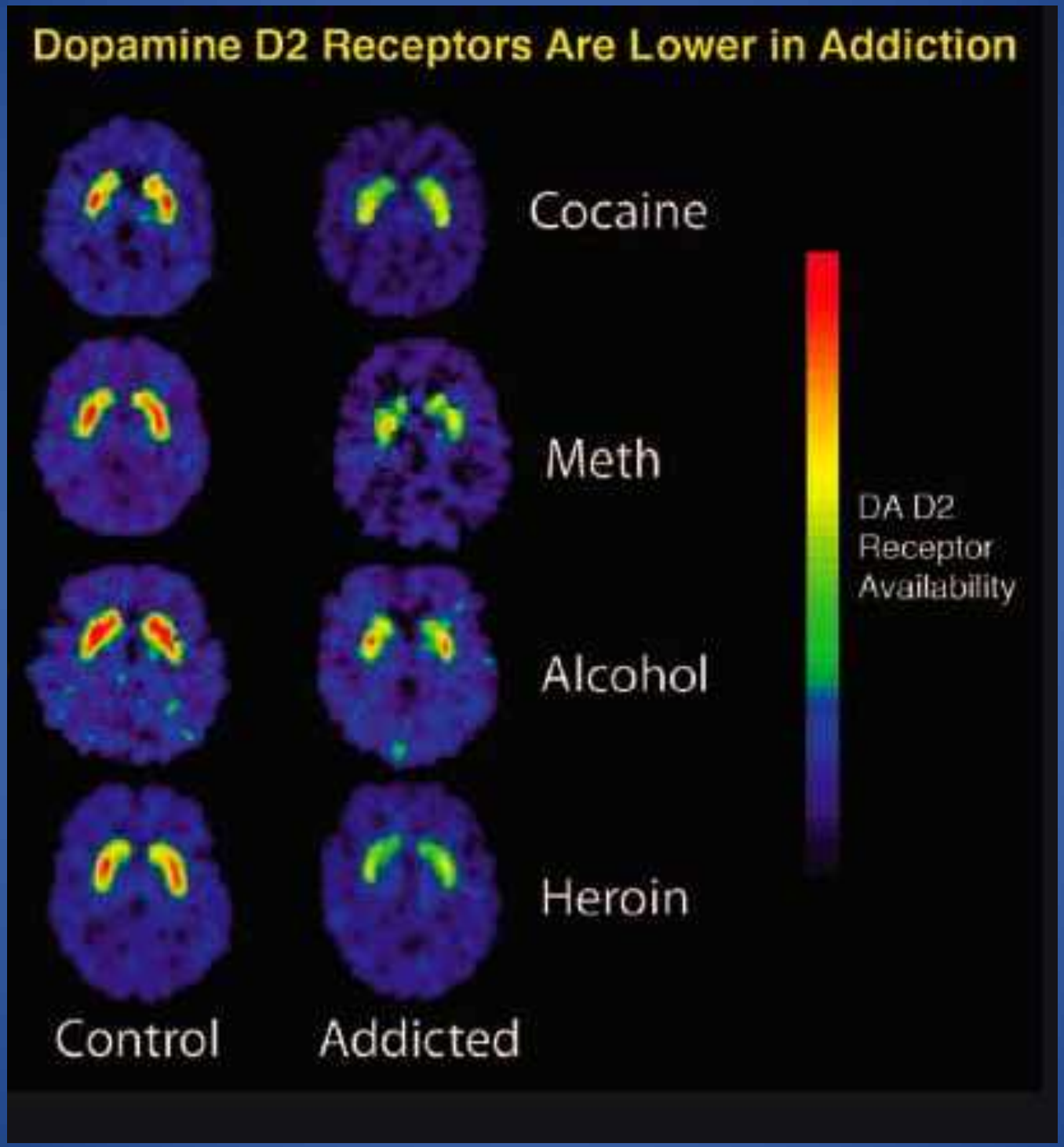
MRI allows to track many different aspects of the brains structure and dynamics in increasingly high resolution. Foto: Forschungszentrum Jülich


40.9
3.25
-3.25
-40.9
H
A
L

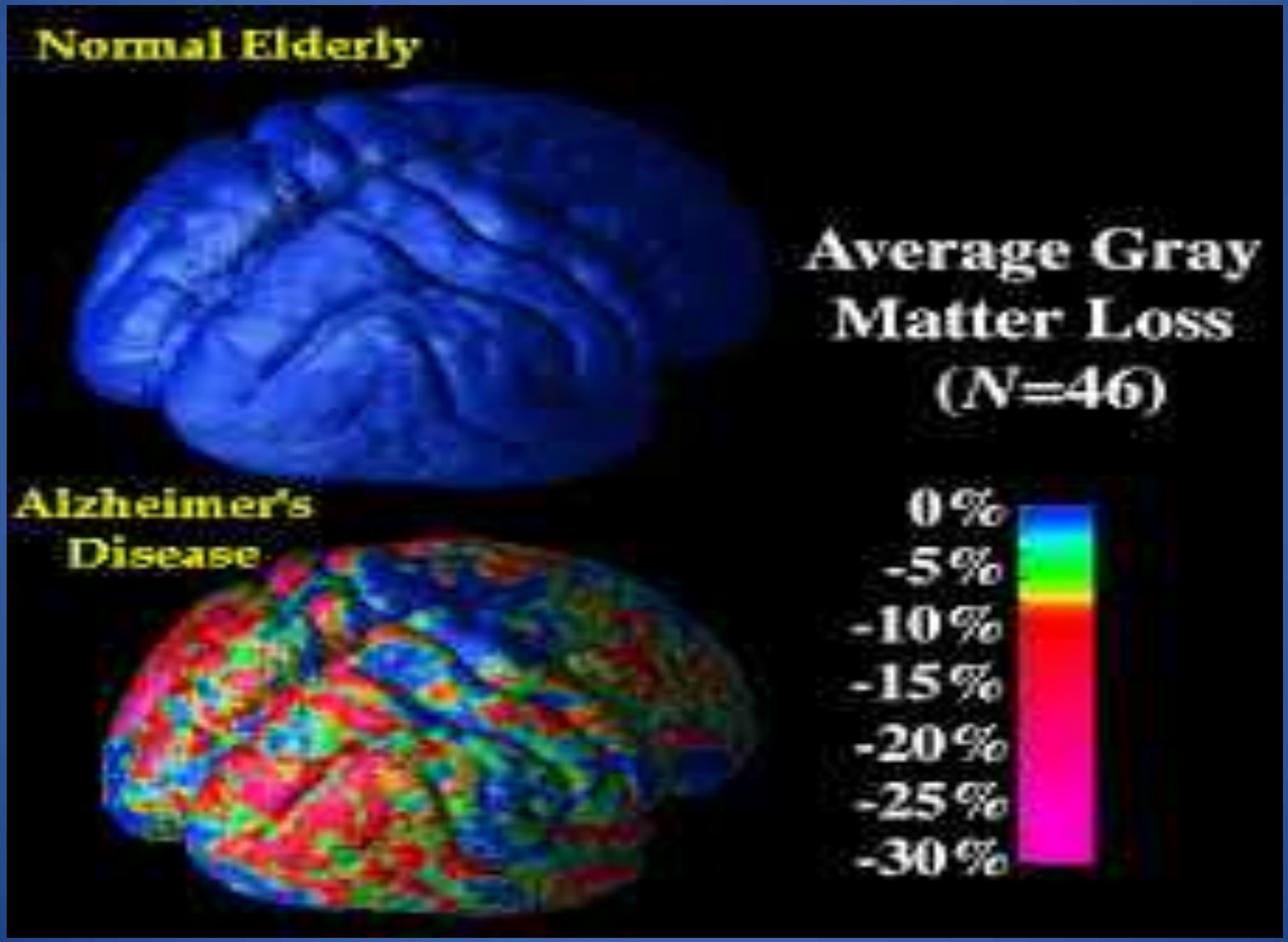


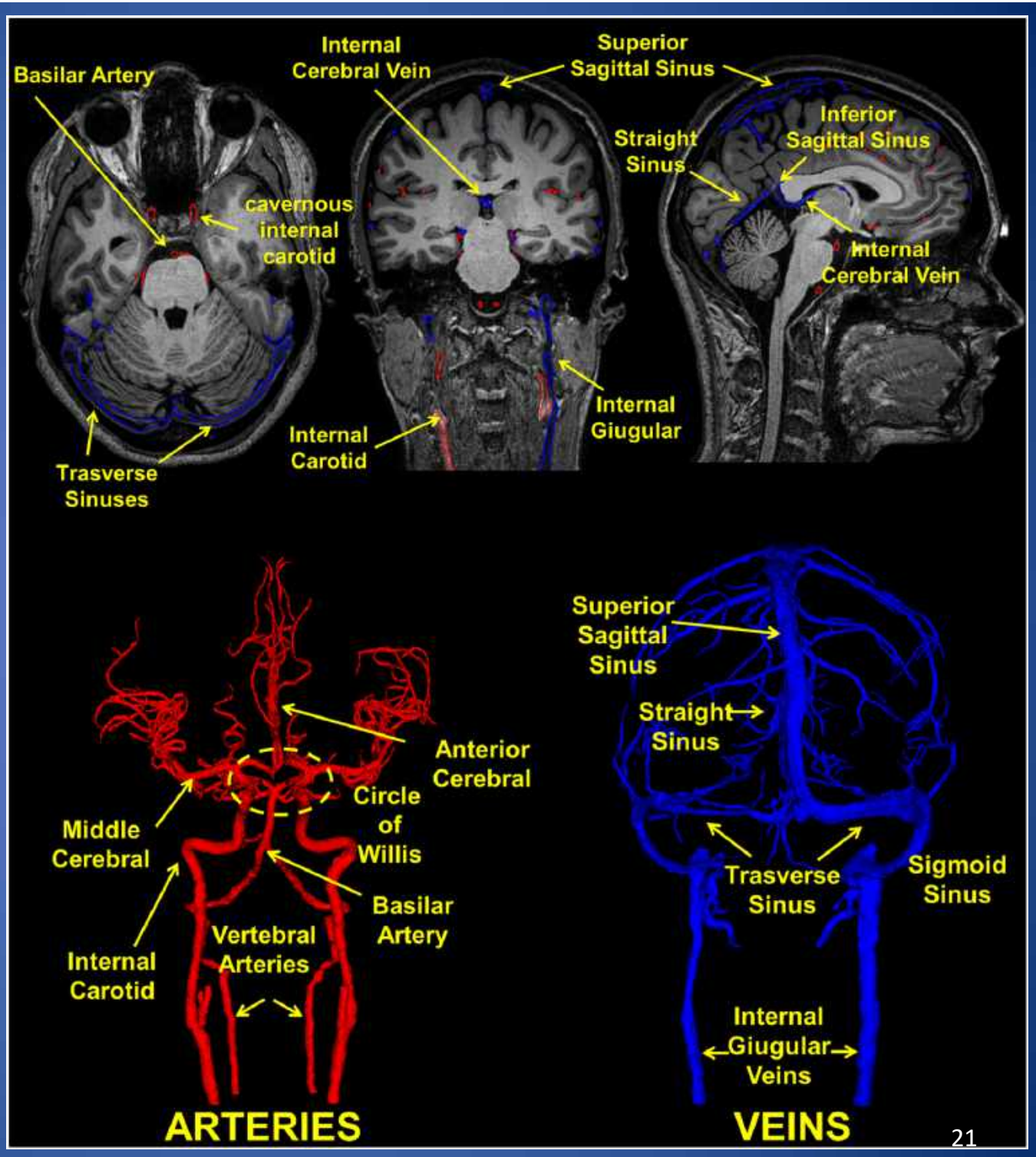

gettyimages
PASIEKA
168835004

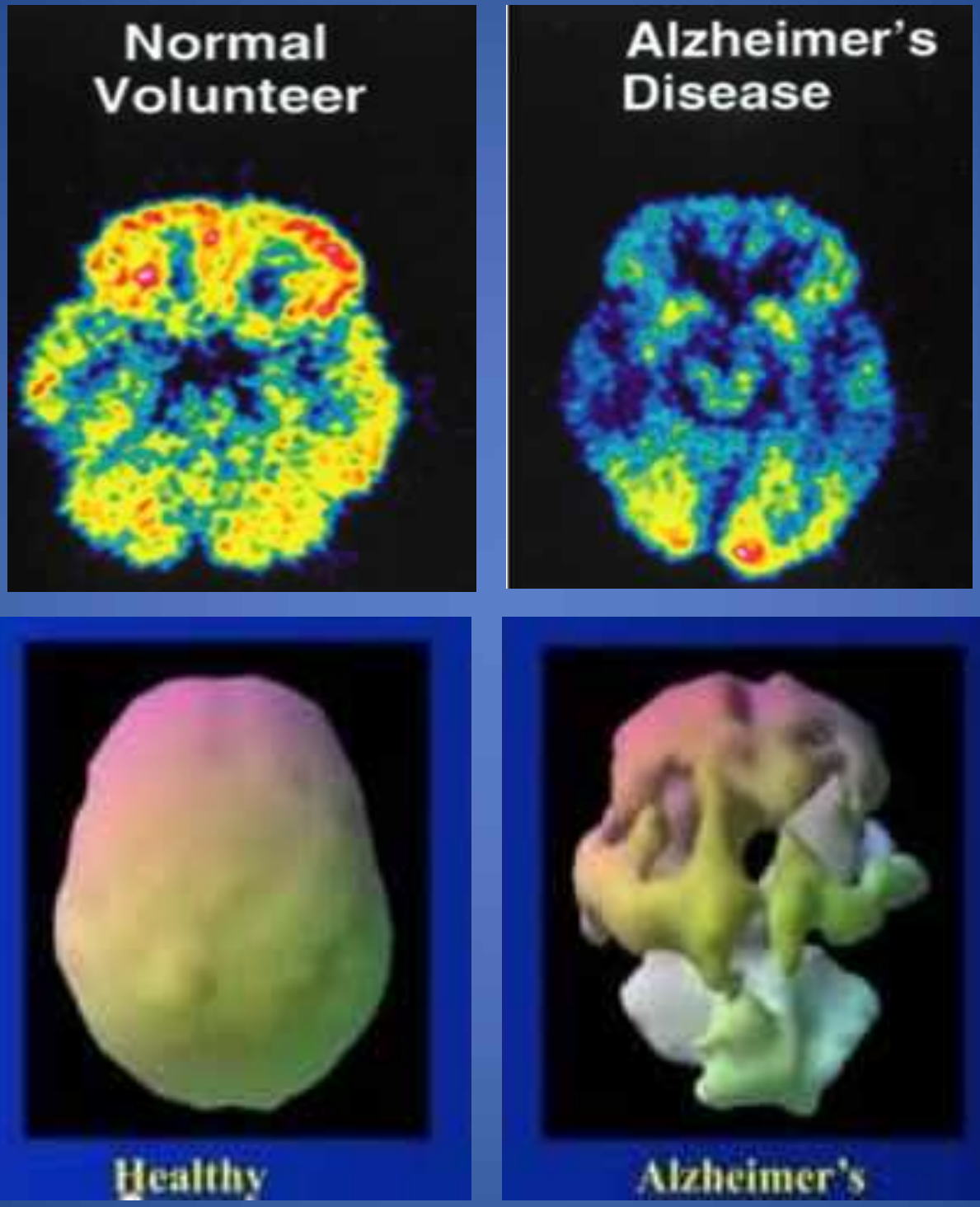

PAUL CUMMING
Imaging Dopamine
Foreword by Arvid Carlsson


Dopamine D2 Receptors Are Lower in Addiction
Cocaine
Meth
Alcohol
Heroin
DA D2
Receptor
Availability
Control
Addicted

Alzheimer's & Anti-Aging Imaging




Basilar Artery
Internal Cerebral Vein
Superior Sagittal Sinus
Inferior Sagittal Sinus
Straight Sinus
cavernous internal carotid
Internal Cerebral Vein
Internal Giugular
Internal Carotid
Trasverse Sinuses
Anterior Cerebral
Circle of Willis
Middle Cerebral
Basilar Artery
Vertebral Arteries
Internal Carotid
ARTERIES
Superior Sagittal Sinus
Straight Sinus
Trasverse Sinus
Sigmoid Sinus
Internal Giugular Veins
VEINS


Normal Volunteer
Alzheimer's Disease
Healthy
Alzheimer's

Quantitative MRIs

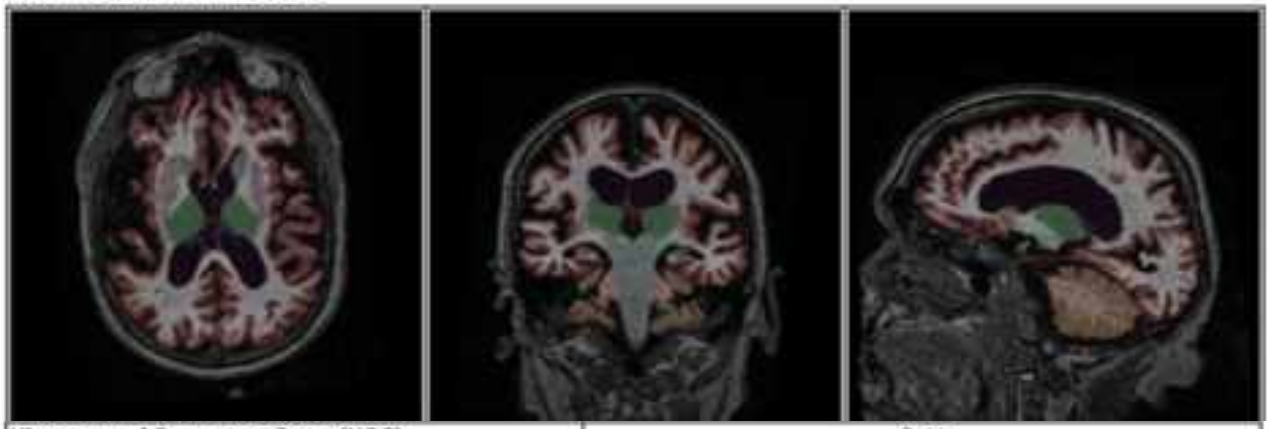
PATIENT INFORMATION

Version 2.3.0

Patient ID:	Patient Name:	Sex: M	Age: 79
Accession Number:	Referring Physician:	Exam Date:	

MORPHOMETRY RESULTS

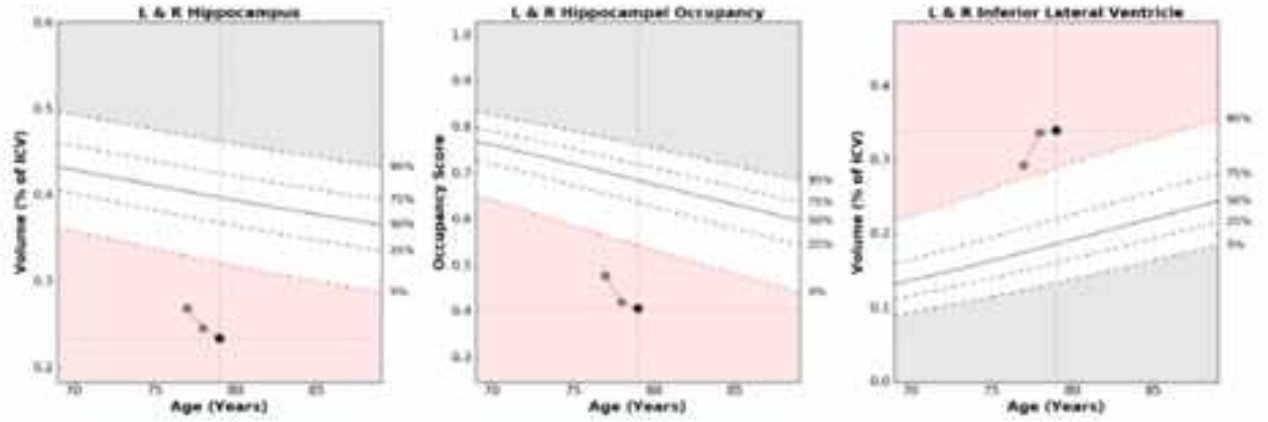
MORPHOMETRY RESULTS



Hippocampal Occupancy Score (HOC)	0.41

Brain Structure	Volume (cm³)	% of ICV (5%-95% Normative Percentile)	Normative Percentile
Hippocampi	4.49	0.23 (0.32 - 0.46)	1
Superior Lateral Ventricles	125.50	6.56 (1.85 - 4.98)	99
Inferior Lateral Ventricles	6.52	0.34 (0.13 - 0.29)	99

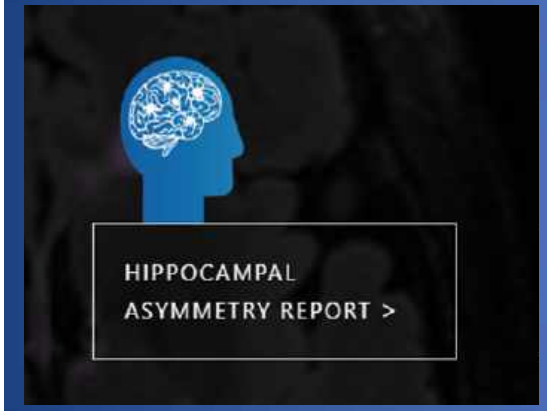
AGE-MATCHED REFERENCE CHARTS




AGE RELATED ATROPHY
REPORT >


PETQuant™
PET FDG Report


BRAIN DEVELOPMENT
REPORT >

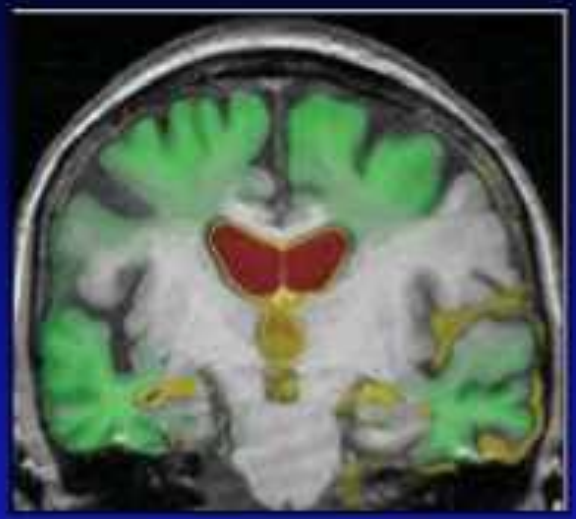

HIPPOCAMPAL
ASYMMETRY REPORT >


MULTI STRUCTURE
ATROPHY REPORT >

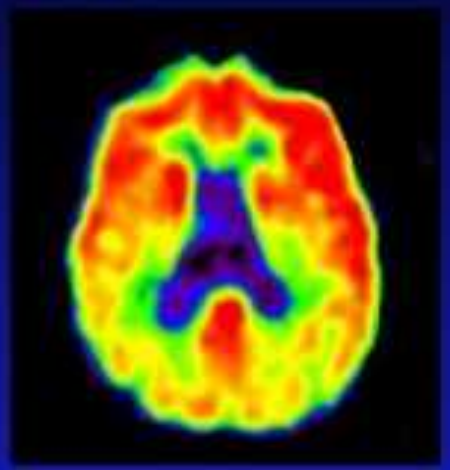

TRIAGE BRAIN ATROPHY
REPORT >

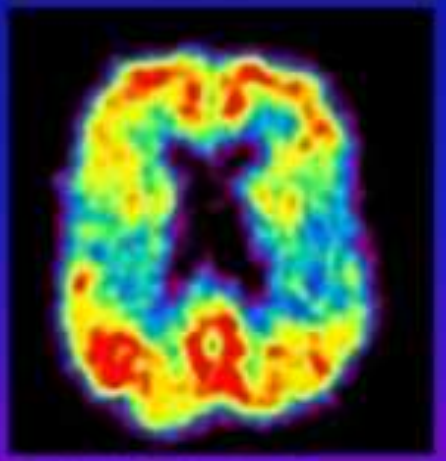
Evolution of Neuroimaging in AD

- Computed Tomography
- MRI
- Volumetric MRI
- Functional MRI
- FDG Glucose PET
- Amyloid Imaging



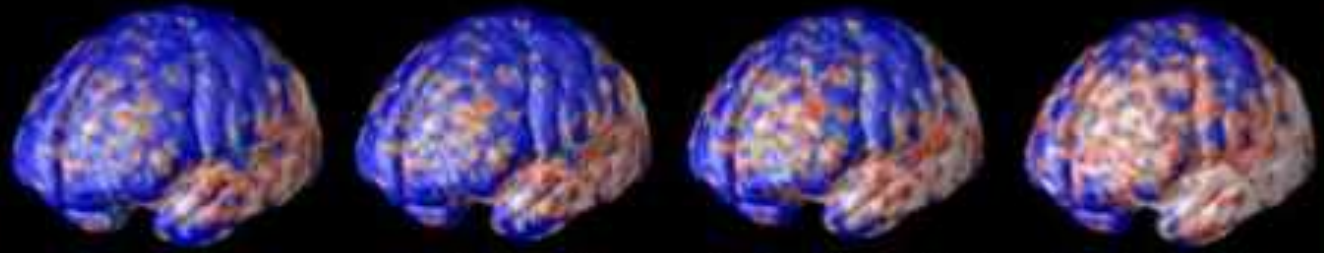
Helmuth J. Science 2002;297:1260-1262





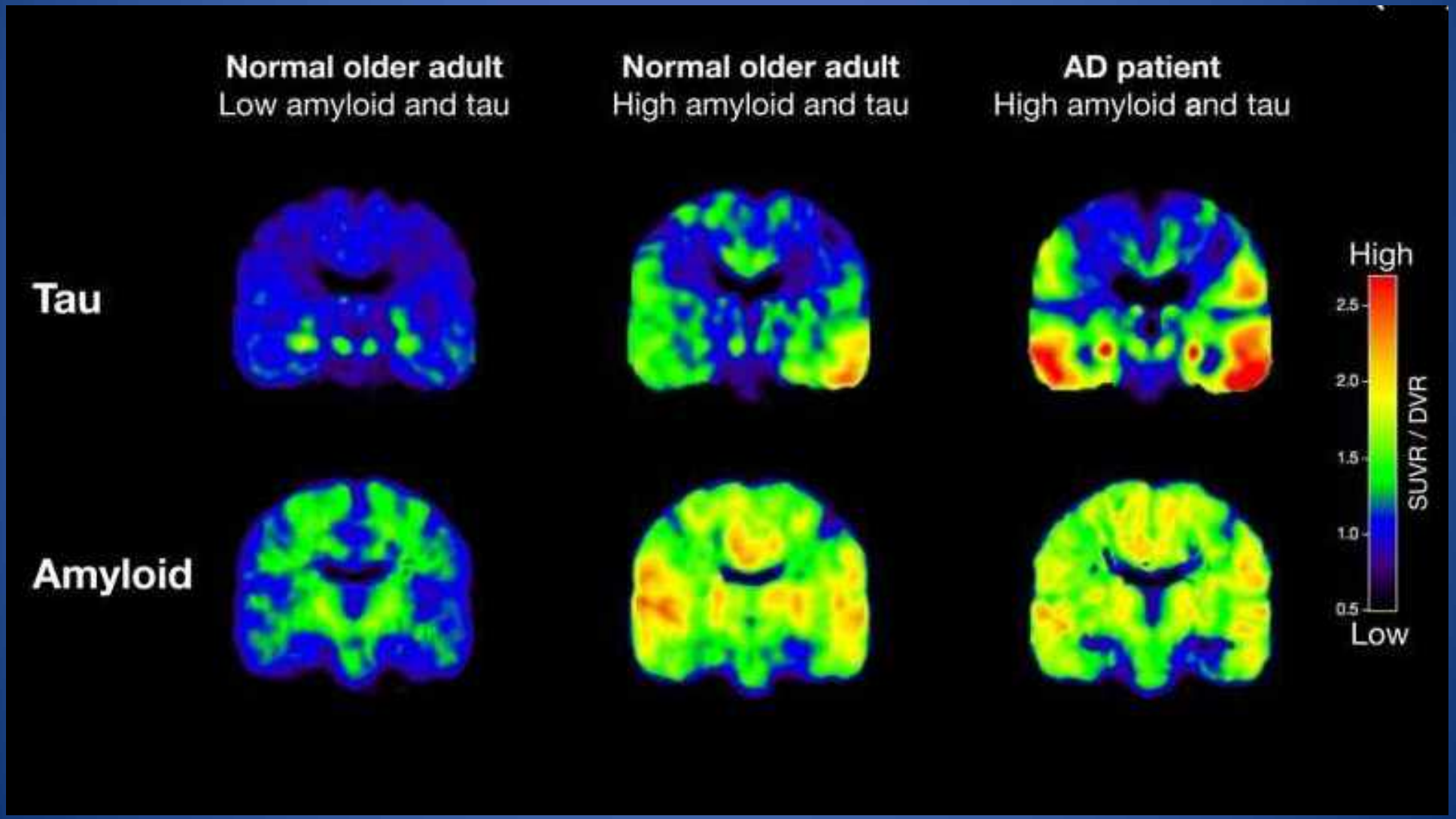
Alzheimer Disease Forum http://www.alzforum.org/new/det ail.asp?id=548

Brain Maps: Alzheimer's Disease Spreading



Lab of Neuro Imaging UCLA School of Medicine. www.loni.ucla.edu/~thompson/AD_4D/dynamic.html

PET scans reveal key details of Alzheimer's protein growth in aging brains



Multimodal work-up of neurodegeneration

Key parameters

Individual specific questions

MRI: Tumors, cerebrovascular lesions etc.

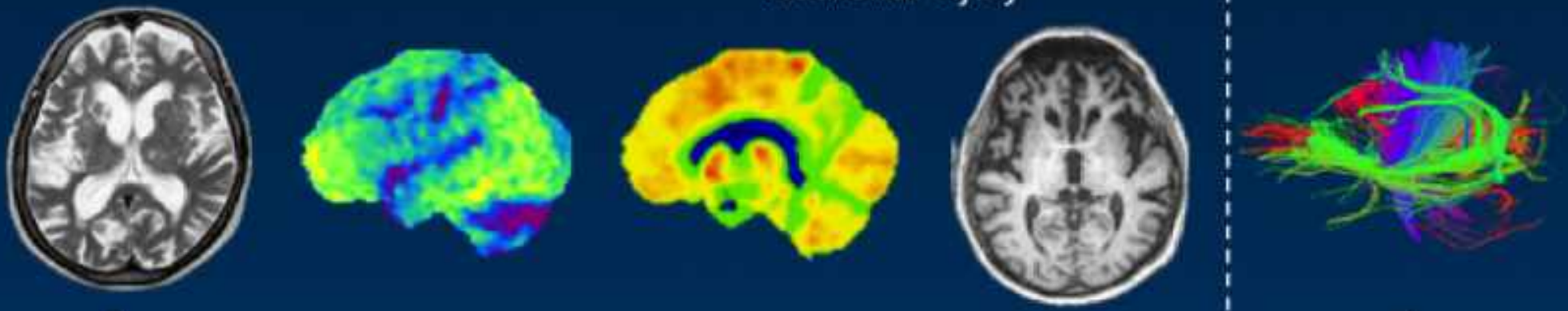
PET: Molecular pathology, amyloid/tau

PET: Neuronal dysfunction (metabolism/perfusion)

MRI: Atrophy, structural changes

PET&/or MRI: Inflammation receptor status connectivity, etc.

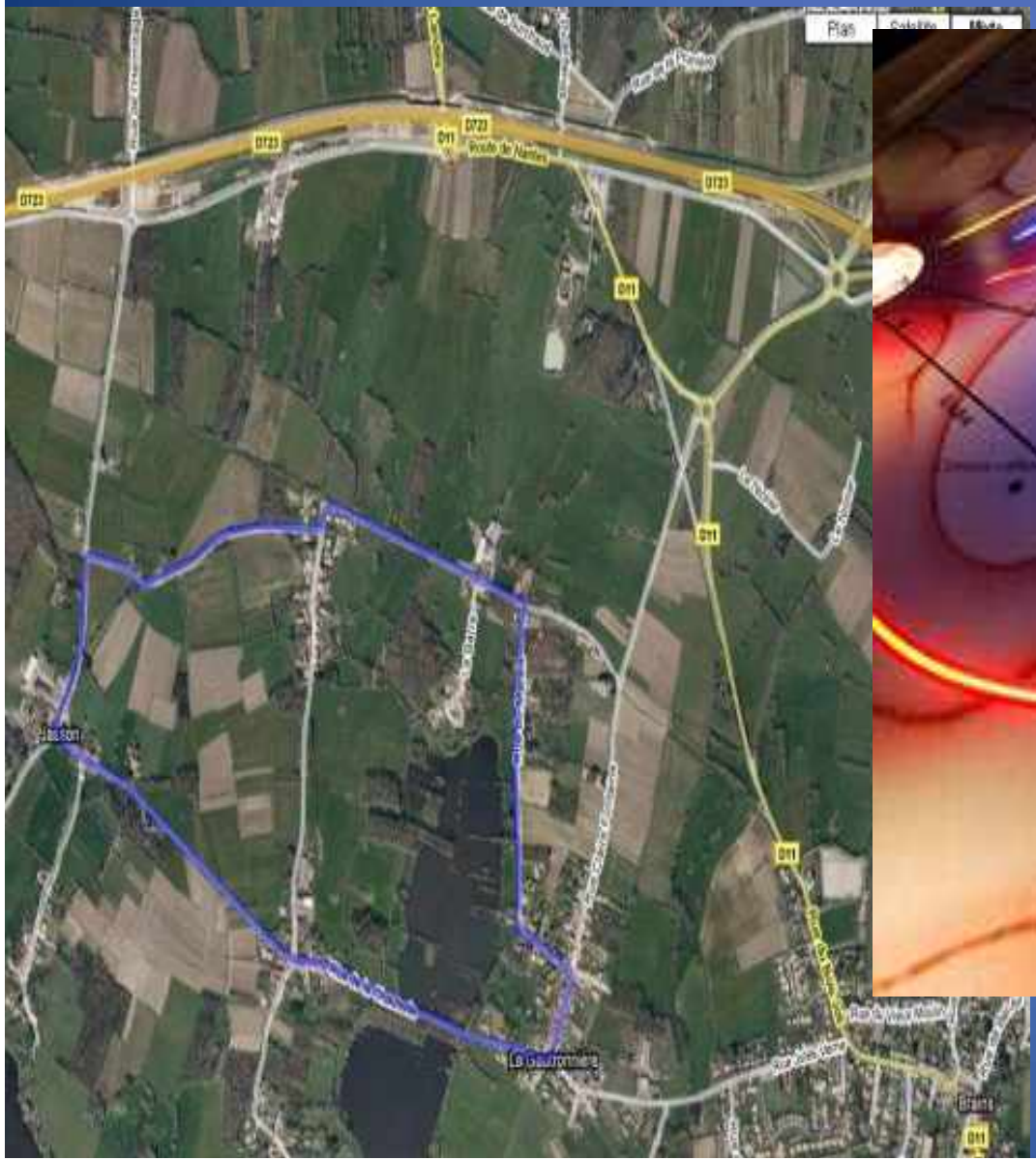
Neuronal injury

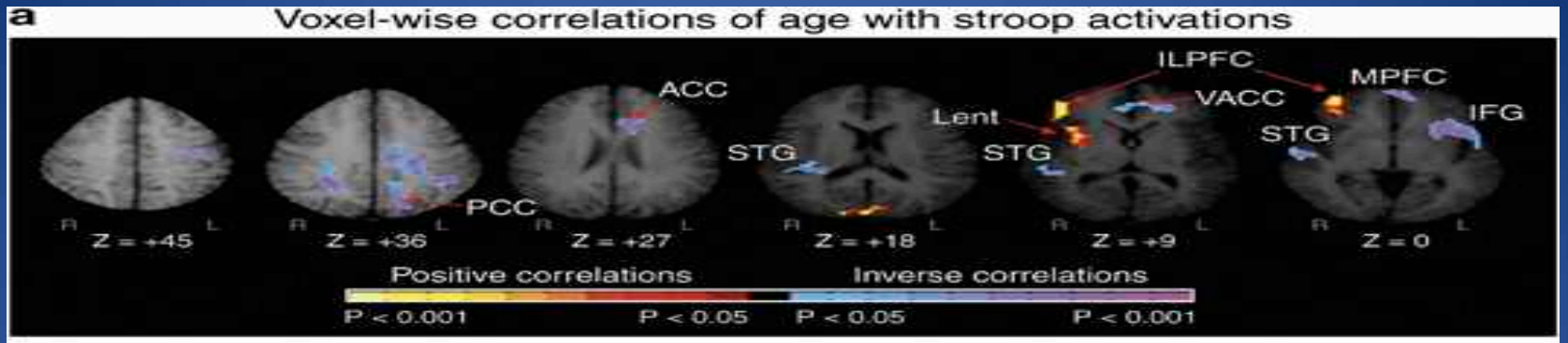


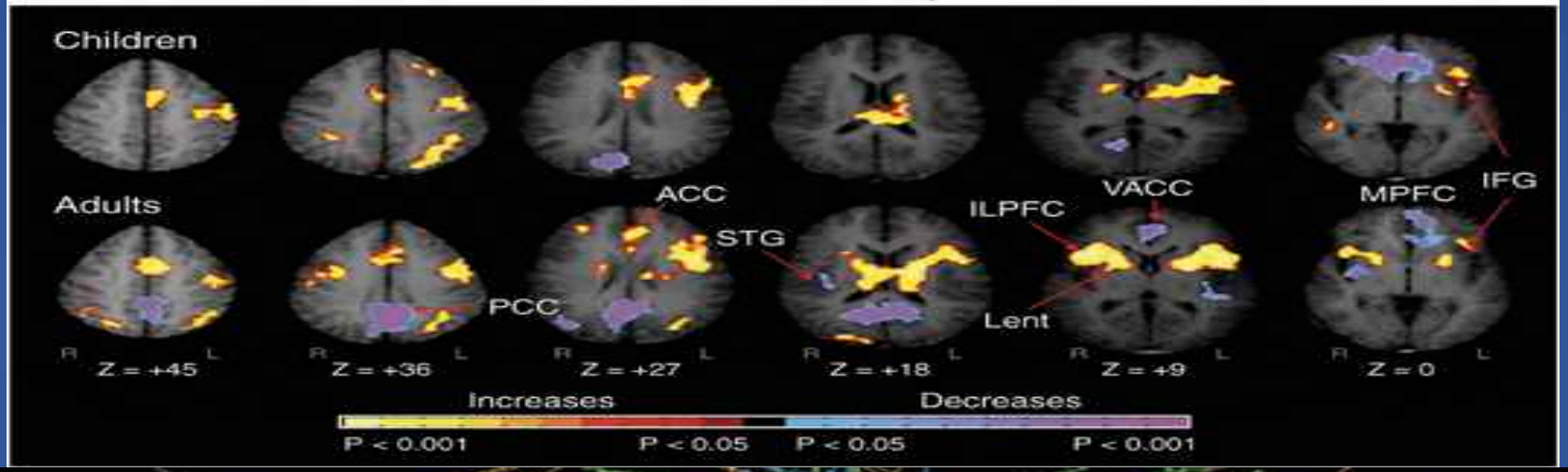
PET/MR:

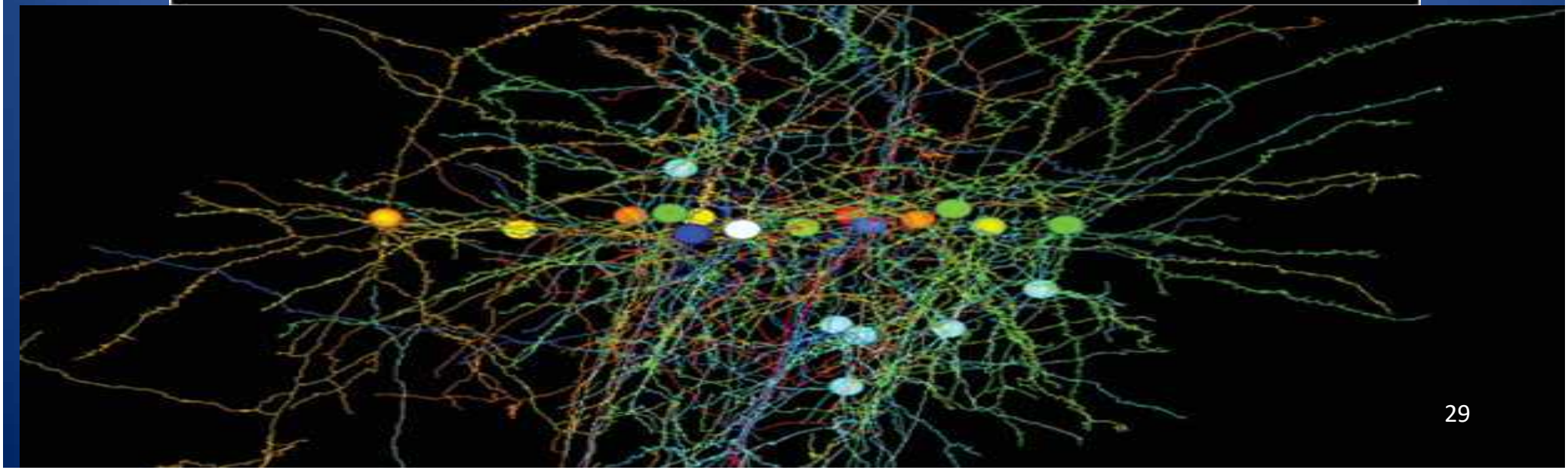
Complete check-up in a one stop fashion in optimized quality (motion/atrophy correction)

Global Positioning System - GPS




a
Voxel-wise correlations of age with stroop activations
ILPFC
MPFC
ACC
VACC
Lent
IFG
STG
STG
STG
PCC
Z = +45
Z = +36
Z = +27
Z = +18
Z = +9
Z = 0
Positive correlations
Inverse correlations
P < 0.001
P < 0.05
P < 0.05
P < 0.001


b
Convetional T-maps
Children
Adults
ACC
VACC
ILPFC
MPFC
IFG
STG
PCC
Lent
Z = +45
Z = +36
Z = +27
Z = +18
Z = +9
Z = 0
Increases
Decreases
P < 0.001
P < 0.05
P < 0.05
P < 0.001



À la carte

This is your brain on music

Mapping musical activity reveals what music stimulates the brain in the same way food, sex and drugs do

BY STEVEN FICK AND ELIZABETH SMILEY

IMAGINING MUSIC: Singing "Twinkle, Twinkle Little Star" in your head stimulates the auditory cortex even though you are not actually hearing the tune. The activity, however, occurs in small, discrete areas (1), and to a lesser degree than if you were actually listening. The inferior frontal gyrus (2) tends to be associated with retrieving memories and is thus stimulated as you recall "How I wonder what you are." Scientists believe the dorsolateral frontal cortex (3) is responsible for holding the song in working memory while it is being imagined.

READING MUSIC: The auditory cortex (1) is organized in terms of muted frequencies, with some cells responding to low frequencies and others to high. Moving from the inside part of the cortex to the outside, different kinds of analyses take place. In the core, basic musical elements, such as pitch and volume, are analyzed, while surrounding regions process more complex elements, such as timbre, melody and rhythm.

PLAYING MUSIC: Few activities use more of the brain than playing music. It requires complex feedback systems that take in information, such as pitch and melody, through the auditory cortex (1) and allow the performer to adjust his or her playing. The visual cortex (2) is activated by reading — or even imagining — a score, the parietal lobe (3) is involved in a number of processes, including computation of finger positions; the motor cortex (4) helps control body movements; the sensory cortex (5) is stimulated with each touch of the instrument; the pre-motor area (6) remains somewhat mysterious but helps perform movements in the correct order and time; the frontal lobe (7) plans and coordinates the overall activity; and the cerebellum (8) helps create smooth, integrated movements.

REACTING EMOTIONALLY TO MUSIC: When you get a shiver up your spine listening to a piece of music, the "reward" structures deep in your mid-brain, such as the thalamus (1), ventral tegmental area (2), orbitofrontal cortex (3) and anterior cingulate (4) are being stimulated. These are some of the same circuits that are activated when a hungry person eats, when an aroused person has sex or when a drug addict snorts cocaine. If you find a song pleasant, activity in the amygdala (5) is inhibited. This part of the brain is typically associated with negative emotion, such as fear.

Go chills up your spine singing the national anthem? Find your feet start to move when you hear ABBA's "Dancing Queen"? Does your heart stumble when you hear your favourite love song? Everyone can name a tune or two that stir their souls. While personal experiences shape musical tastes, scientists are discovering that we all use the same basic brain circuits to process music.

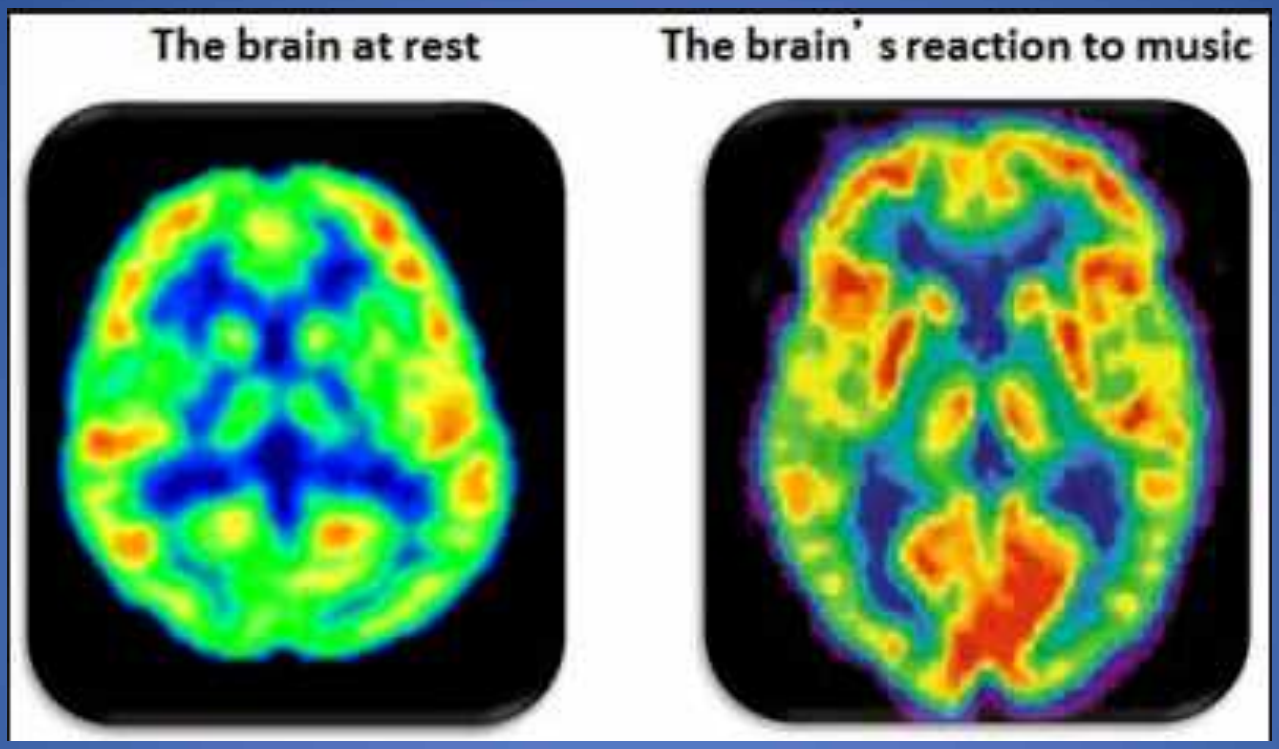
"Everyone responds to music," says Robert Zatorre, a neuroscientist at the Montreal Neurological Institute of McGill University who studies music's impact on the brain. "So there must be something in our brains that predisposes us to it."

Using MRI (magnetic resonance imaging) and PET (positron emission tomography), scientists have mapped the brain activity of volunteers listening to or playing music and have found that the brain essentially performs like an orchestra. Each instrument in an orchestra has a unique function, but when heard in isolation, we would hear less meaning. Conversely, if you could see an orchestra's full sound, the role of each instrument is difficult to isolate and decipher. "The brain is not a mosaic of independent little sections," says Zatorre. "It is the ensemble activity that yields overall patterns."

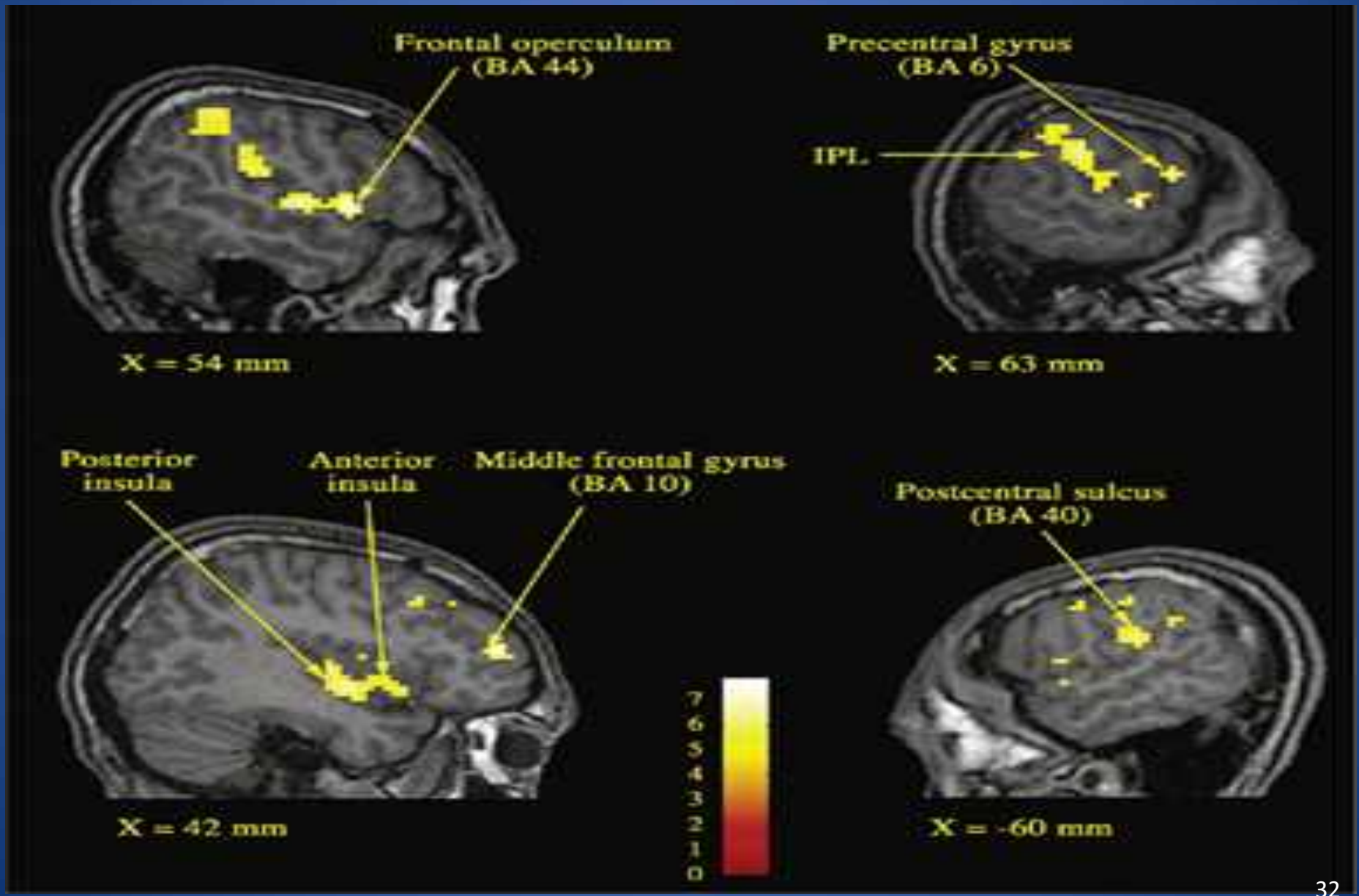
This research is helping us reveal the root of musical dysfunction and the brain's adaptation to playing music. About one in a hundred musicians suffer from a focal dystonia, for example, where one fingers begin to move together as if joined. In violinists, the portion of the motor cortex that controls the four fingers of the left hand, which do most of the work, seems to be enlarged. This adaptation helps the violinist play better, but scientists have found that too much practice can eventually lead to confused signals in the brain. As a result, the musician can no longer move the two digits independently.

But playing the complex neural interactions that occur in a brain under the influence of music has an even broader goal. It paves the way for understanding in areas of brain disorders. "To solve diseases such as Alzheimer's, we need to achieve a good understanding of the entire system," says Zatorre. "It's an exciting avenue, because it involves almost every brain system that is known to exist."

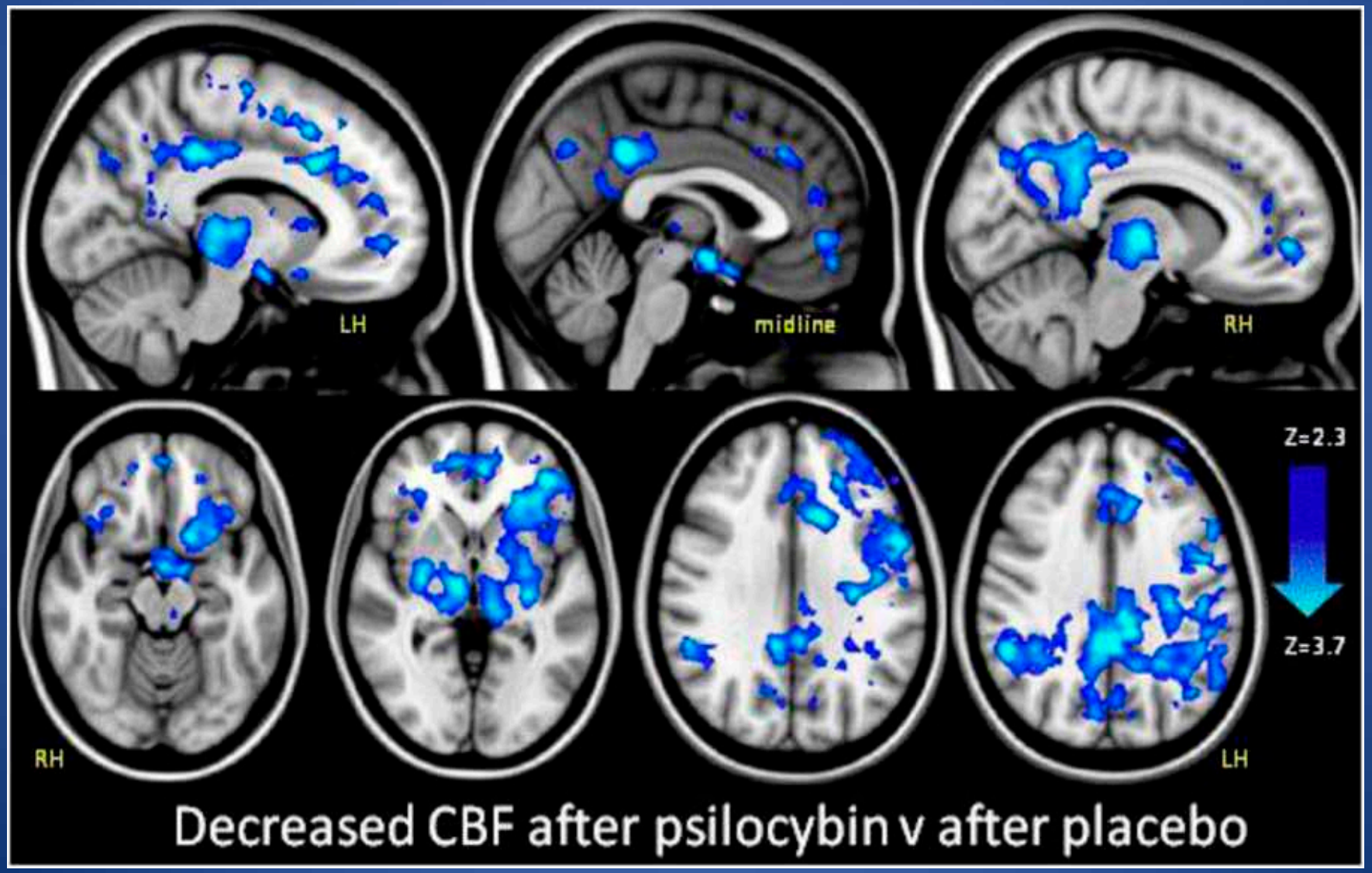
Your Brain on Music



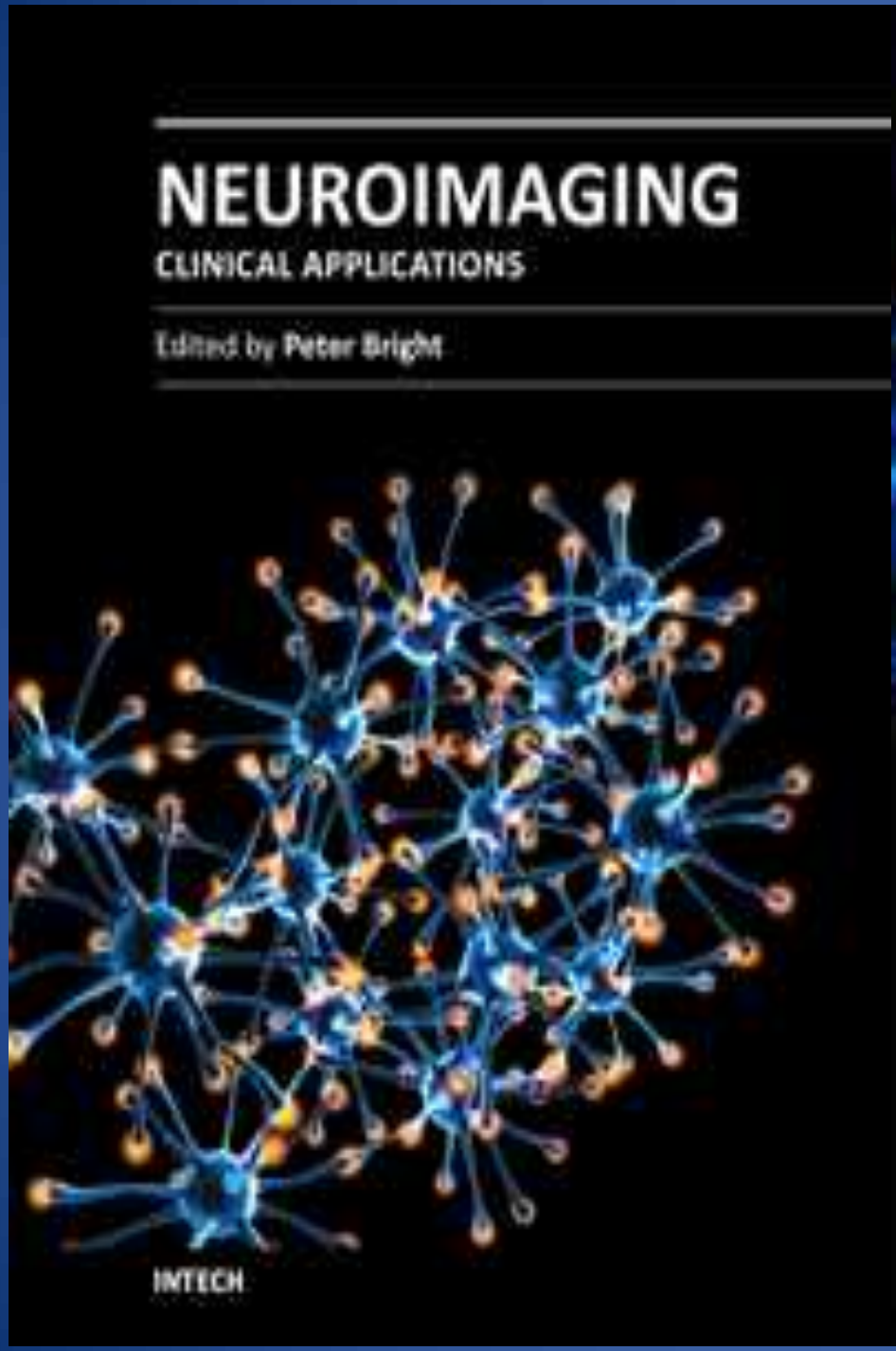
Sex Addiction



fMRI Scans Reveals How "Magic Mushrooms" Inflict Psychedelic Effect On The Brain




THE BRAIN INITIATIVE
BRAININITIATIVE.ORG


NEUROIMAGING
CLINICAL APPLICATIONS
Edited by Peter Bright
INTECH


BRAIN
CONNECTIVITY

BRAIN INITIATIVE TIMELINE

2013:
- Obama announces BRAIN Initiative.
- NIH, NSF, and DARPA commit $100M for 2014.

2014:
- FDA and IARPA join.
- Initiative establishes long-term vision and research priorities.

2016 – 2020:
- $400M per year funding period dedicated to the development of new tools and technologies

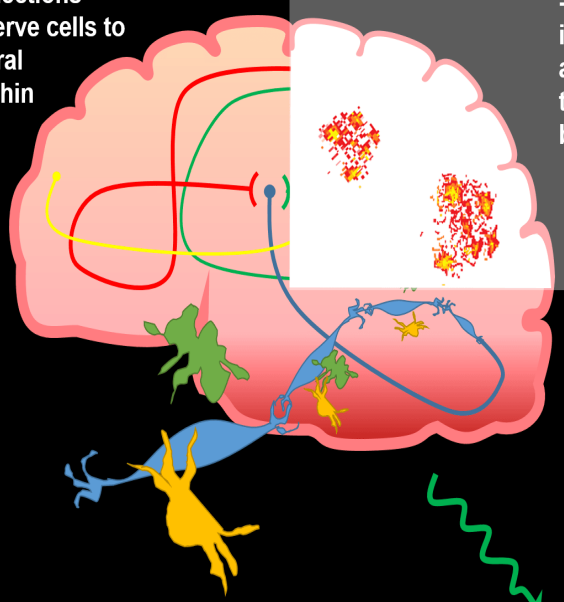
2021 – 2025:
- $500M per year funding period for application of new tools to study of the brain

RESEARCH PRIORITY AREAS

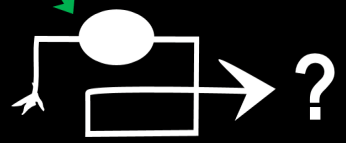
1) Brain Cell Types
- Identify the many different cells that comprise the brain and determine their functions

2) Tools for Circuit Diagrams
- Map connections between nerve cells to define neural circuits within the brain

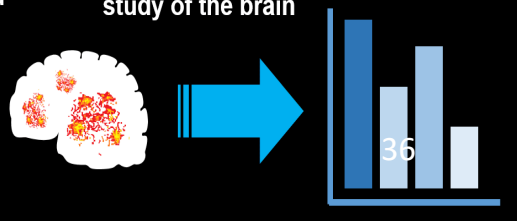
3) Technology to Monitor Neural Activity
- Monitor activity of individual nerve cells and neural circuits over the breadth of the entire brain simultaneously



4) Precise Interventional Tools
- Determine the role of different neural circuits in behavior by targeted manipulation



5) Theory and Data Analysis Tools
- Develop new methods to work with data acquired during study of the brain



6) Human Neuroscience
- Study the human brain and work toward treatments for disorders

7) Integrated Approaches
- Combine the tools and findings of other priority areas for a comprehensive understanding of brain function

FEDERAL PARTNERS

NIH — Development of new tools and techniques

NSF — Fundamental biology and technology development

DARPA — Rehabilitation of warfighters and civilians

FDA — Regulation of neurological medical devices

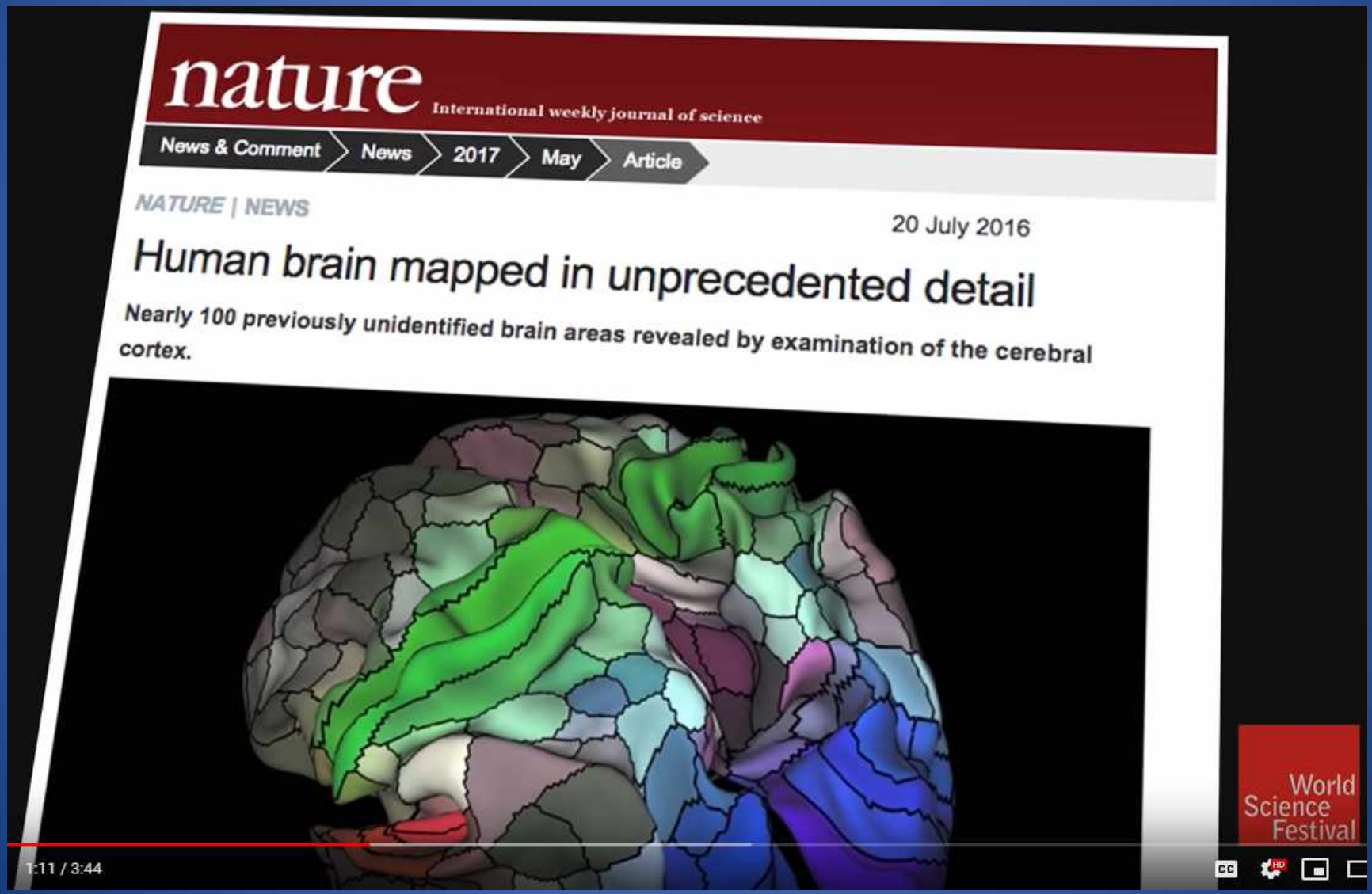
IARPA — Cognition and computation in the brain

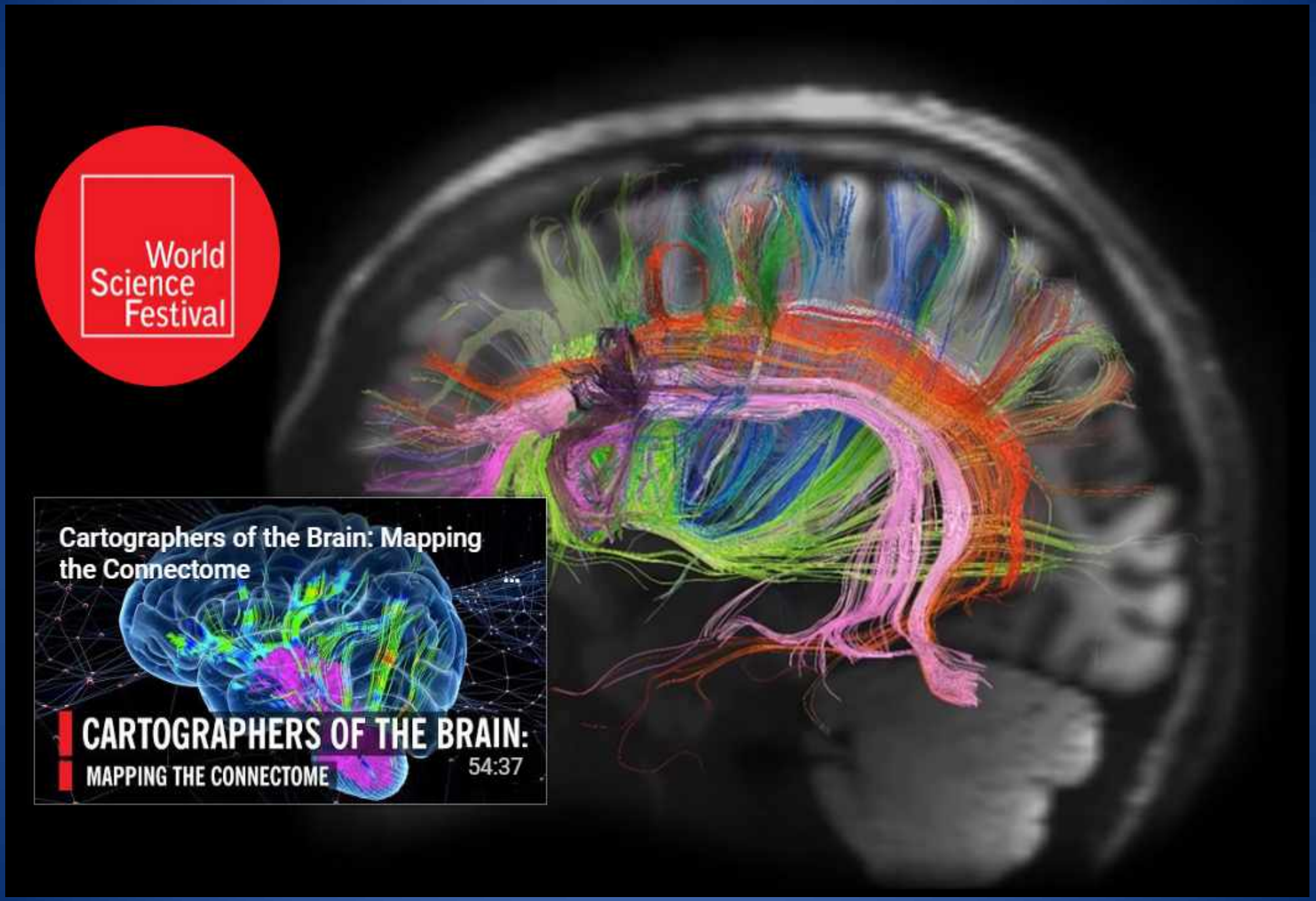
Decade of the Mind

- **Success will require research that reaches across disparate fields such as:**
  - **Cognitive science**
  - **Medicine neuroscience**
  - **Psychology,**
  - **Mathematics**
  - **Engineering,**
  - **Neurotechnology**
  - **Computer science**

  Additional important insights will need to come from areas as diverse as :
  - **Systems biology,**
  - **Cultural anthropology**
  - **Social science**
  - **Robotics**
  - **Automation technology**

The Human Connectome Project HCP




World Science Festival
Cartographers of the Brain: Mapping the Connectome
CARTOGRAPHERS OF THE BRAIN:
MAPPING THE CONNECTOME
54:37

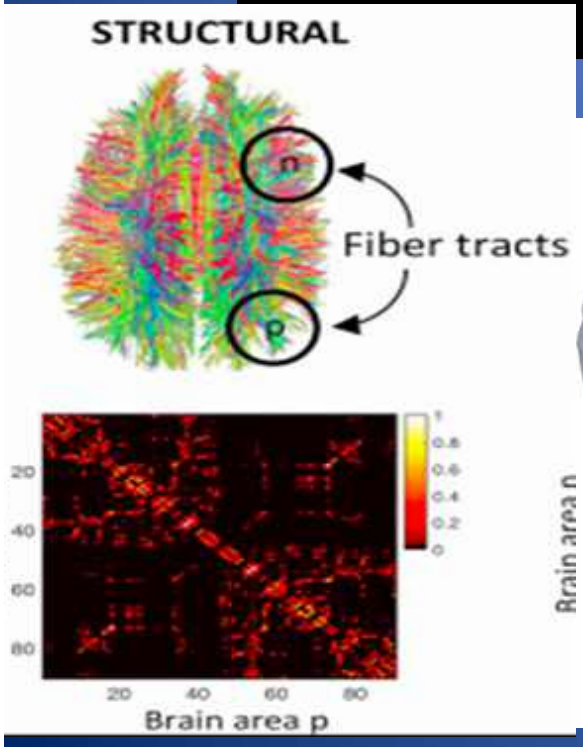
The Human Connectome Project HCP

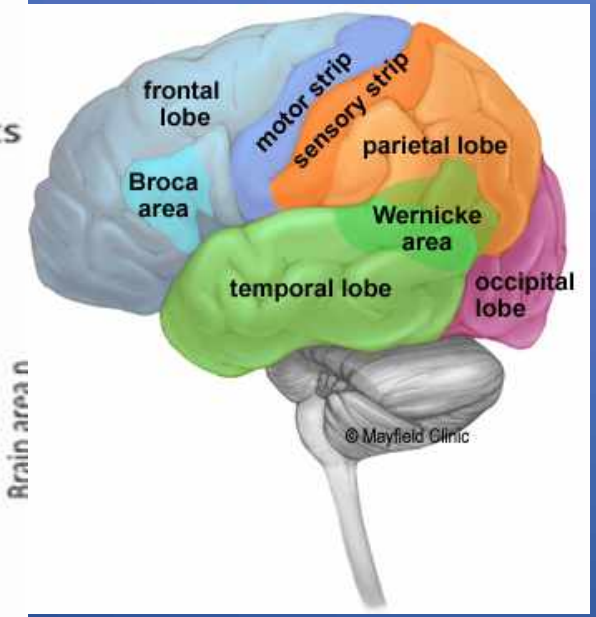
brain imaging techniques

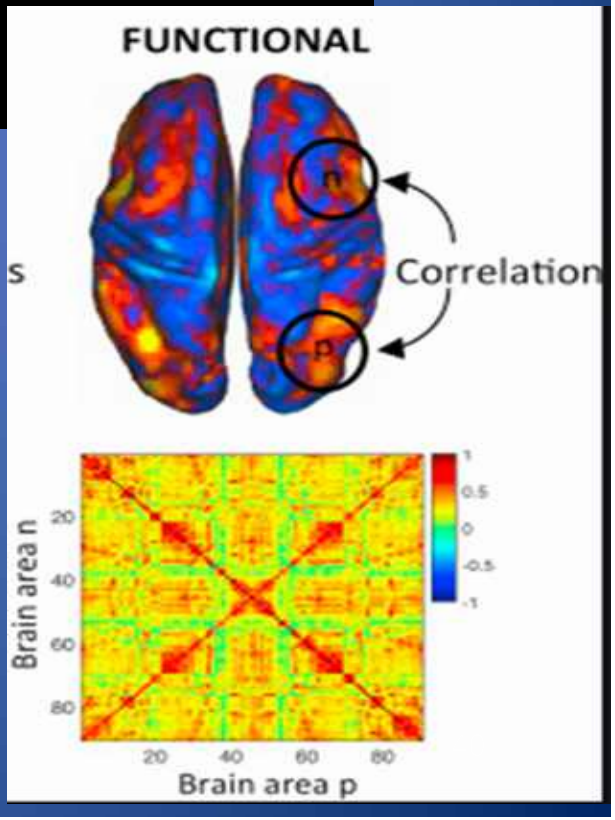
structural vs. functional

CT
MRI

PET
fMRI

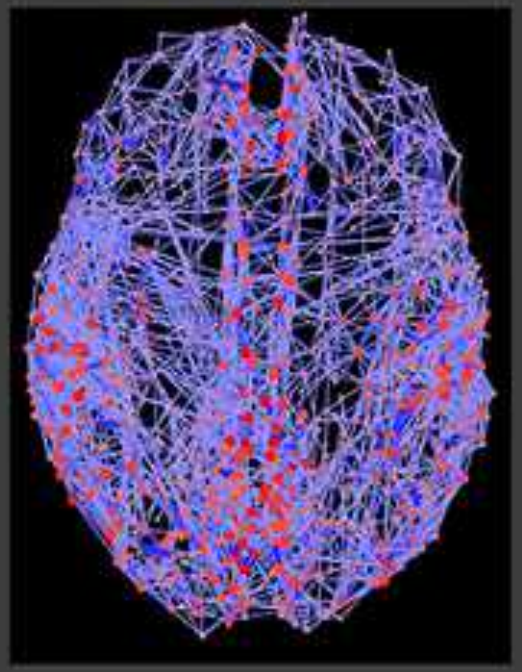






The Human Connectome

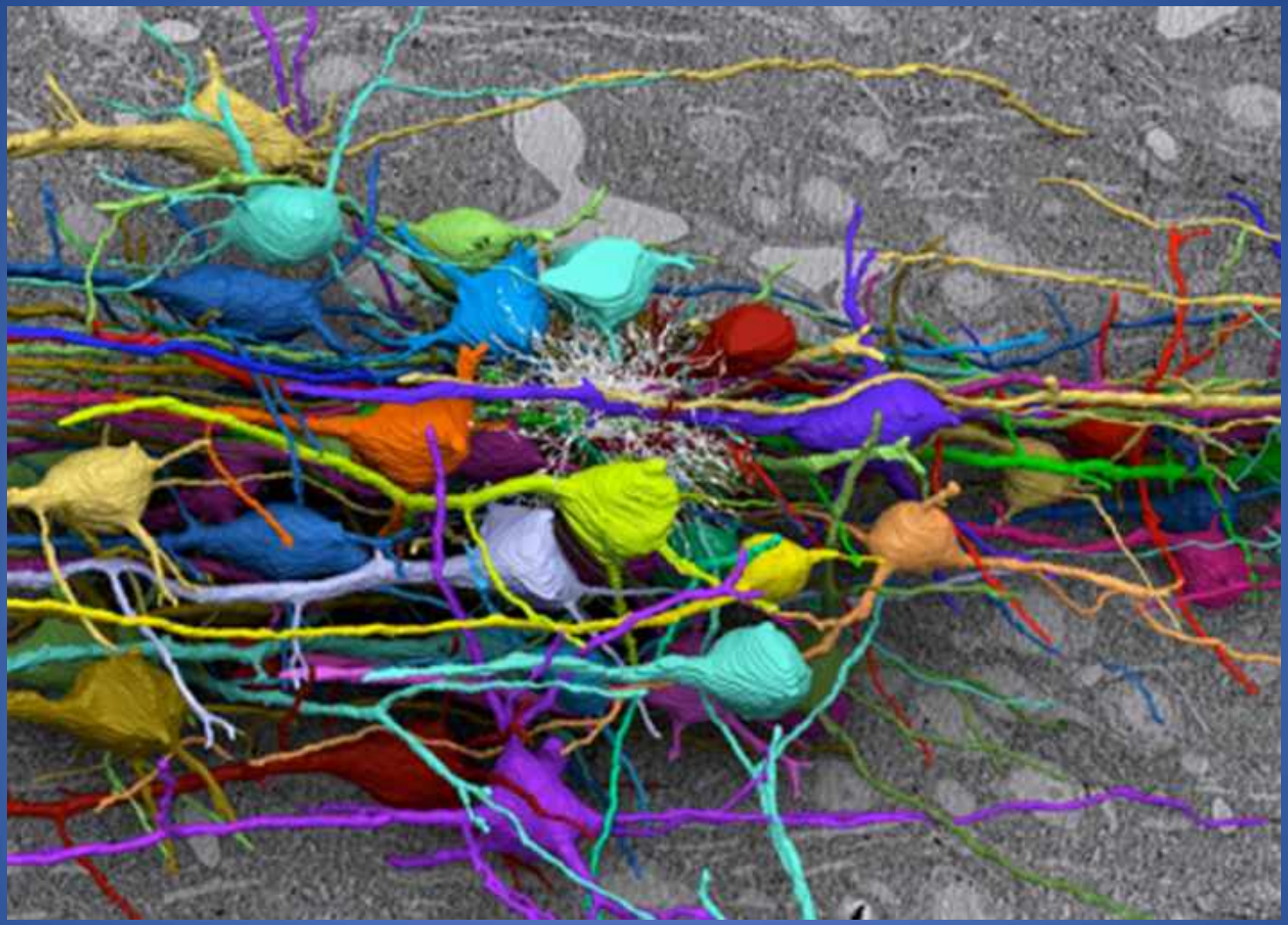
Anatomy
Klingler's method for fiber tract dissection uses freezing of brain matter to spread nerve fibers apart. Afterwards, tissue is carefully scratched away to reveal a relief-like surface in which the desired nerve tracts are naturally surrounded by their anatomical brain areas.



Connectome
Shown are the connections of brain regions together with "hubs" that connect signals among different brain areas and a central "core" or backbone of connections, which relays commands for our thoughts and behaviors.

Neuronal Pathways
A new MRI technique called diffusion spectrum imaging (DSI) analyzes how water molecules move along nerve fibers. DSI can show a brain's major neuron pathways and will help neurologists relate structure to function.

Connectome Computation

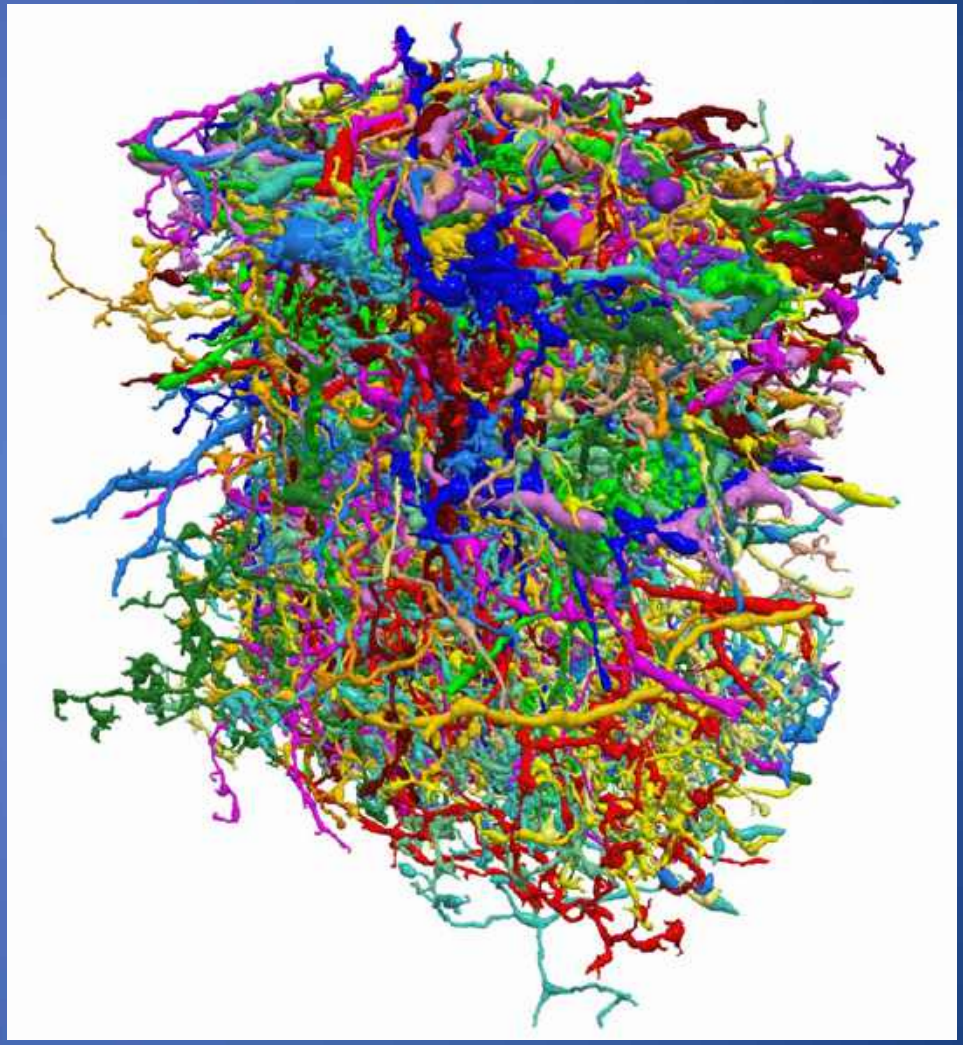


Connectome Computation

How a Fly Brain Detects Motion - MIT Technology Review

A reconstruction of 379 neurons involved in motion detection in the fruit fly.

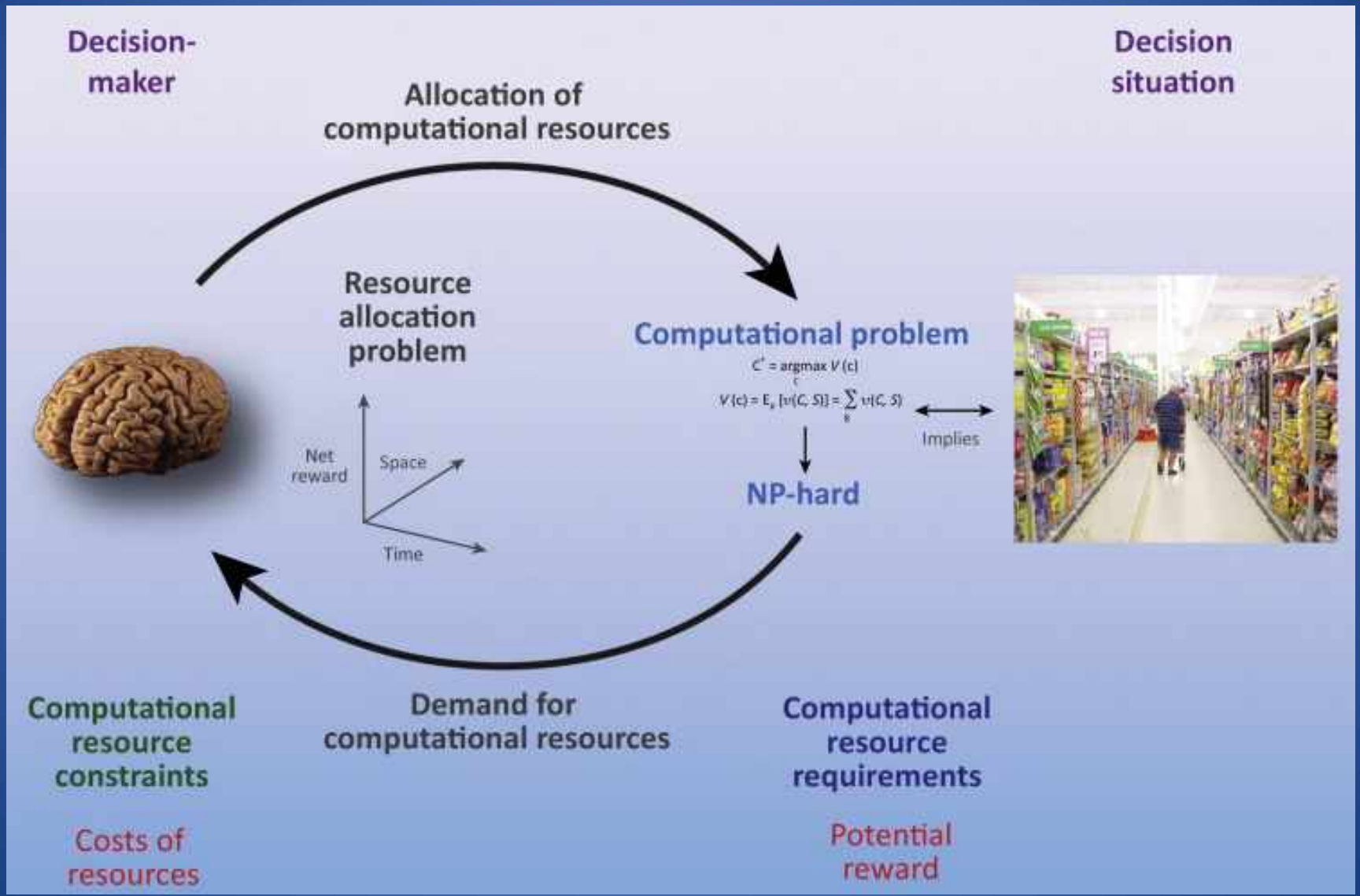
By mapping the brain structure in such detail, the researchers gained new insight into how the brain detects movement. Their work is the latest example of many ongoing efforts in neuroscience to understand how the brain functions by building intricate diagrams of neuronal connections, or connectomes



Computational Analaysis
(Modeling and Predicting Human Behavior)

Computational Complexity and Human Decision-Making

Trends in Cognitive Neuroscience



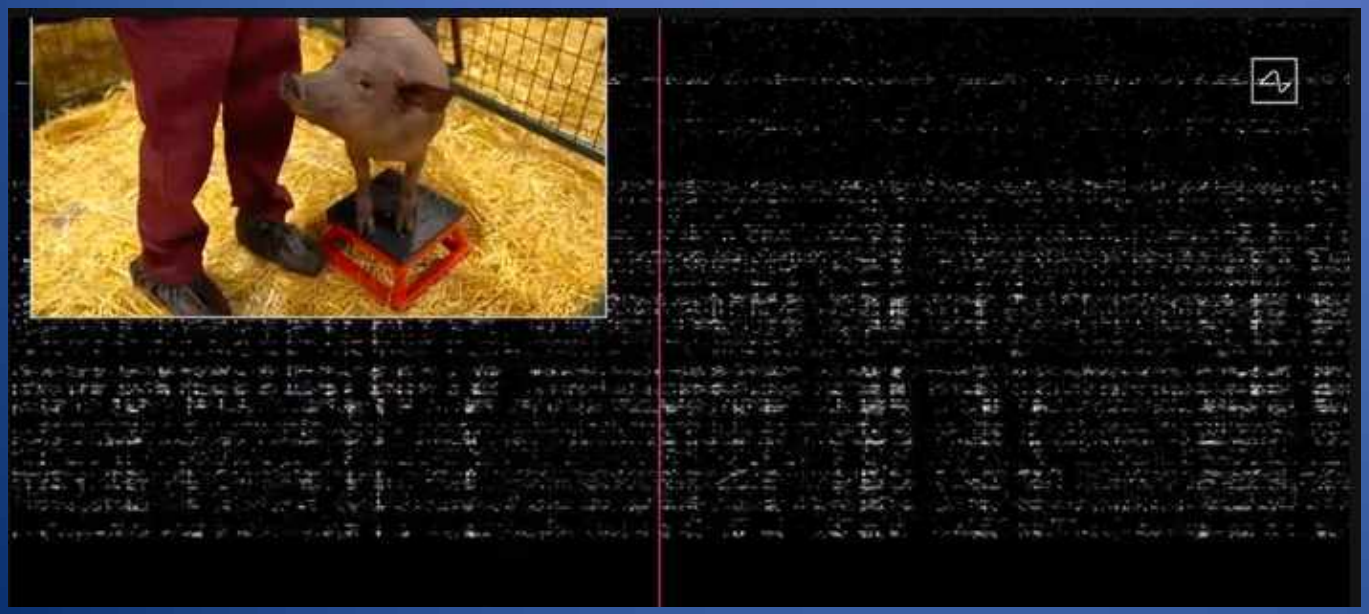
Peter Bossaerts , Carsten Murawski

OPINION| VOLUME 21, ISSUE 12, P917-929, DECEMBER 01, 2017

Elon Musk – Neuralink

The entrepreneur and Tesla founder unveiled the new design of the chip, as well as the full-scale surgical robot and a group of pig test subjects.

Elon Musk unveils updated Neuralink brain implant design and surgical robot



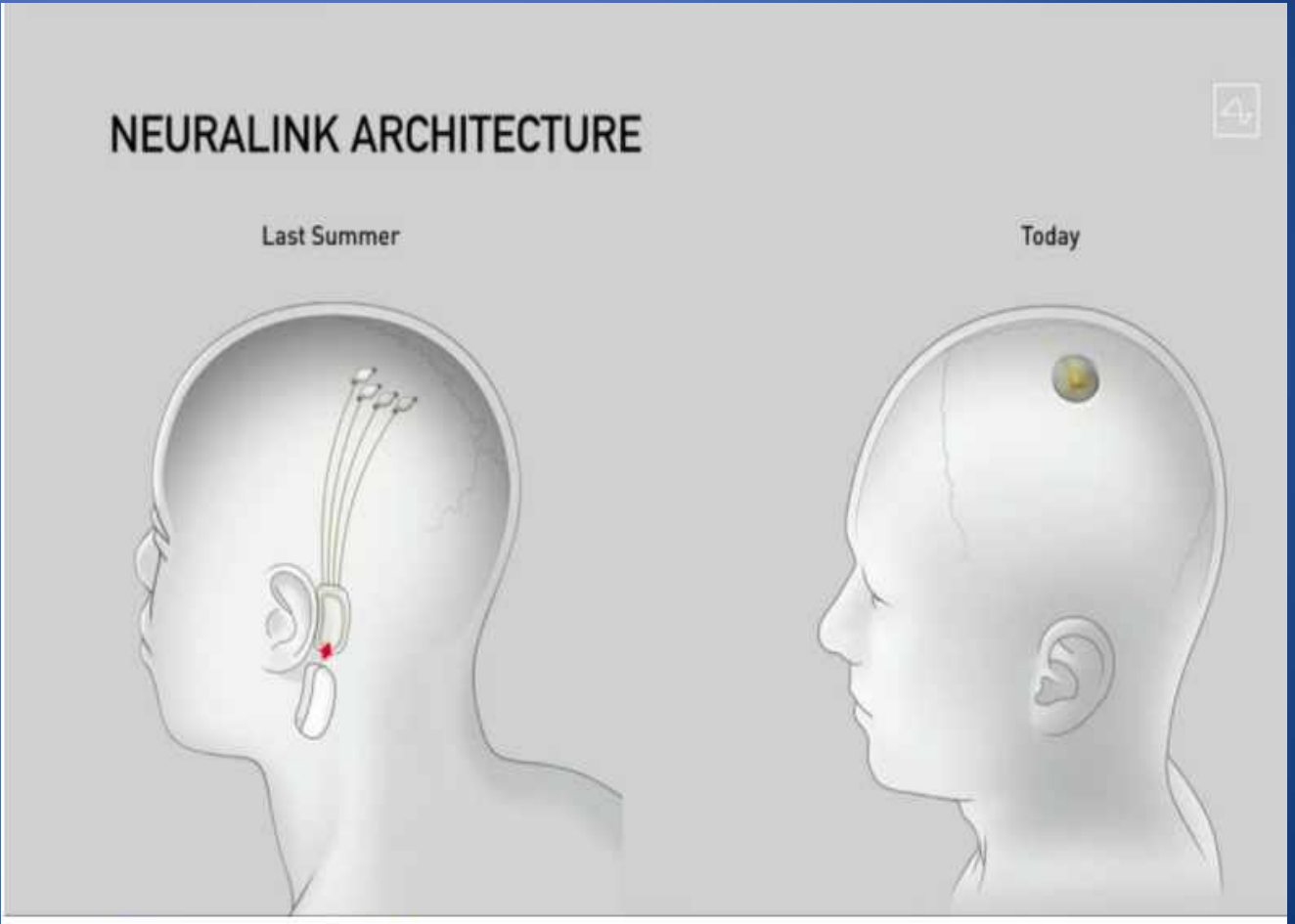
The robot pictured above has neuro-surgically inserted the chip into several pigs.

Visual to your left shows tiny EEG readings of real time activity in the brain.

Neuralink received a Breakthrough Device Designation from the FDA in July. The startup is now preparing for its first human implantation, pending required approvals and further safety testing.

Elon Musk's neuroscience startup **Neuralink** has revealed the **"dramatically simplified" design** for an implant that aims to create **brain-to-machine interfaces**.

Neuralink is developing to connect human brains with computer interfaces via artificial intelligence.



The Neuralink has been simplified from a device behind the ear to one on top of the skull

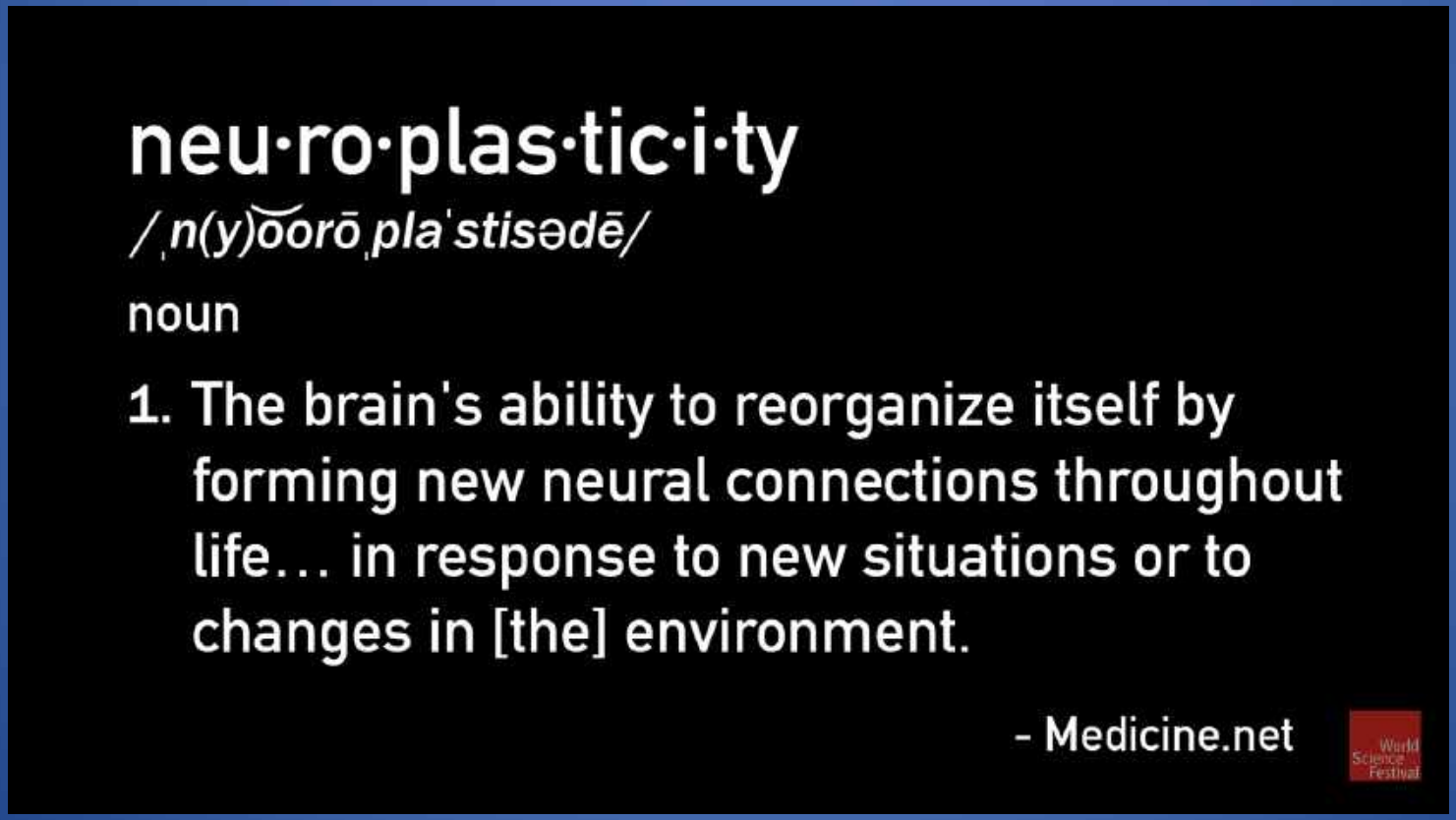
Article Natashah Hitti, 2 September 2020
https://www.dezeen.com/2020/09/02/neuralink-elon-musk-brain-implant-technology/

Elon Musk – Neuralink

- *The coin-sized chip would enable humans to control technology with their mind*
- **"It's kind of like a FitBit in your skull," said Elon Musk.**
- *The surgical robot is designed to be "comforting" for patients*
- *The implant could allegedly solve neurological disorders*
- **Musk also showed a pig that previously had a chip inserted into its brain, but had since been removed, to show that the procedure is reversible without any serious side-effects.**

Mapping Neuroplasticity ?

An astonishing new science called "neuroplasticity" is overthrowing the centuries-old notion that the human brain is immutable. - Norman Doidge, M.D.,
Psychiatrist and Psychoanalyst

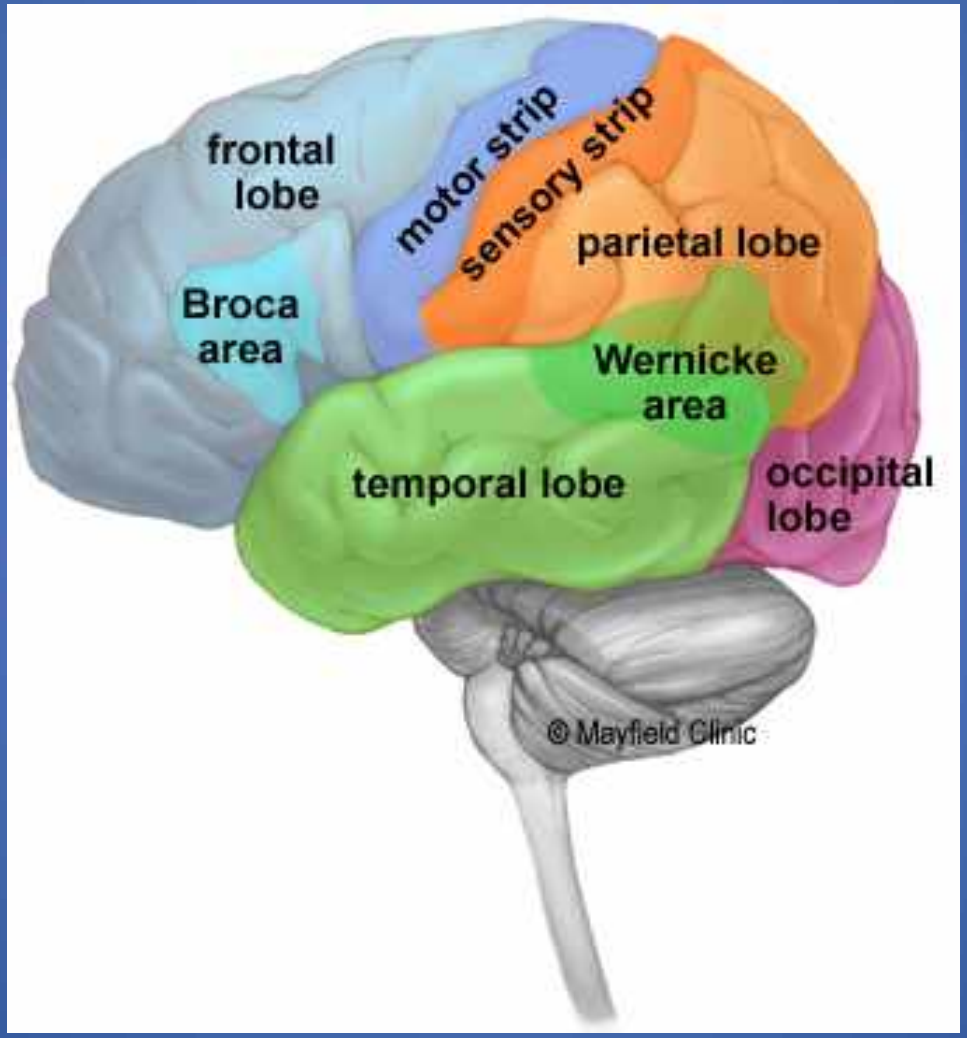


Neuroplasticity

The Backwards Brain Bicycle - Smarter Every Day 133 - YouTube

YouTube · SmarterEvervDav

Neuro-immuno-endo-psychopharmacology



ADHD

DEPRESSION

ANXIETY

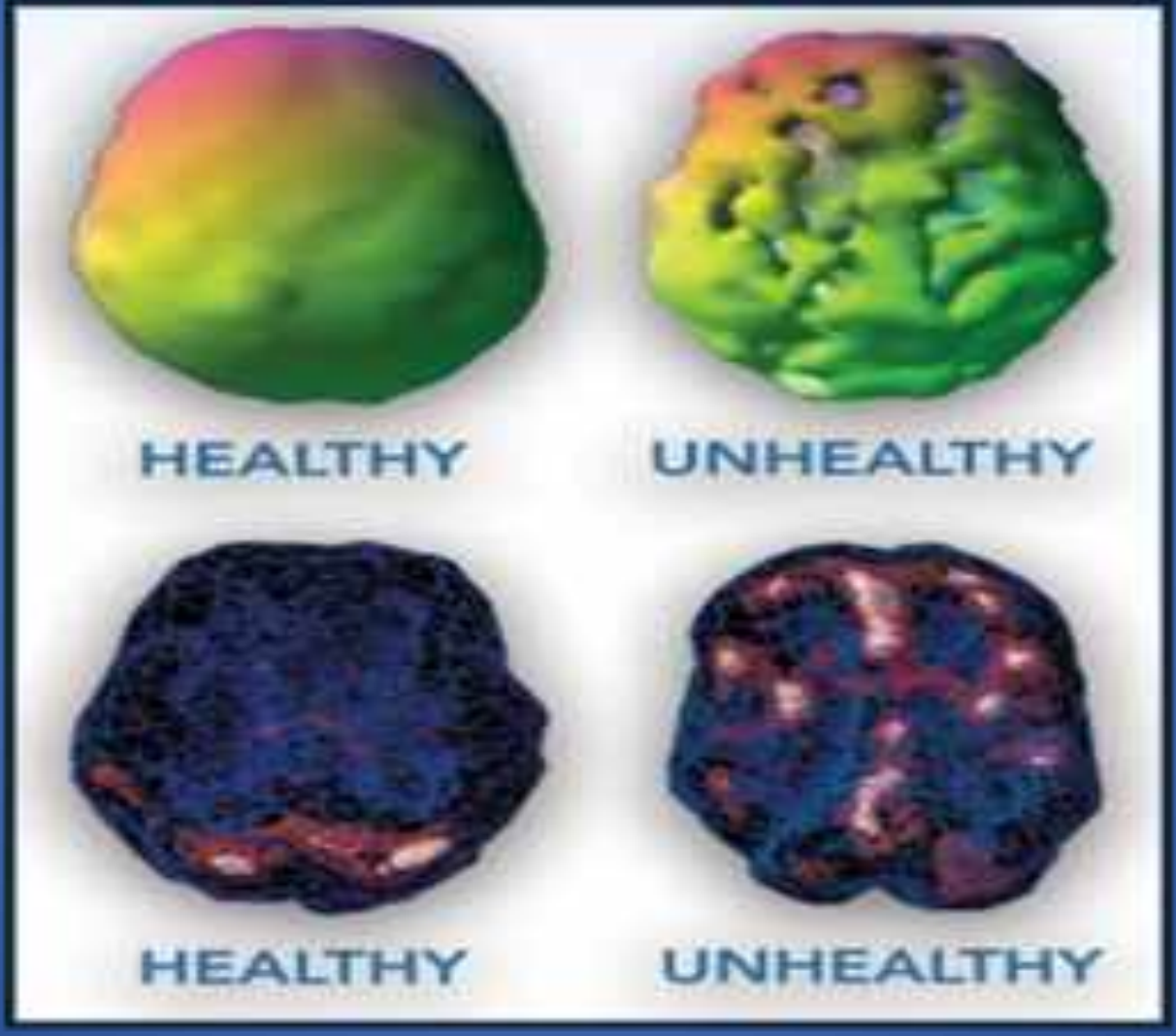
Depression

Anxiety

Panic

Insomnia

How Do You Know, Unless You Look?



S.P.E.C.T.

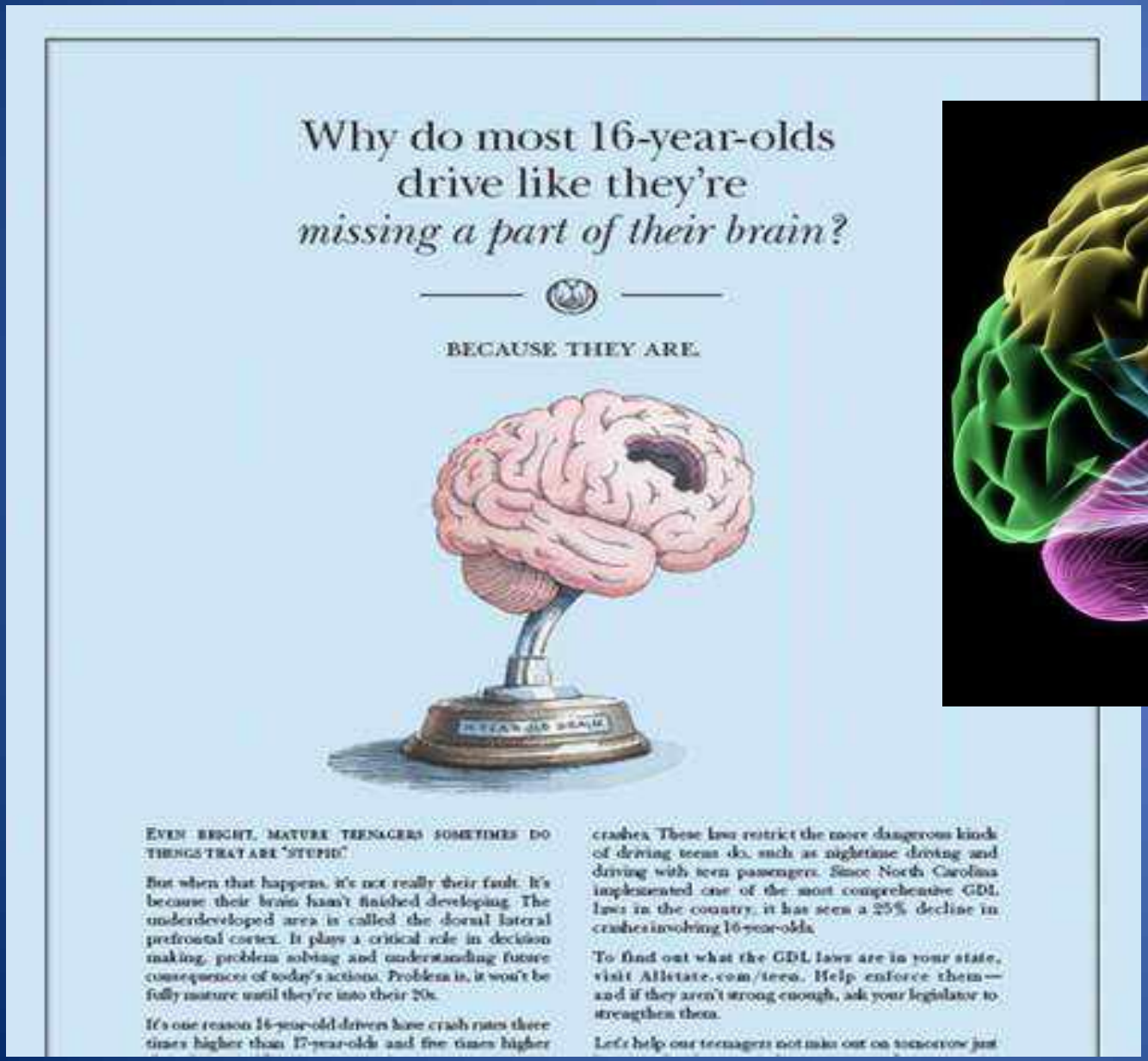
Single-Photon Emission Computer Tomography

AVERAGE SCAN TIME – 15-20 MINUTES

Shiny Eyes


WHICH BRAIN DO YOU WANT?
4 YEARS OF ALCOHOL AGE 21
3 YEARS OF METH AGE 22
2 YEARS OF MARIJUANA AGE 16
HEALTHY, DRUG FREE BRAINS AGE 16
3 YEARS OF COCAINE AGE 22
6 YEARS OF INHALANTS AGE 21
3 YEARS OF SMOKING AGE 16
3-D surface views of the brain, acquired by SPECT imaging, looking at cerebral blood flow and metabolism

The Developing Pre-Frontal Cortex



Why do most 16-year-olds drive like they're *missing a part of their brain?*

BECAUSE THEY ARE.

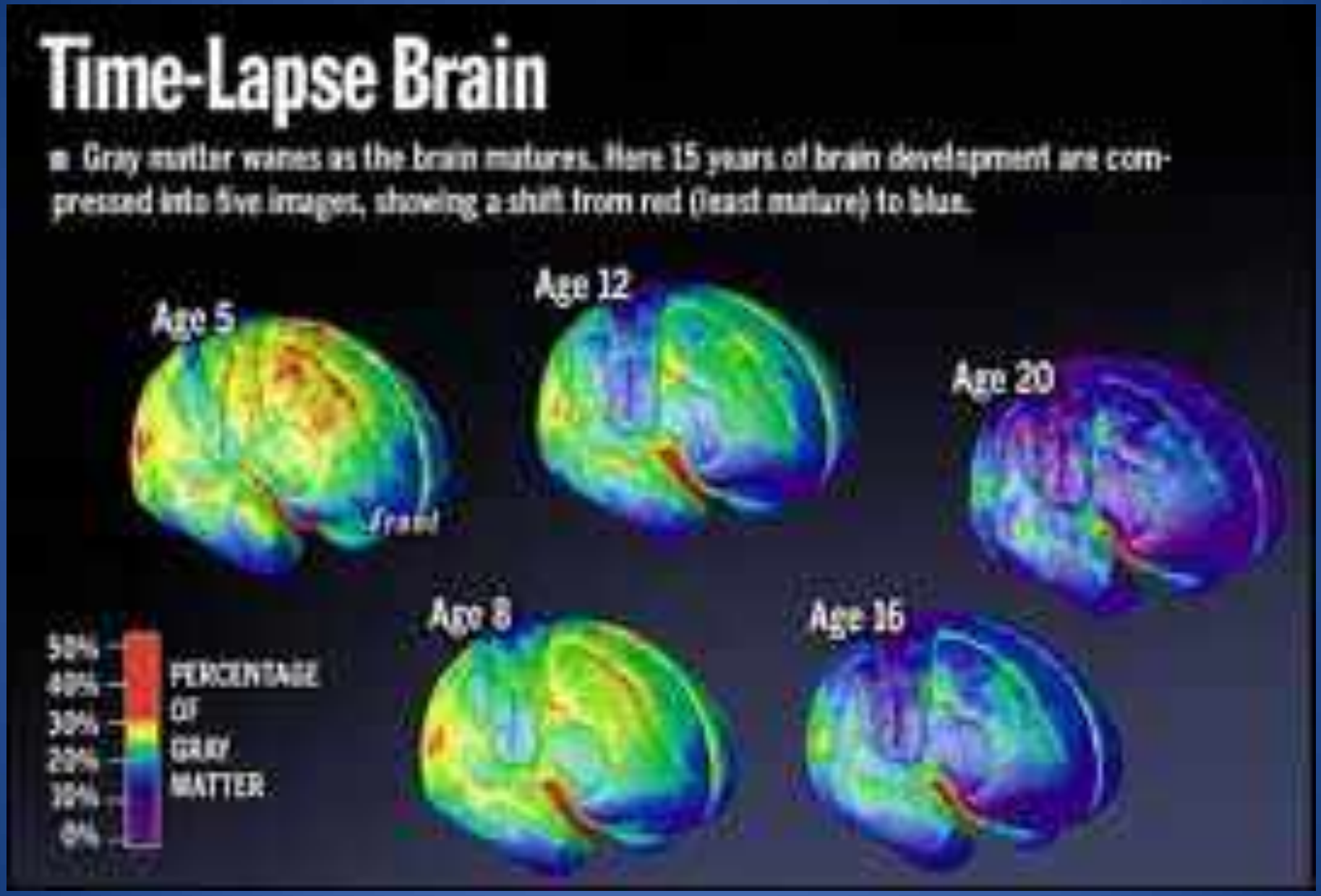
EVEN BRIGHT, MATURE TEENAGERS SOMETIMES DO THINGS THAT ARE "STUPID."

But when that happens, it's not really their fault. It's because their brain hasn't finished developing. The underdeveloped area is called the dorsal lateral prefrontal cortex. It plays a critical role in decision making, problem solving and understanding future consequences of today's actions. Problem is, it won't be fully mature until they're into their 20s.

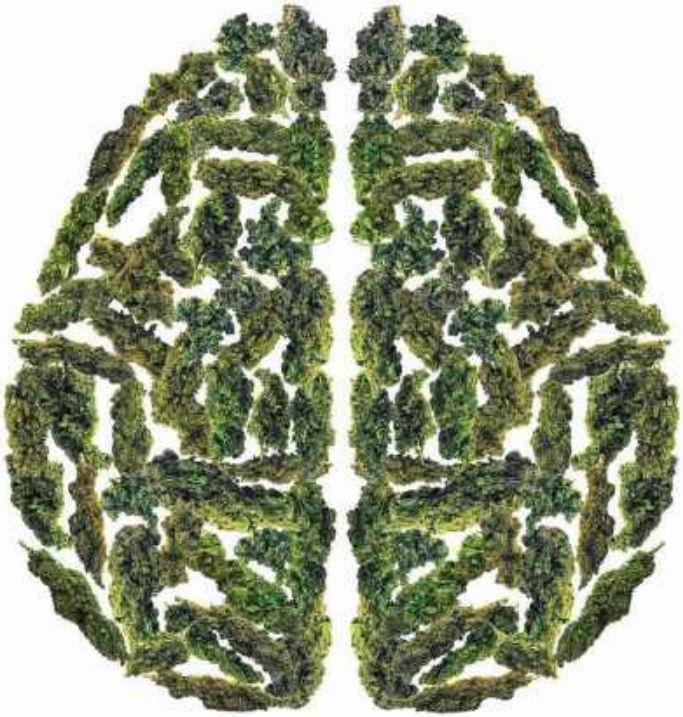
It's one reason 16-year-old drivers have crash rates three times higher than 17-year-olds and five times higher crashes. These laws restrict the more dangerous kinds of driving teens do, such as nighttime driving and driving with teen passengers. Since North Carolina implemented one of the most comprehensive GDL laws in the country, it has seen a 25% decline in crashes involving 16-year-olds.

To find out what the GDL laws are in your state, visit Allstate.com/teen. Help enforce them—and if they aren't strong enough, ask your legislator to strengthen them.

Let's help our teenagers not miss out on tomorrow just

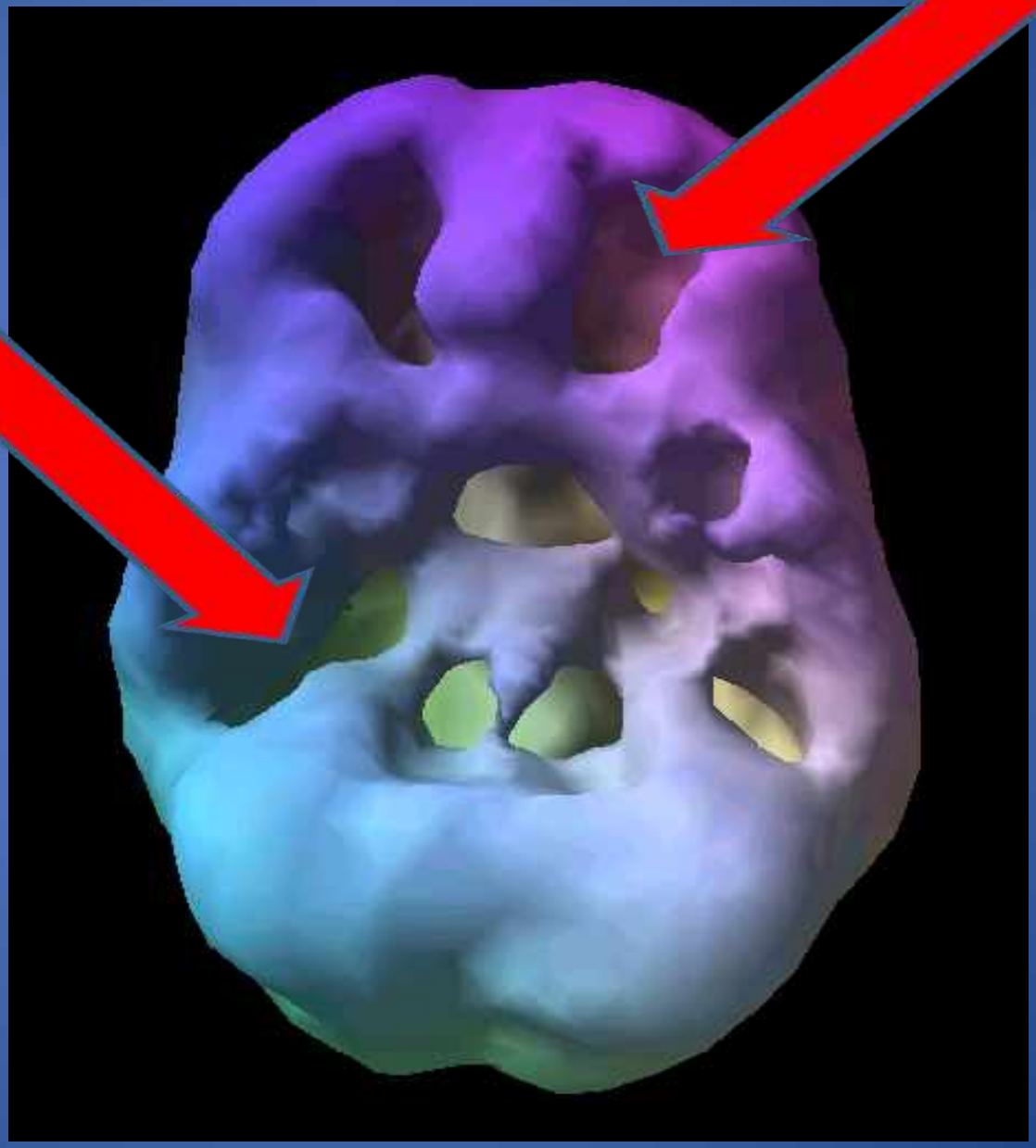

Time-Lapse Brain
Gray matter wanes as the brain matures. Here 15 years of brain development are compressed into five images, showing a shift from red (least mature) to blue.
Age 5
Age 12
Age 20
Age 8
Age 16
Front
50%
40%
30%
20%
10%
0%
PERCENTAGE OF GRAY MATTER

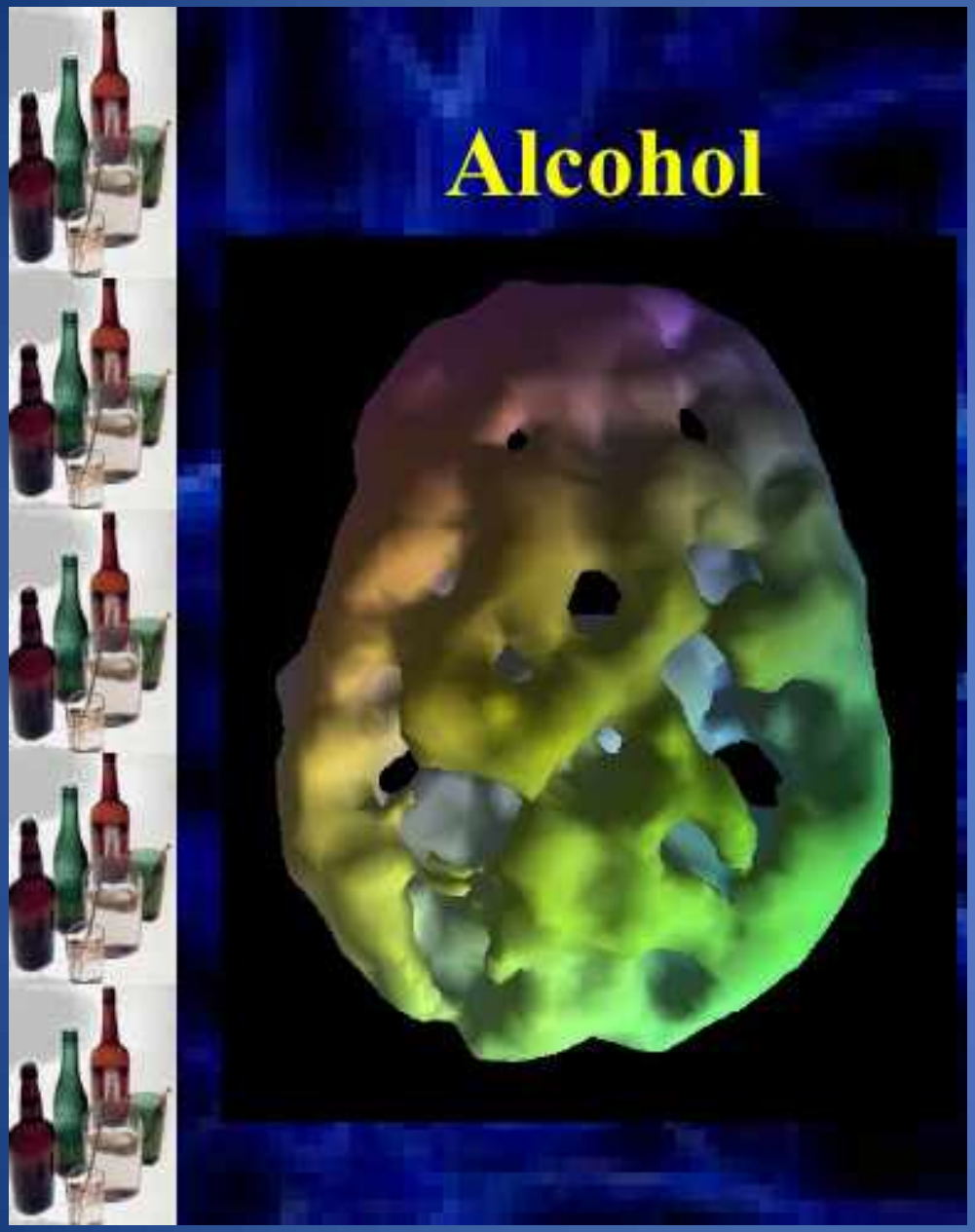
Visual Motivation




shutterstock.com · 102981386

Marijuana




Alcohol


Alcohol


JCT
EAST
LA
308
LA
70
AIRMED


NATIONALLY CERTIFIED
NREMT
PARAMEDIC


TEXAS
DEPARTMENT OF HEALTH
EMT
PARAMEDIC

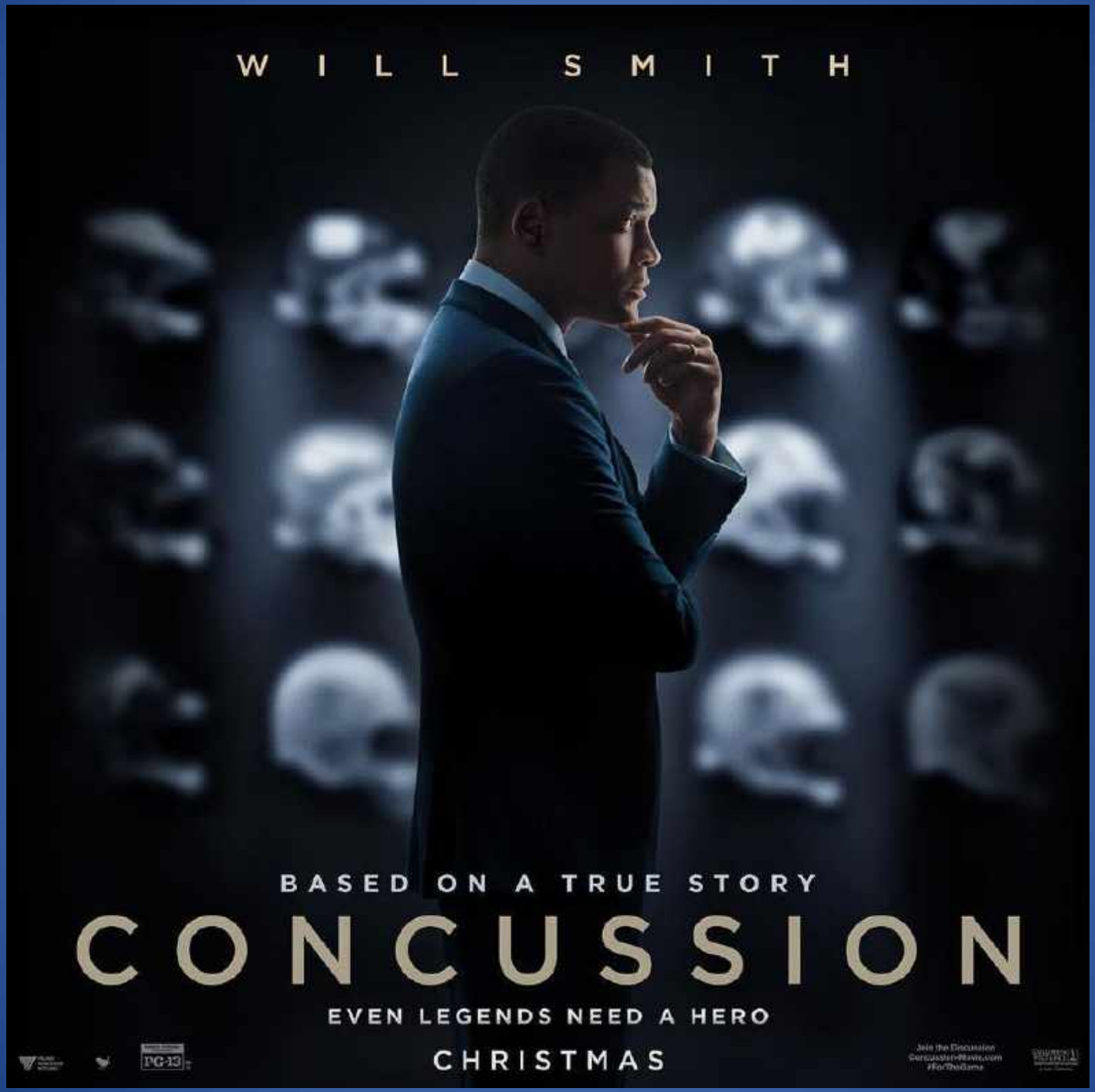
The Young and Impaired Prefrontal Cortex

"Addiction without treatment…is progressive…and can result in disability or premature death."

http://www.asam.org/advocacy/find-a-policy-statement/view-policy-statement/public-policy-statements/2011/12/15/the-definition-of-addiction

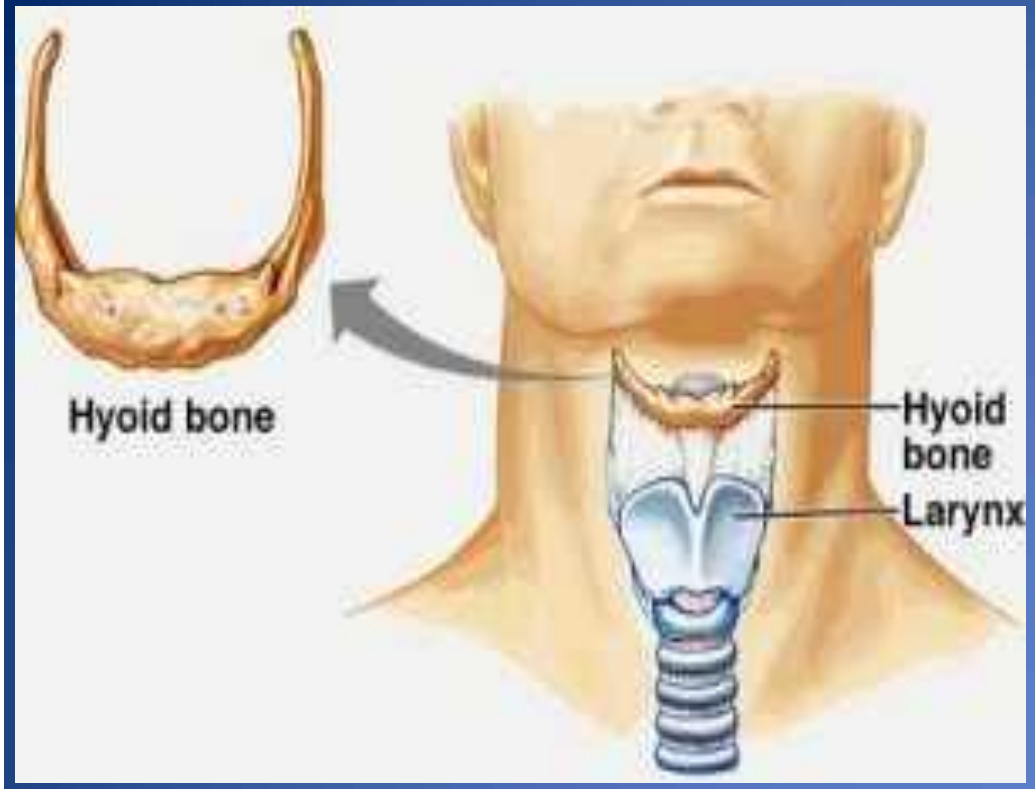
Smoking and Drinking with “Informed Consent”

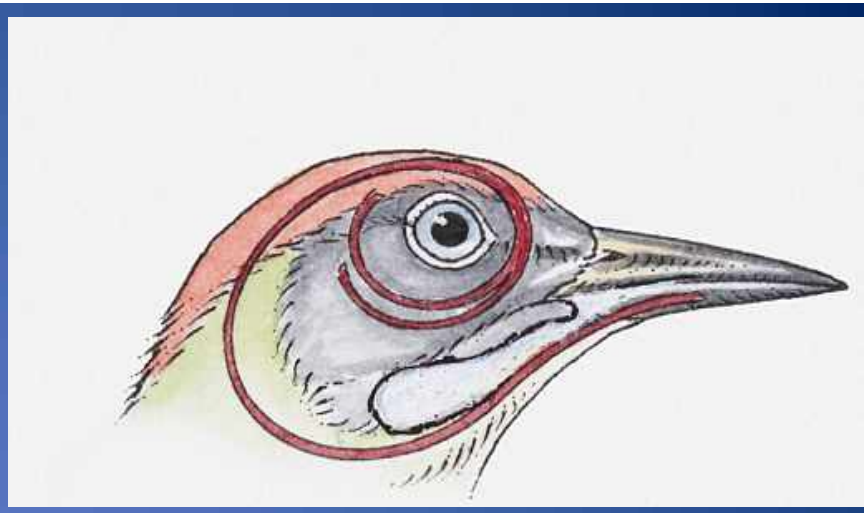
Traumatic Brain Injury and Behavioral Manifestations

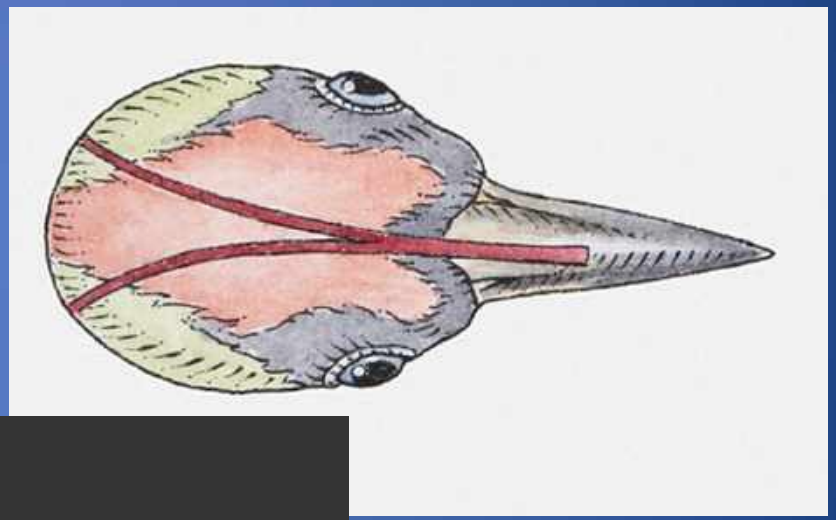

WILL SMITH
BASED ON A TRUE STORY
CONCUSSION
EVEN LEGENDS NEED A HERO
CHRISTMAS
PG-13

Prefrontal Cortex Injuries

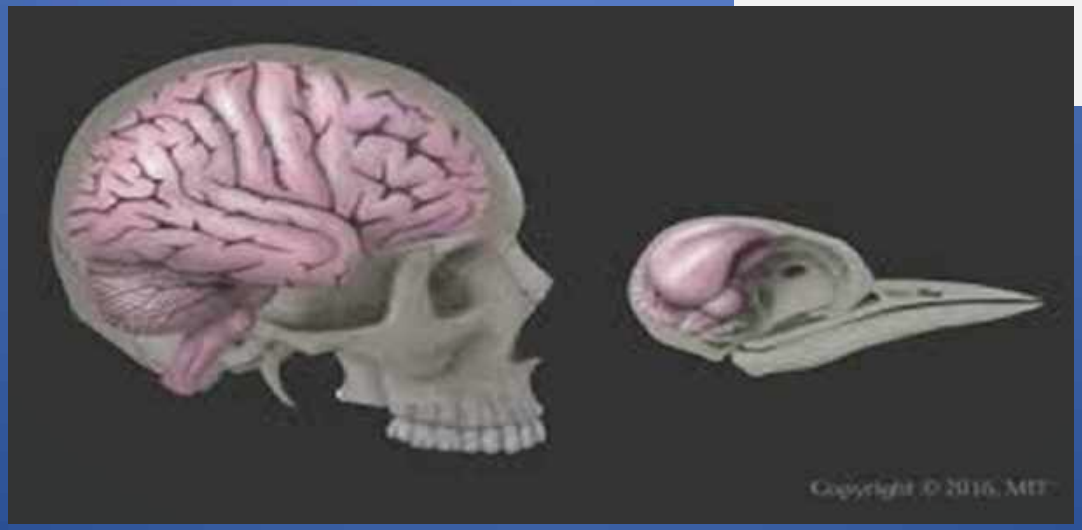
Why Don't Woodpeckers Get Headaches?



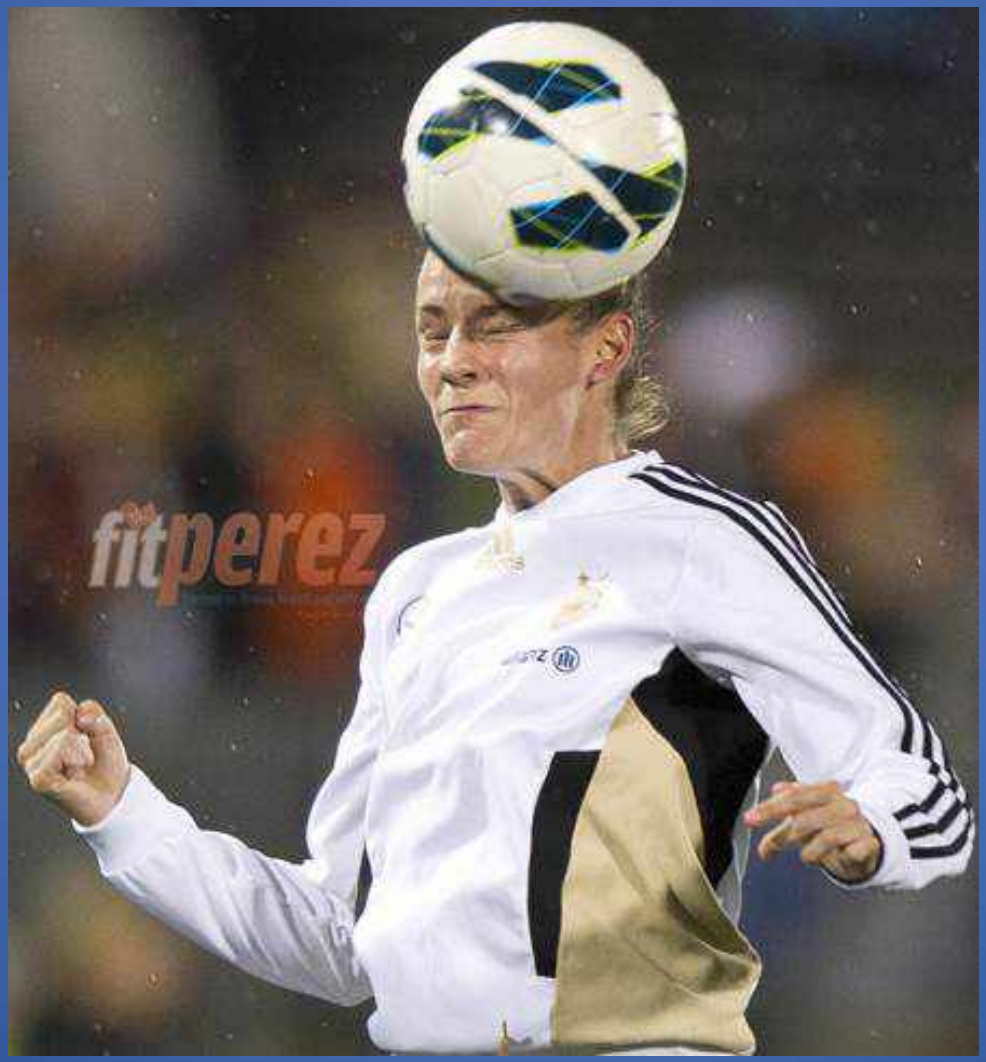




The hyoid bone, located in the bird's cranium, secures and diverts vibrational forces away from the brain.

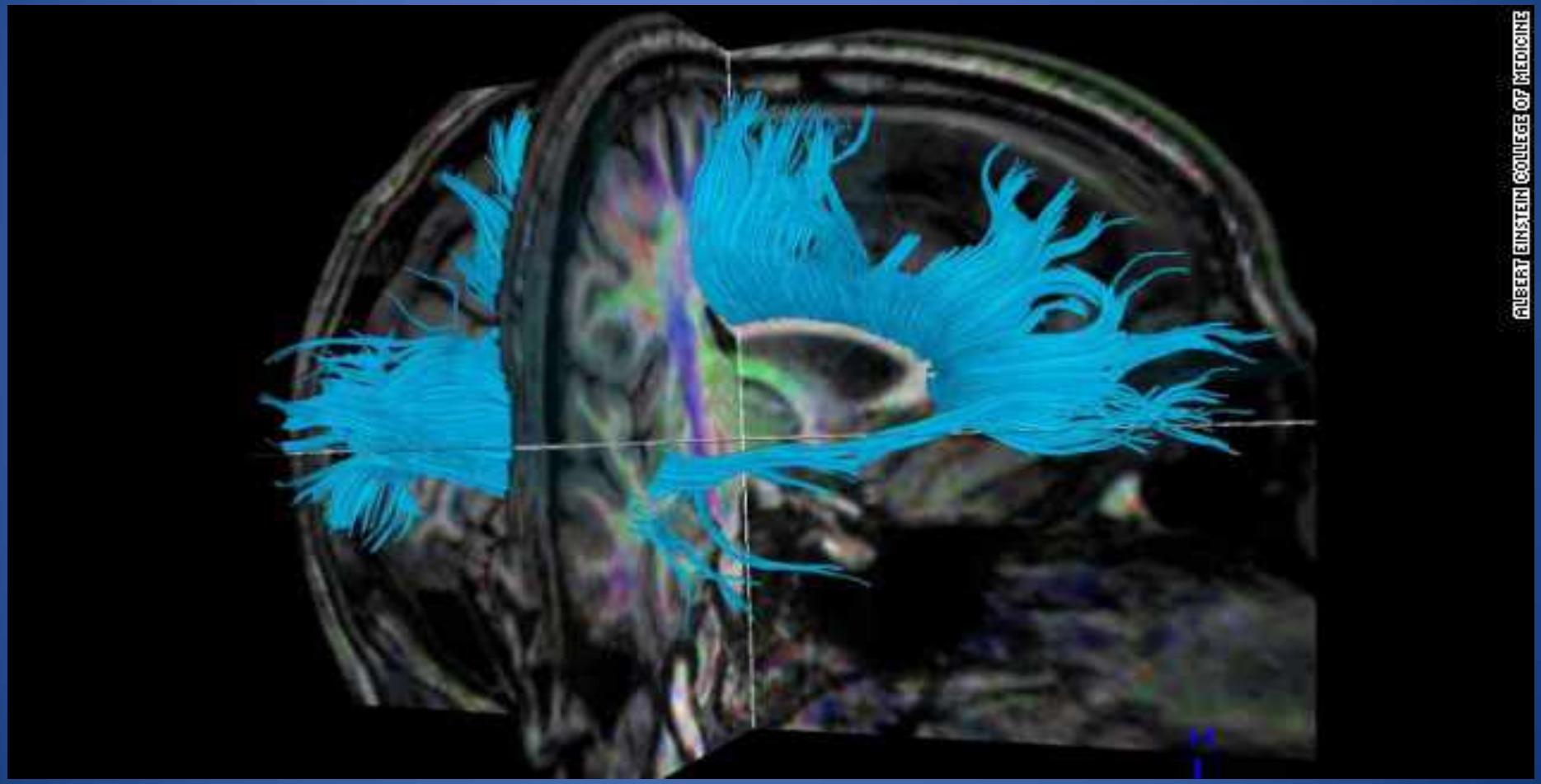


Lipton and colleagues studied 37 young, healthy, amateur soccer players who headed the ball between as few as 32 and as many as 5,400 times during the preceding 10-month season.



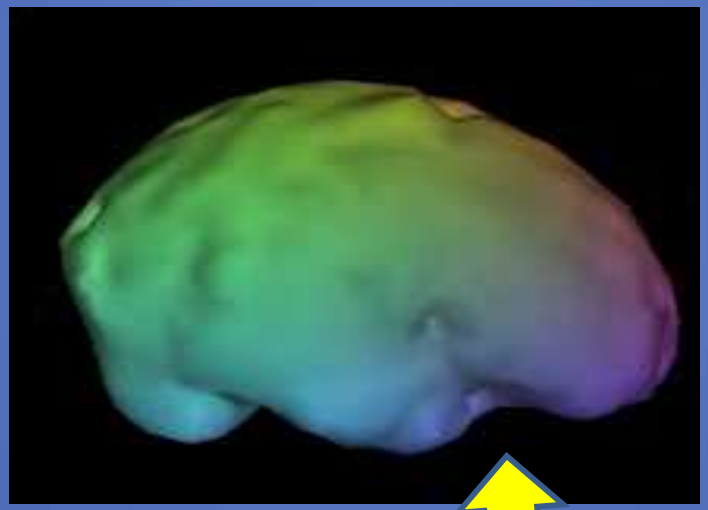
Neuroradiology
Soccer Heading Is Associated with White Matter Microstructural and Cognitive Abnormalities
Michael L. Lipton, MD, PhD, et al September 2013 Volume 268, Issue 3

Repetitive subconcussive head trauma in the setting of heading during soccer may be associated with white matter microstructural and neurocognitive changes similar to those seen in patients with traumatic brain injury.



Neuroradiology
Soccer Heading Is Associated with White Matter Microstructural and Cognitive Abnormalities
Michael L. Lipton, MD, PhD, et al September 2013 Volume 268, Issue 3

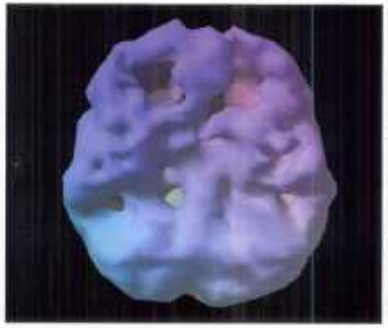
Injury Location and Behavior



ADD / ADHD

Rest, Concentration & Concentration with Medication

undersurface view, rest
mild decrease prefrontal area



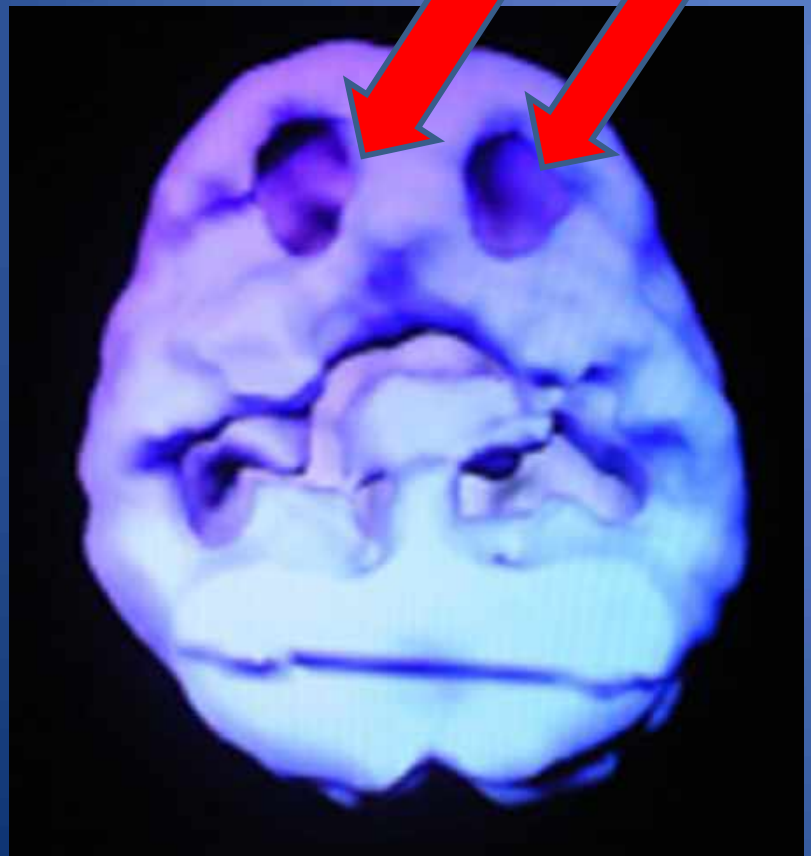
undersurface view, concentration
marked decrease prefrontal cortexand left temporal lobe

undersurface view, w/Adderall
overall marked improved activity

Pre Frontal Cortex (PFC)

Executive Function
Decision Making
Impulse Control
ADHD/ADD

NE, Dopamine, PEA
Caffeine, Nicotine



- **Procrastination**
- **Picking a Fight**

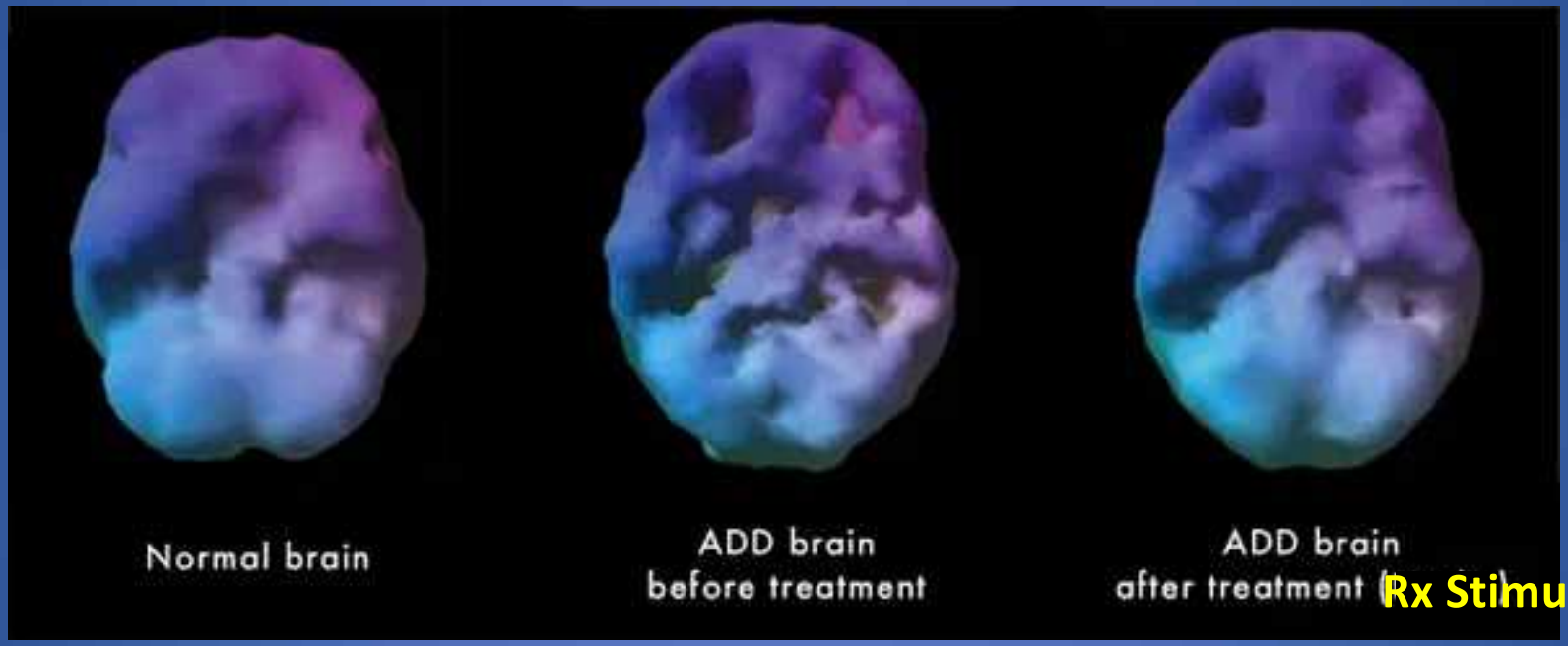
Treatment Considerations

Traditional:

- **Stimilants**

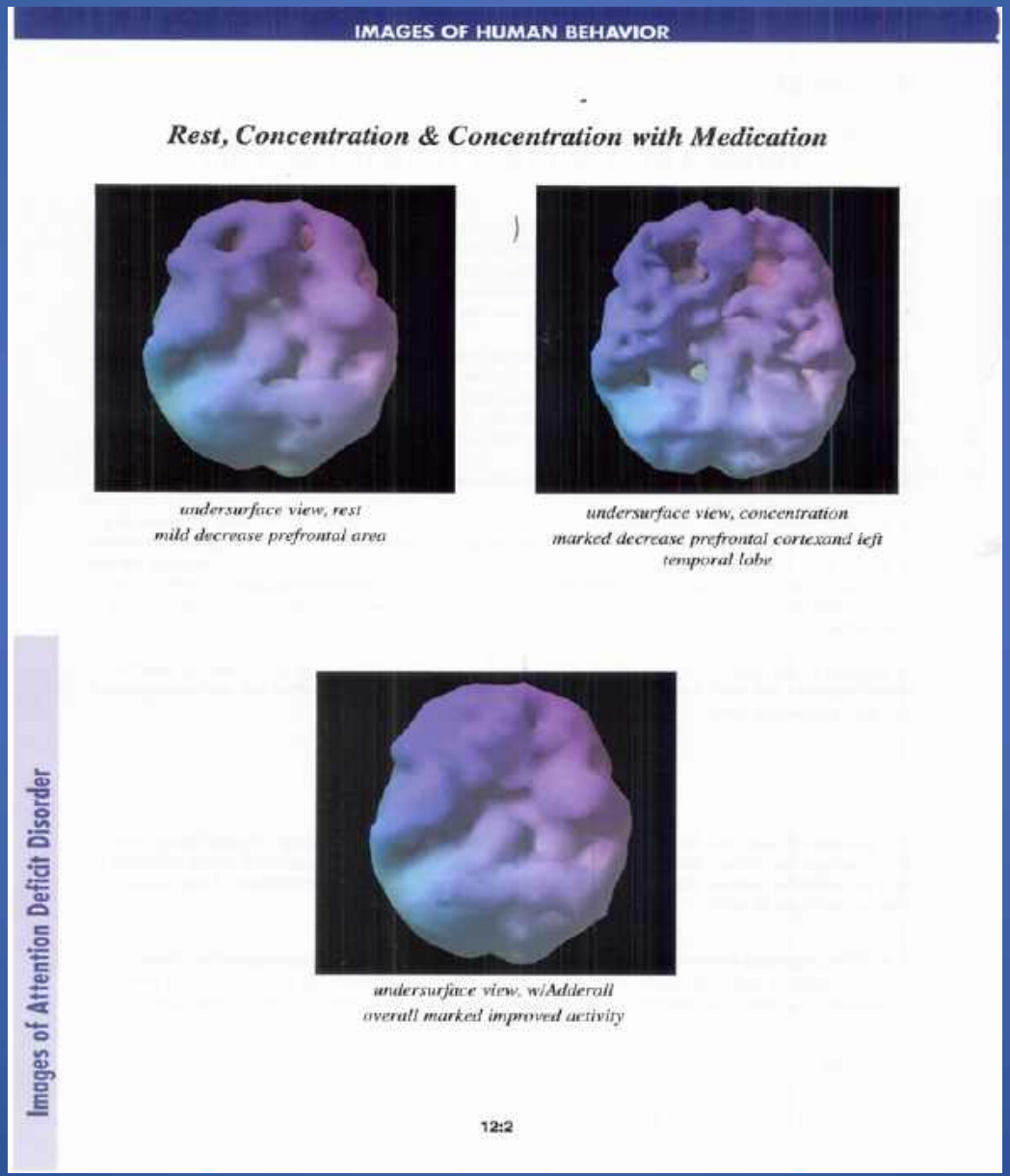
Alternative:

- **L-Tyrosine**
- **PEA**
- **Muccana Pruriens**



www.amenclinics.com
Dr. Daniel Amen, MD

Treatment Order Matters



IMAGES OF HUMAN BEHAVIOR

Rest, Concentration & Concentration with Medication

undersurface view, rest
mild decrease prefrontal area

undersurface view, concentration
marked decrease prefrontal cortexand ieft temporal lobe

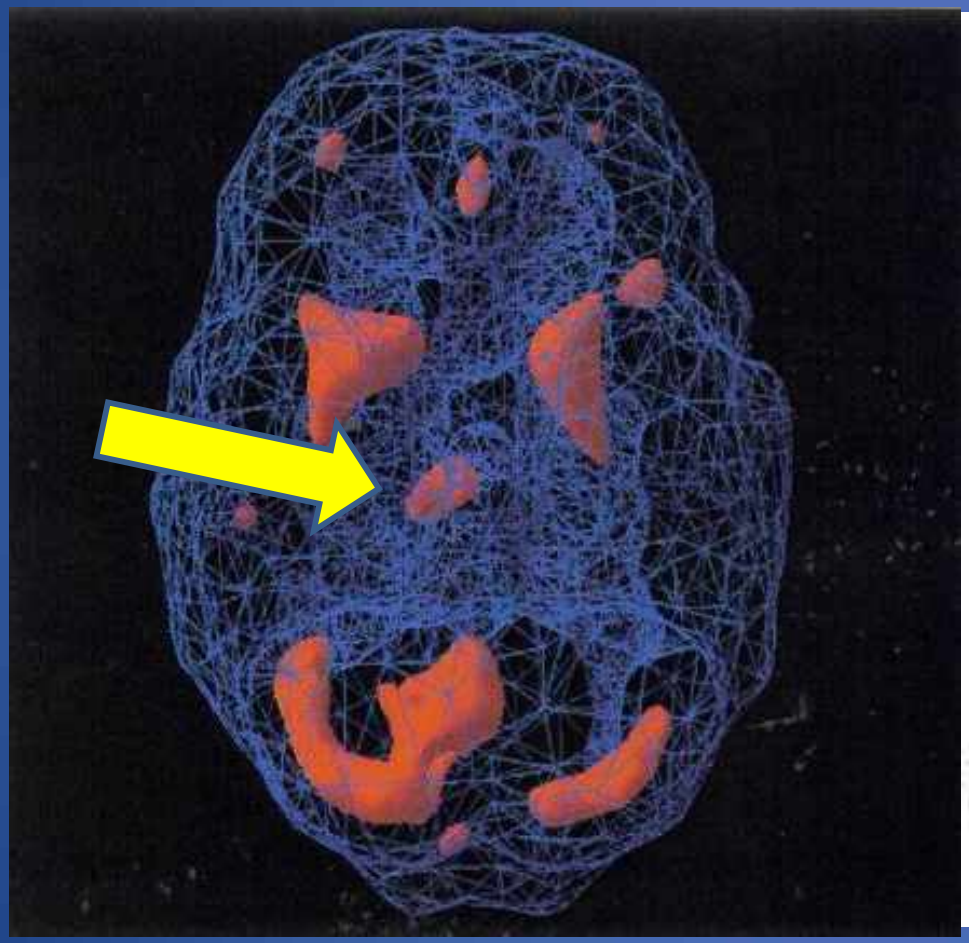
undersurface view, w/Adderall
overall marked improved activity

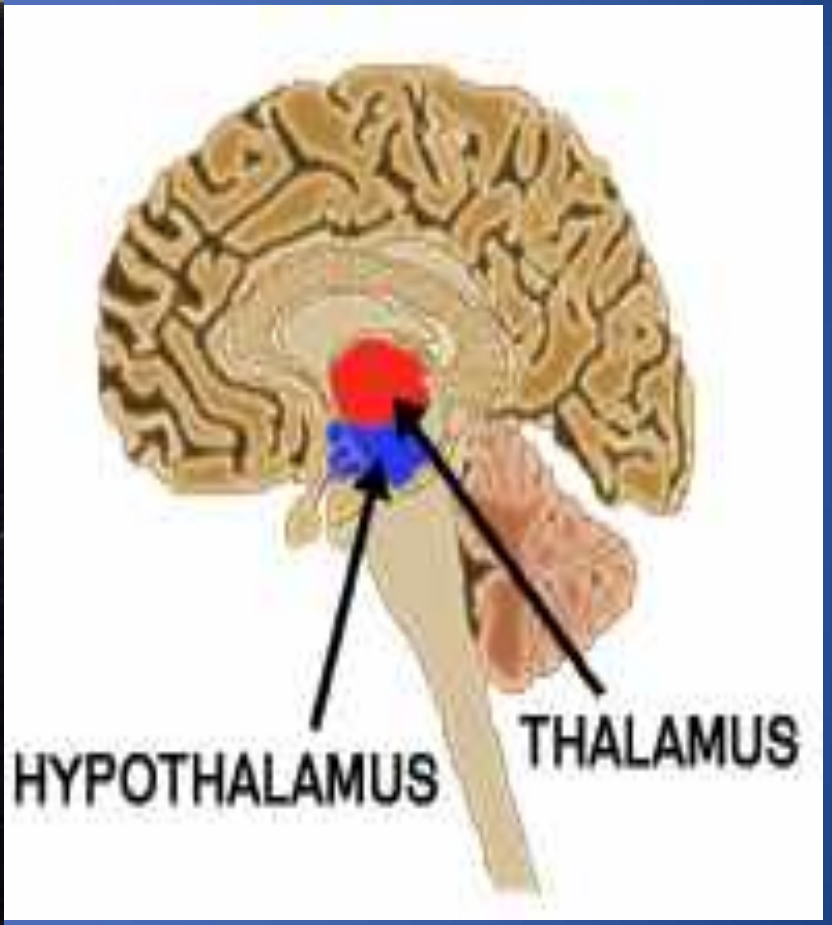
12:2

Images of Attention Deficit Disorder

Pay Attention to Your Patients Drug of Choice

Thalamus (Depression)





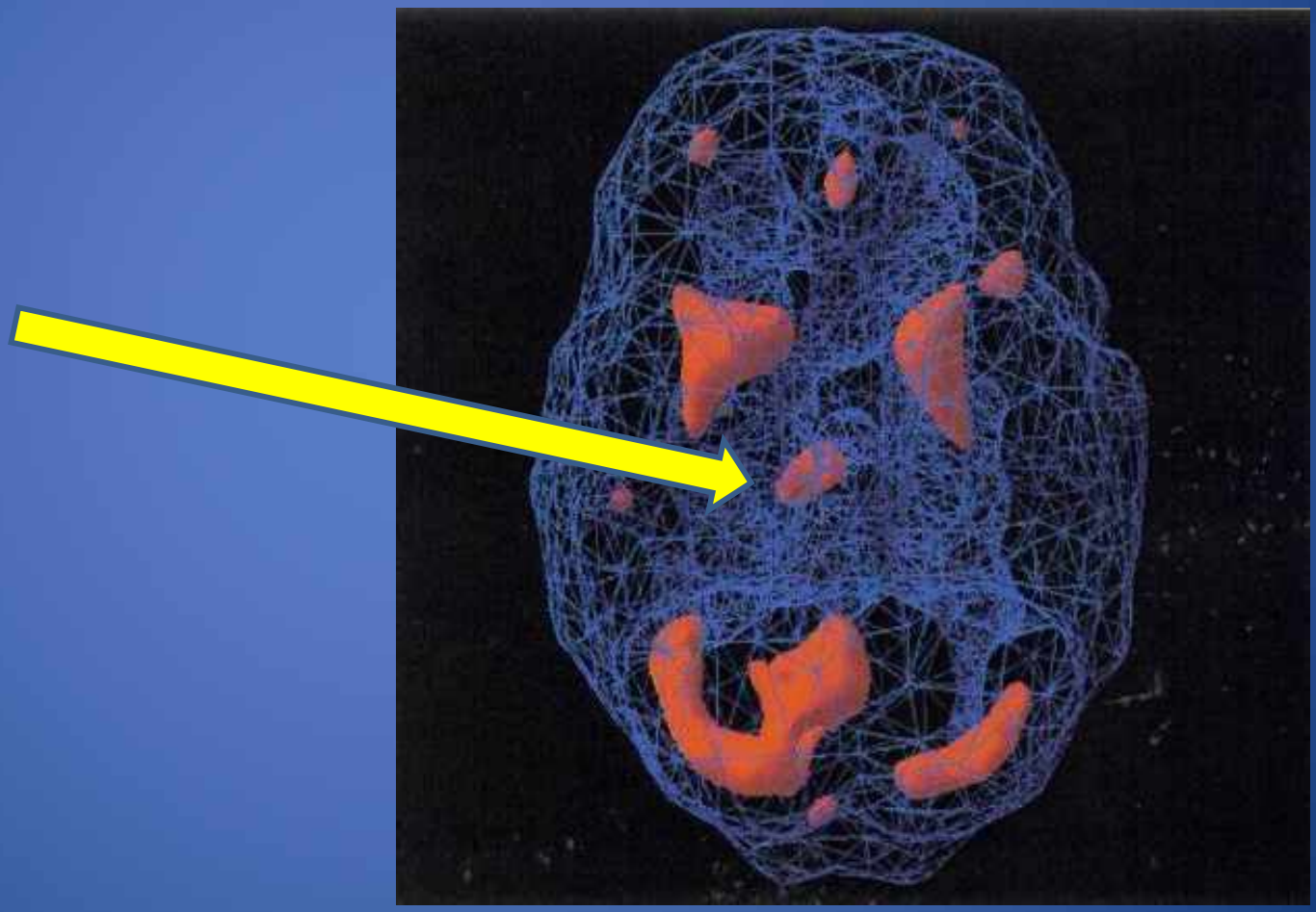
Thalamus (Depression)

Traditional

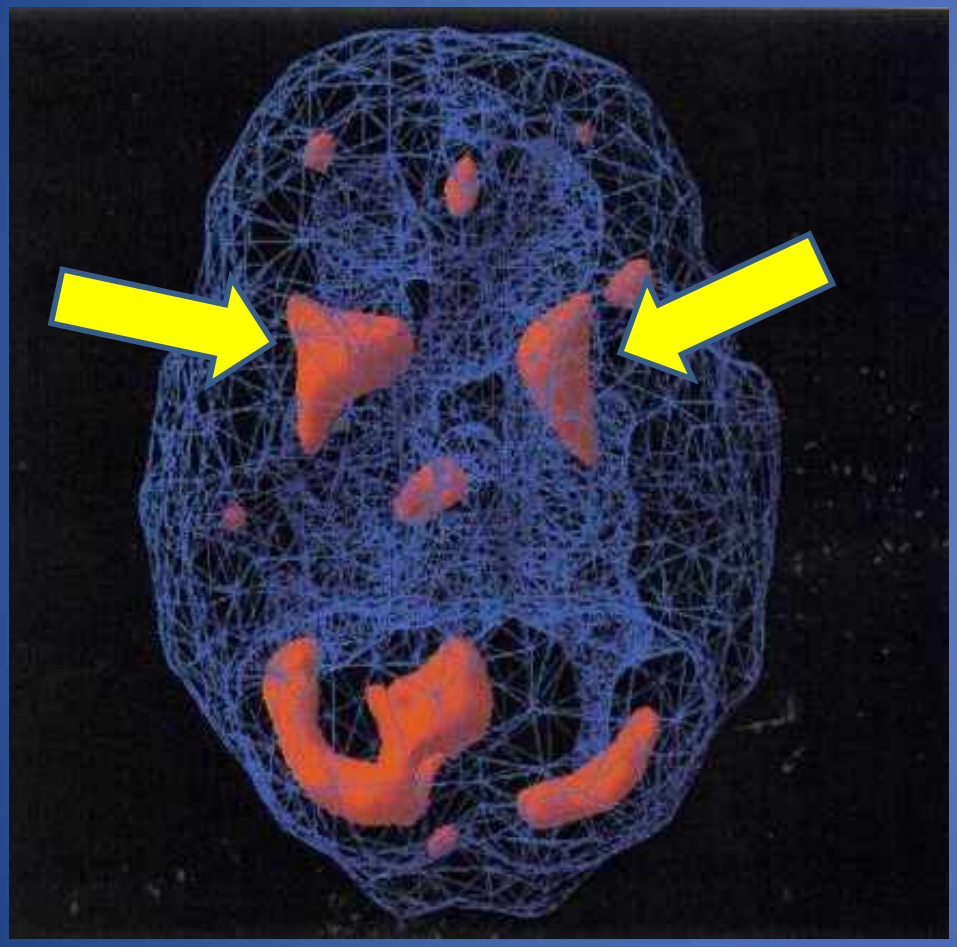
- TCA
- SSRI

Alternative:

- L-Tryptophan
- T-HTP



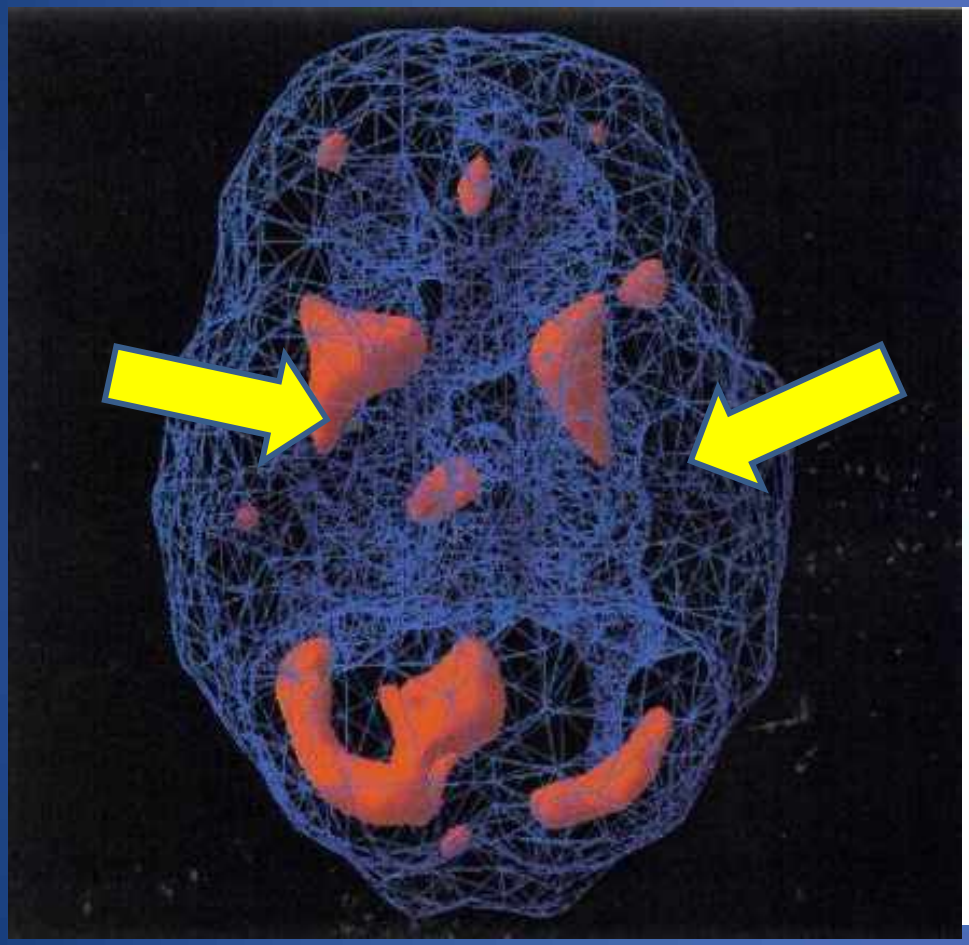
Basal Ganglia (ANXIETY)

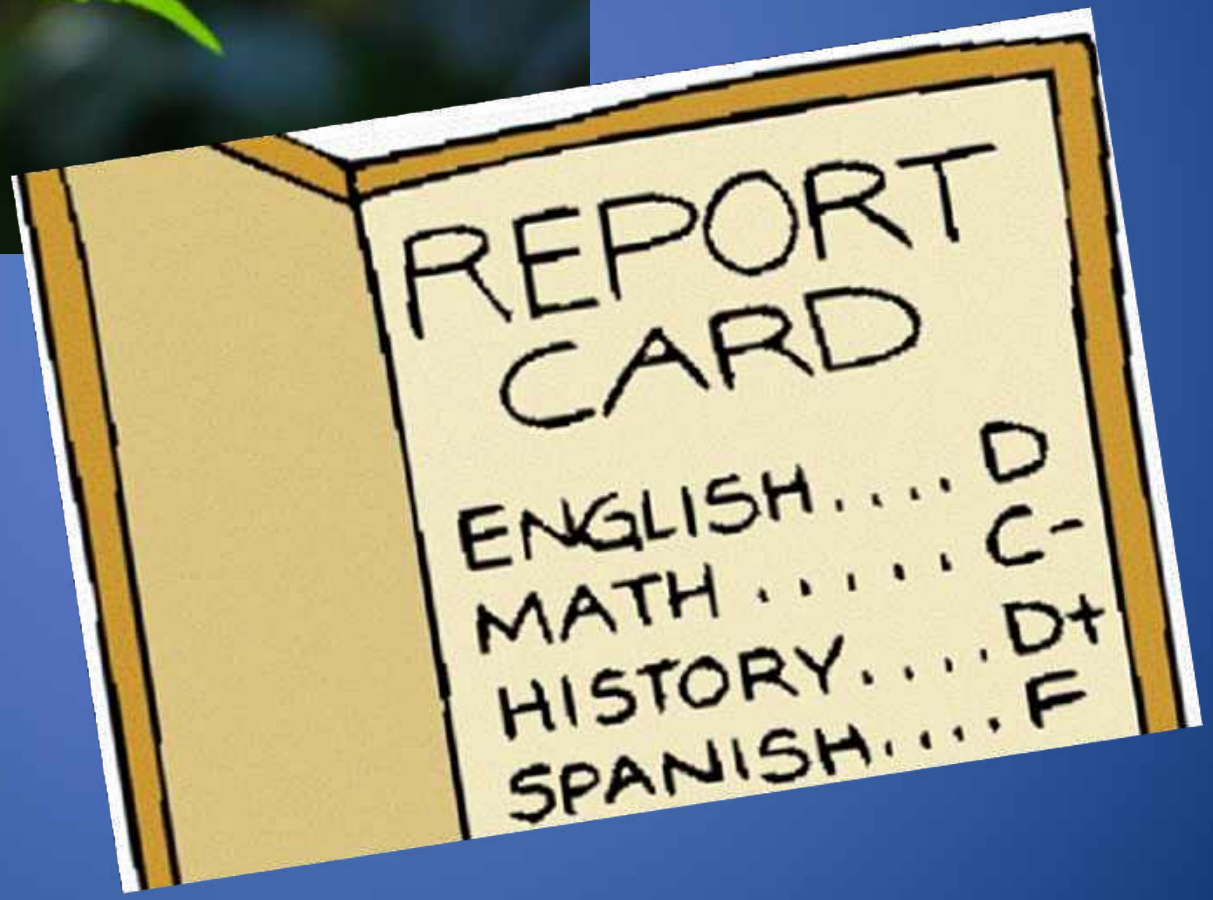



Marijuana!
HEY, AT LEAST IT'S NOT CRACK!

Cannabis

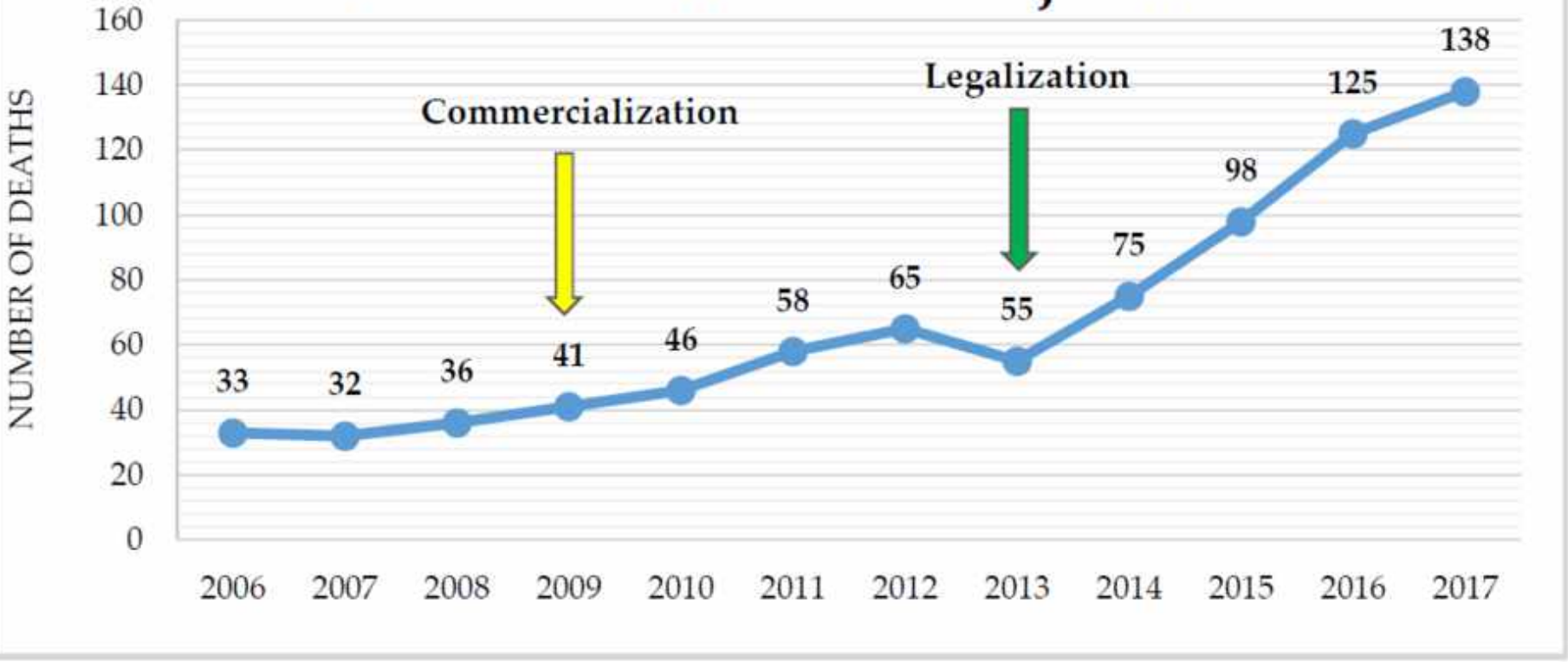
Basal Ganglia (Anxiety) Consider GABAergic , Taurine, and/or Anti-Glutamatergic




REPORT
CARD
ENGLISH.... D
MATH..... C-
HISTORY.... D+
SPANISH.... F

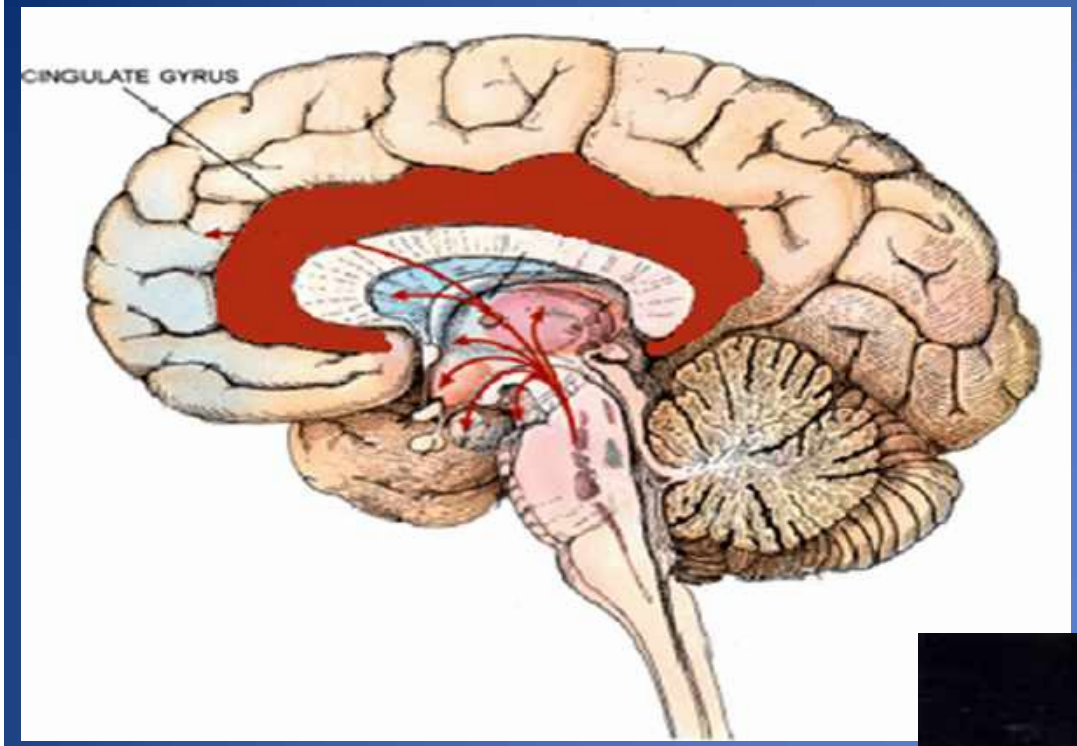
Weed Out the Confusion: One-Third of Teens Think Driving Under The Influence of Marijuana is Legal in States Where Recreational Use By Adults is Permitted

Traffic Deaths Related to Marijuana when a Driver Tested Positive for Marijuana



SOURCE: National Highway Traffic Safety Administration, Fatality Analysis Reporting System (FARS), 2006-2011 and Colorado Department of Transportation 2012-2017

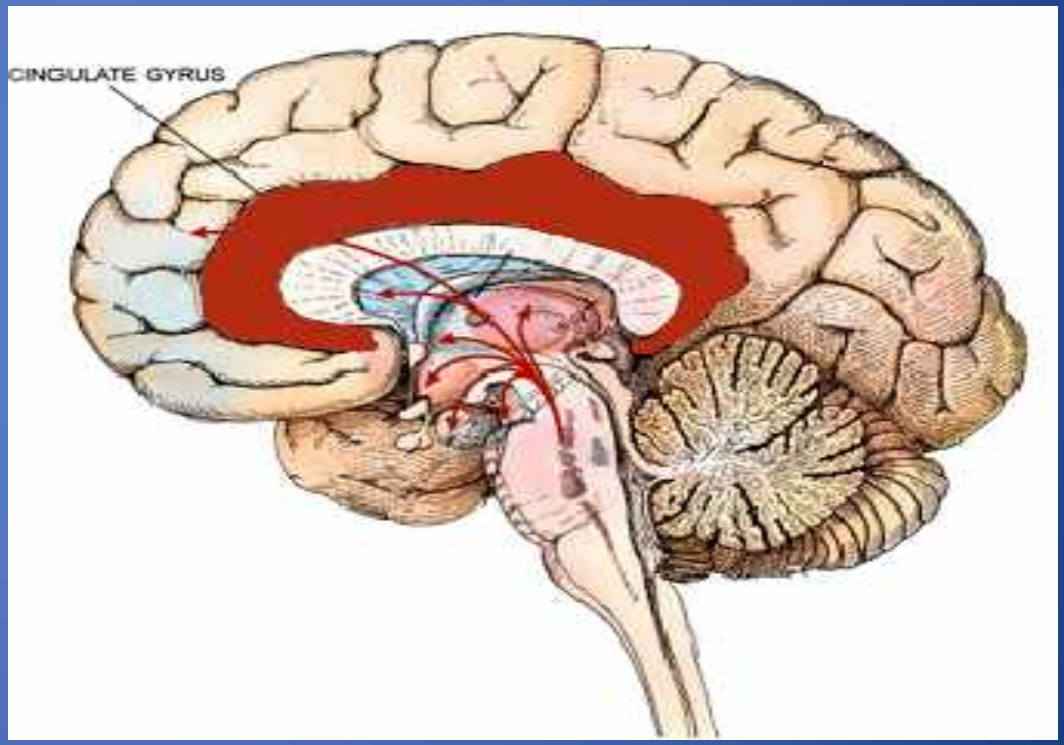
https://www.stopdruggeddriving.org/problem



Cingulate Gyrus

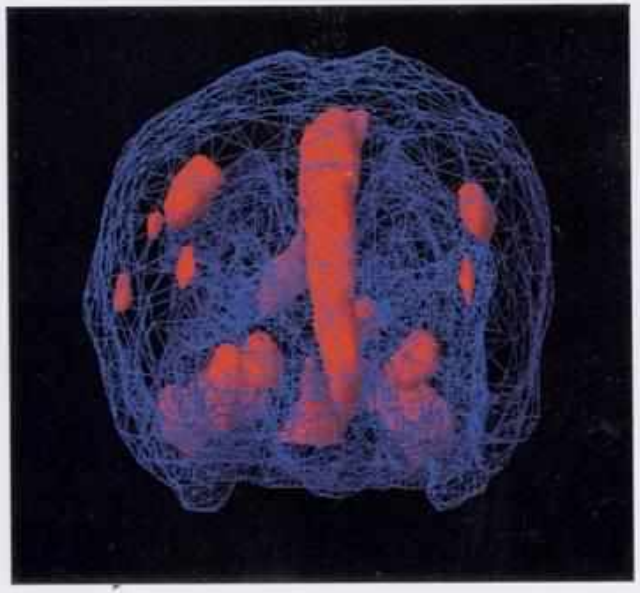
Cingulate Gyrus Problems

- Cognitive Inflexibility
- OCD
- Hoarding
- Rigidity
- Addictions
- ODD
- PTSD
- Vigilance
- Holding a Grudge
- Gambling
- Road Rage

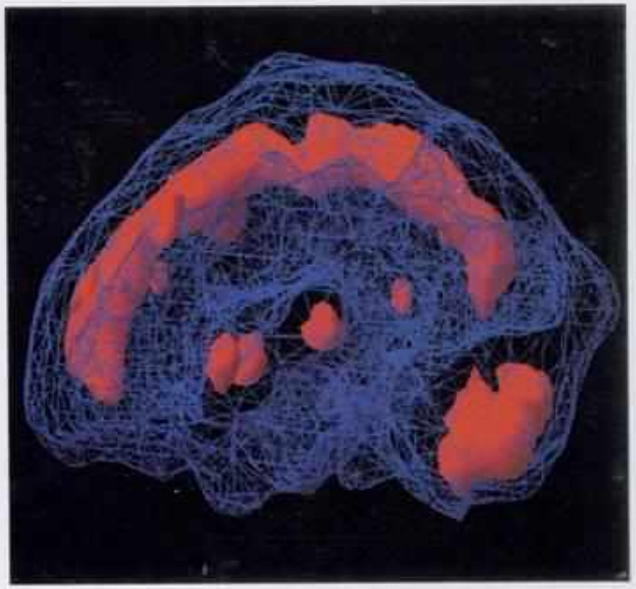


Pathological Gambling

top down active view



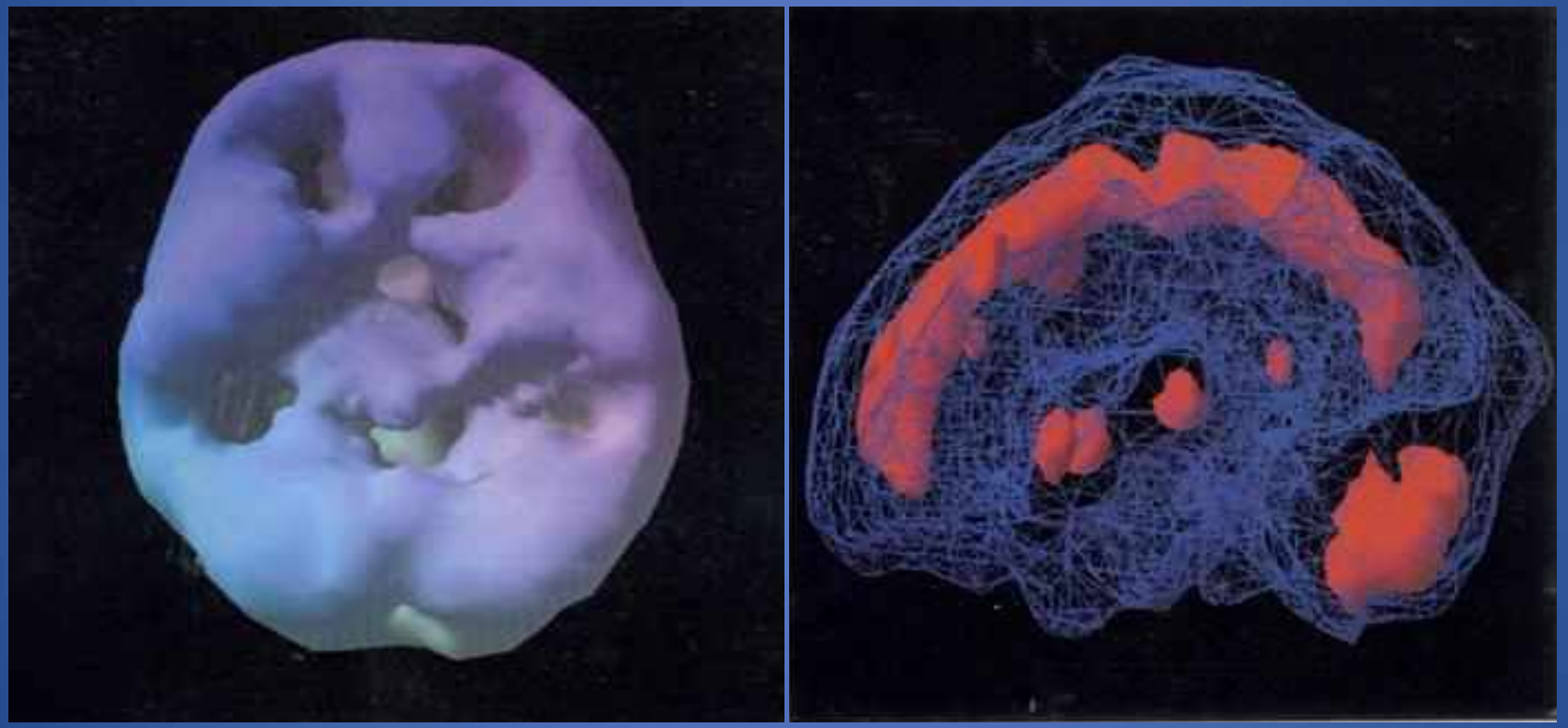
front on active view



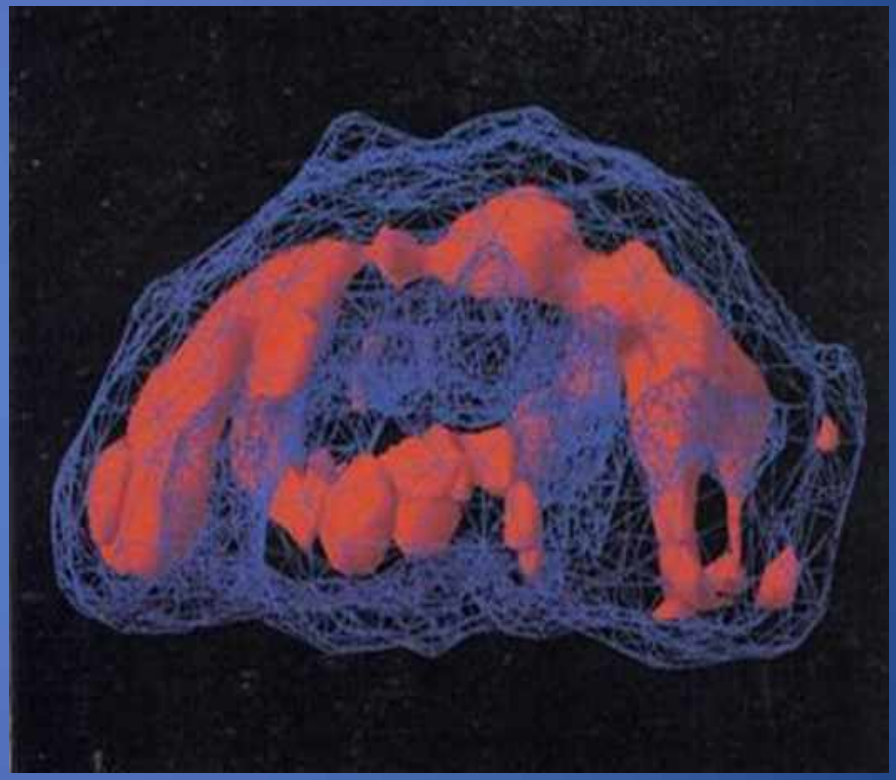
side active view

marked increased anterior cingulate activity

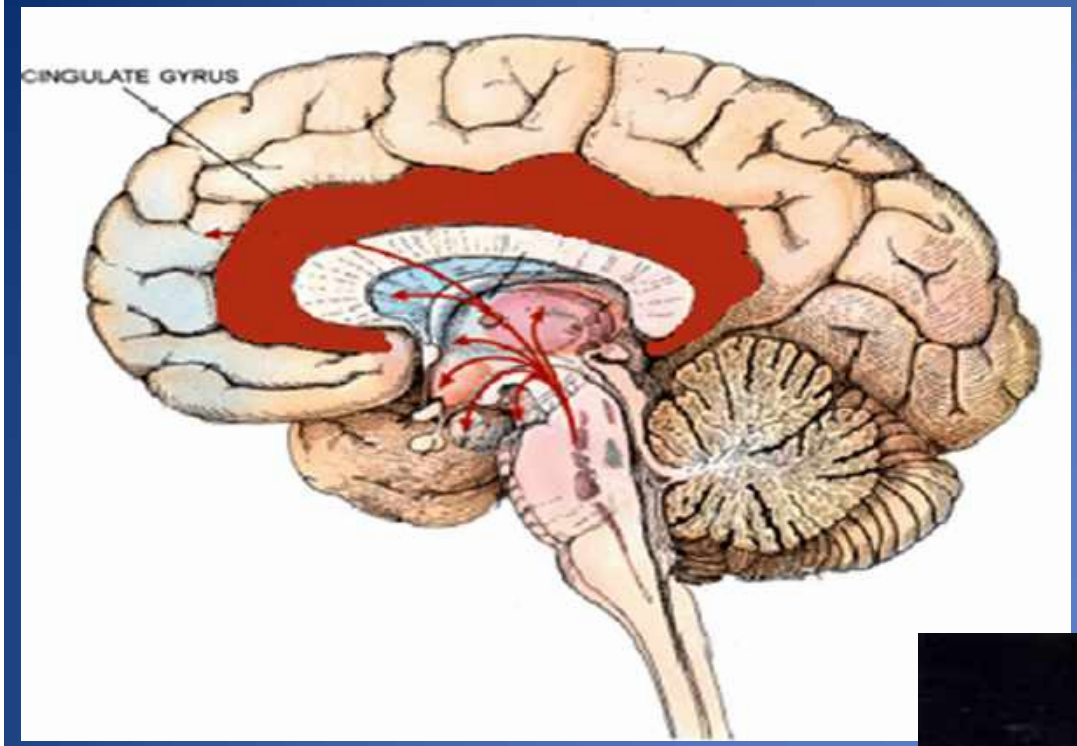
Impulsive Gambling



Road Rage



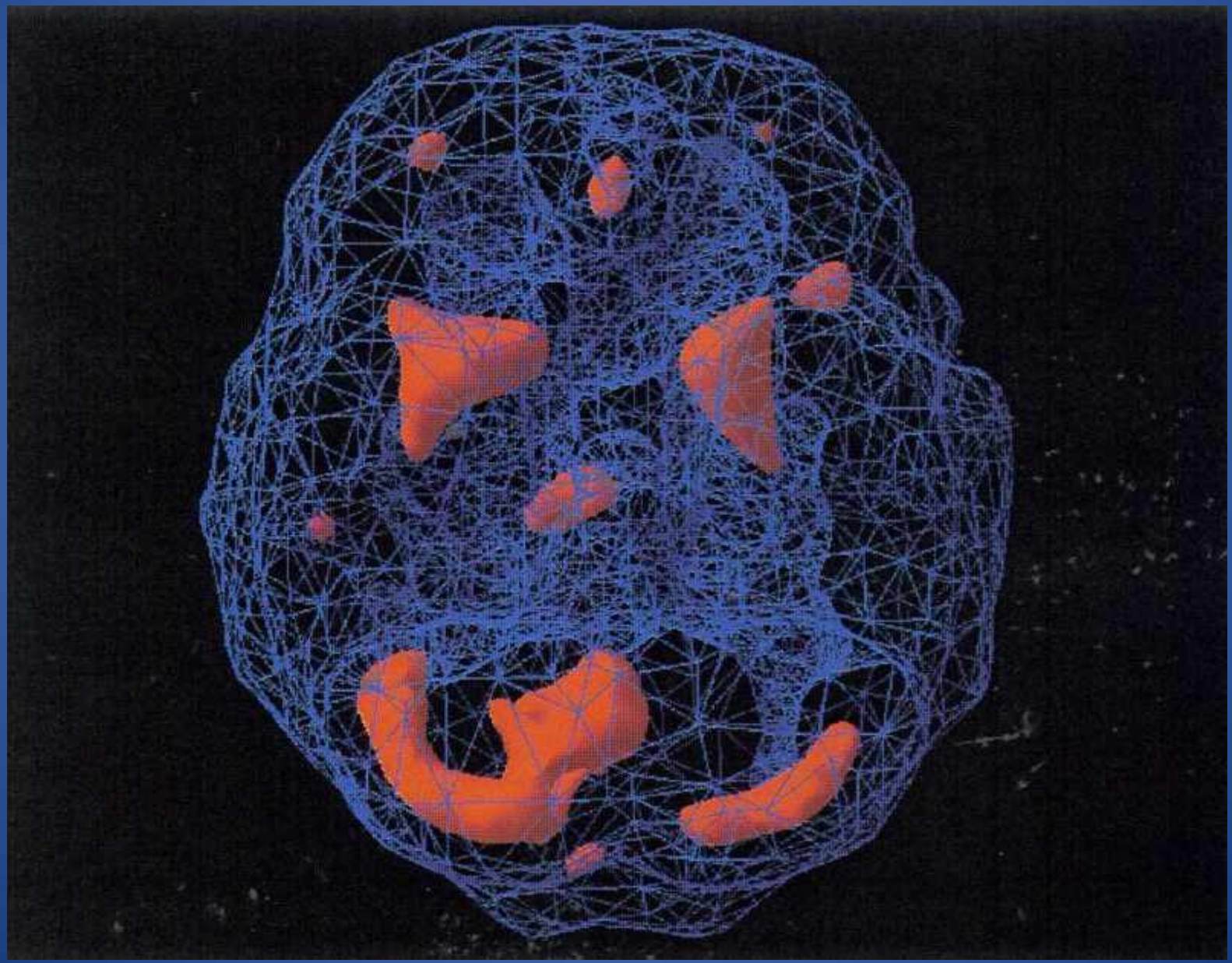
Impulsive & Compulsive



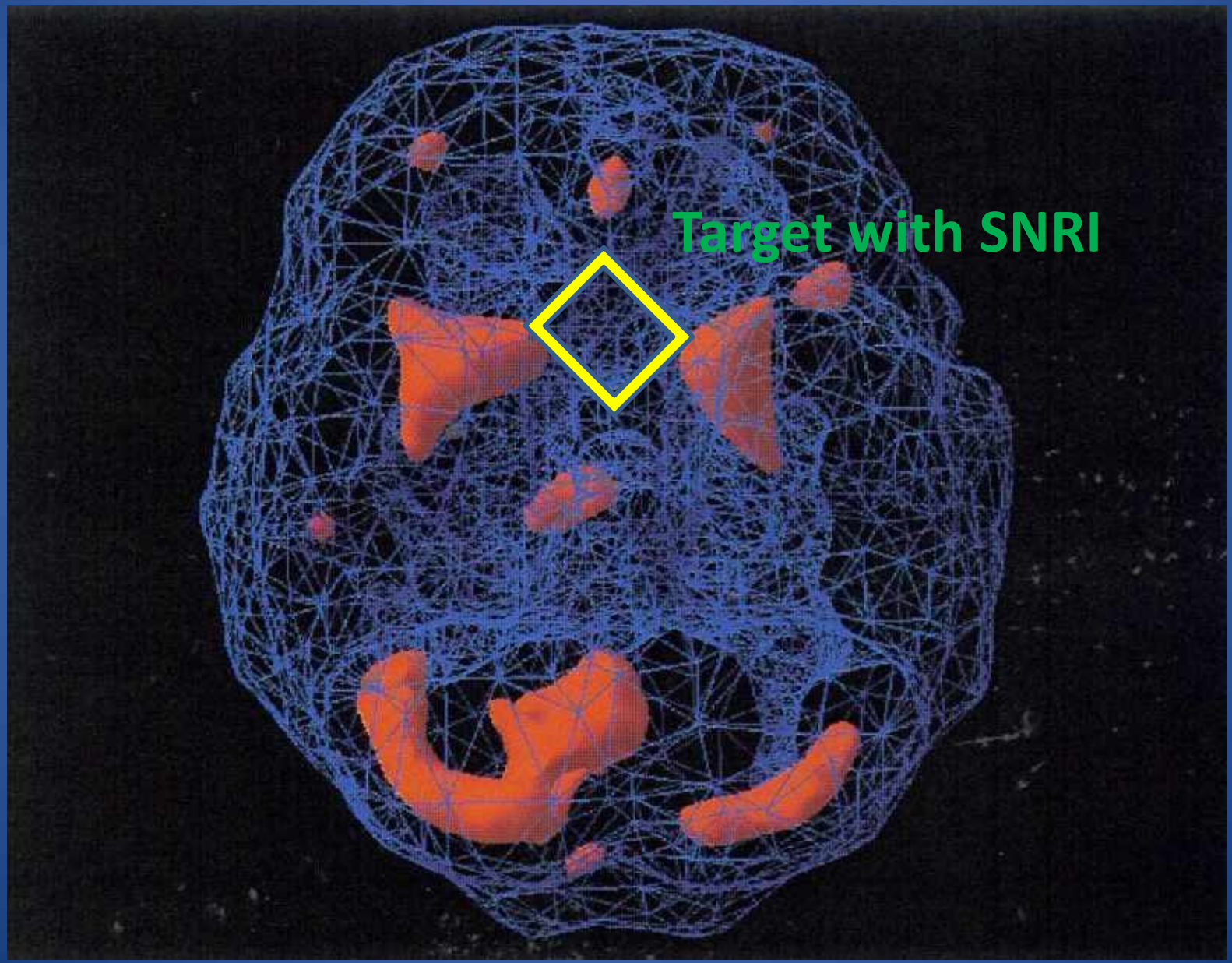
Cingulate Gyrus

Target with Serotonergic Drug
or Supplement as the "Gear Shifter"

Depression, Anxiety, OCD, PTSD



Depression, Anxiety, OCD, PTSD
The Diamond Pattern



Temporal Lobe

Memory	Mood / Temper	Psychosis
Choline	GABA	Dopamine
Dopamine	Glutamate Dopamine	Glutamate
	Mood Stabilizer	Antipsychotic

Firestorms of the Brain
The Use of Neuroimaging in Court

No Alcohol

top-down active view
ring of fire pattern

Alcohol Intoxicated State

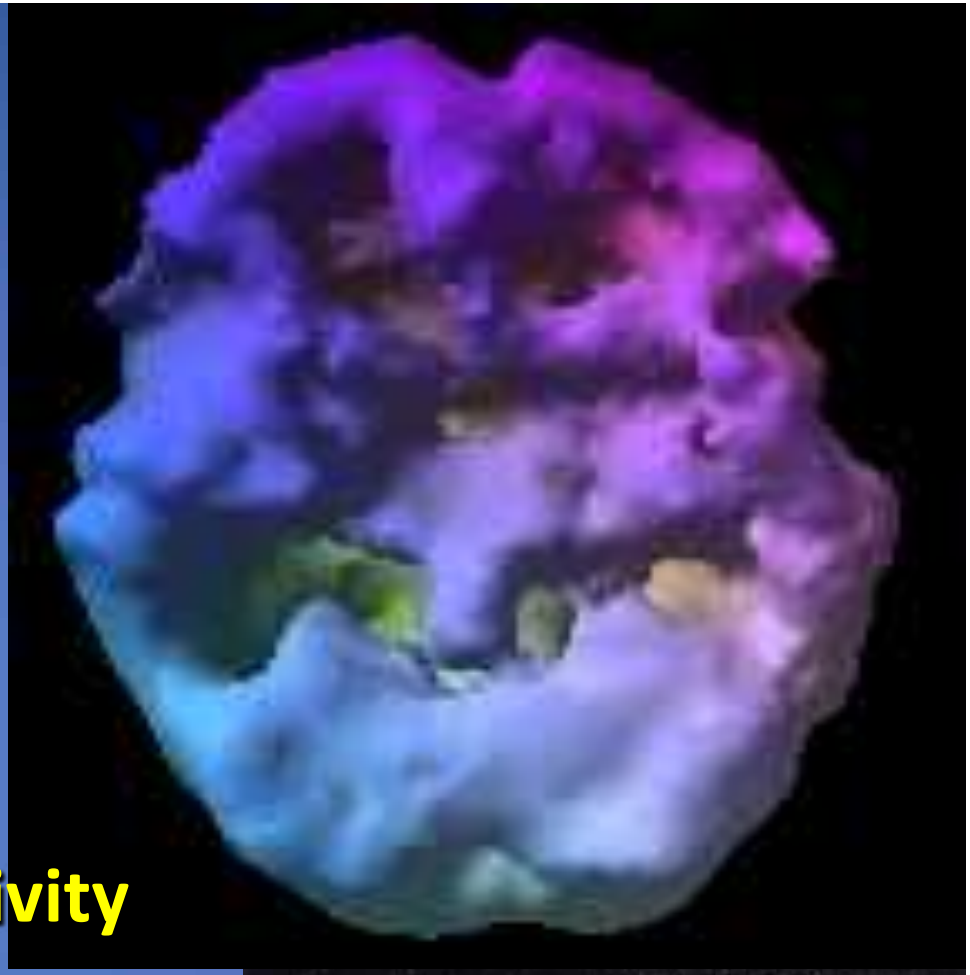
top-down active view
overall dampening effect on the brain
still increased cingulate activity

underside surface view
good overall activity without alcohol

underside surface view
marked decreased in temporal lobes
(tendencies toward aggression),
marked decreased prefrontal cortex
(no internal supervision)

Firestorms of the Brain
The Use of Neuroimaging in Court

Violent Behavior



TRIAD:

Decreased Prefrontal Cortex Activity

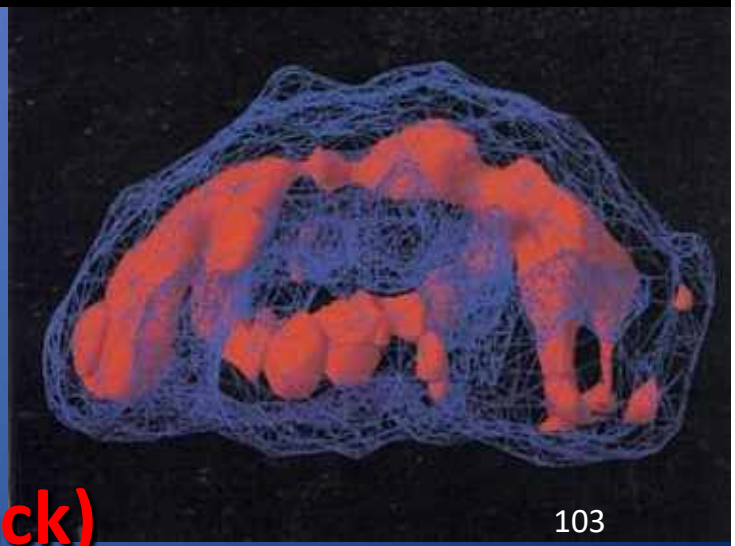
(Impulsivity)

Abnormal Left Temporal Lobe

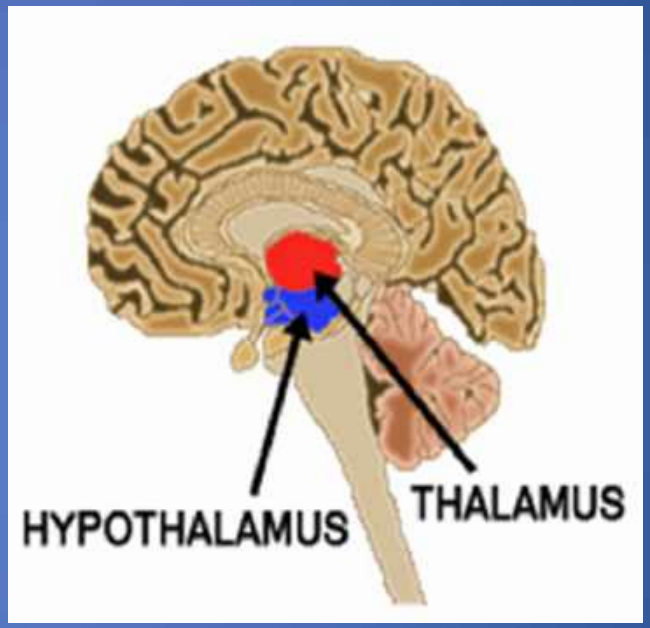
(Agression)

Overactive Cingulate Gyrus

(Vigilience, OCD, planned executed attack)



ADD and Depression and Potential Mood Disorder (Bipolar)



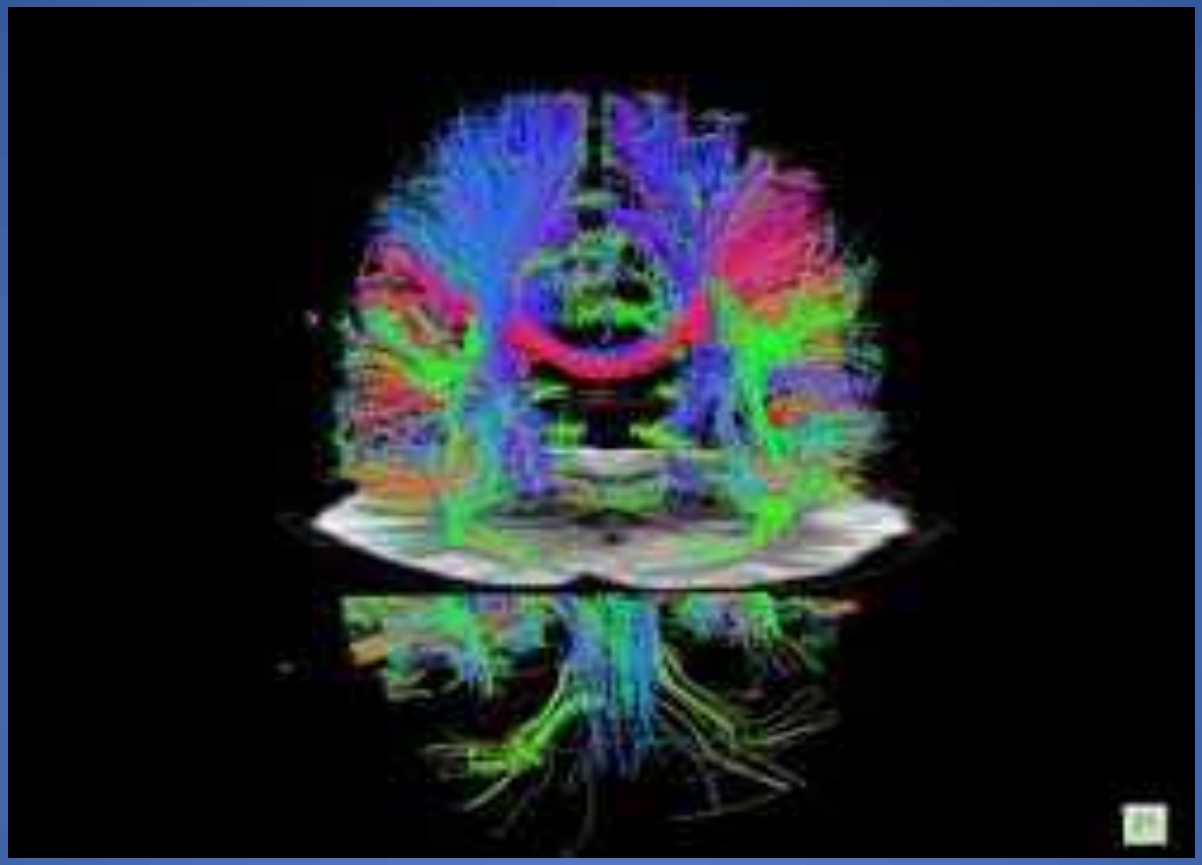
Consider Mood Stabilizer and later SNRI and or stimulant cautiously

Recognizing Neurotransmitter Patterns

Norepinephrine

Dopamine

Epinephrine



Serotonin

GABA

Glutamate

The medical literature, as well as a wealth of clinical observation, continues to support the use of urine in testing for neurotransmitter levels and guiding therapies designed to bring balance to the nervous system.

	Result		Collected	Normal Range
Epinephrine RO	**5.8** Low	0 7 12 25	3:10PM 6/2/2011	Day: 7-12 Night: 4-6
Norepinephrine RO	**17.2** Low	0 30 45 100	3:10PM 6/2/2011	Day: 30-45 Night: 15-23
Dopamine RO	**58.7** Low	0 115 175 460	3:10PM 6/2/2011	Day: 115-175 Night: 75-120
DOPAC RO	**719.2** Low	0 790 1560 3000	3:10PM 6/2/2011	Day: 790-1,560 Night: 530-930
Serotonin RO	**70.6** Low	0 120 185 460	3:10PM 6/2/2011	Day: 120-185 Night: 100-150
5-HIAA RO	**1,305.0** Low	0 2100 5000 7500	3:10PM 6/2/2011	Day: 2,100-5,000 Night: 2,000-3,300
Glycine RO	**348.8** Low	0 455 980 2500	3:10PM 6/2/2011	Day: 455-980 Night: 390-750
Taurine RO	**98.0** Low	100 540 2400	3:10PM 6/2/2011	Day: 100-540 Night: 65-360
GABA RO	**3.9** Low	0 4.7 7 18	3:10PM 6/2/2011	Day: 4.7-7.0 Night: 3.8-5.7
Glutamate RO	**10.2** Low	0 15 32 100	3:10PM 6/2/2011	Day: 15-32 Night: 12-22
PEA RO	**12.5** Low	0 30 70 200	3:10PM 6/2/2011	Day: 30-70 Night: 20-40
Histamine RO	**6.5** Low	0 14 24 75	3:10PM 6/2/2011	Day: 14-24 Night: 8-14

Excitatory and Inhibitory Neurotransmitters

- **Excitatory**
  - **Epinephrine**
  - **Norepinephrine**
  - **Dopamine**
  - **Glutamate**
  - **PEA**
  - **Histamine**
- **Inhibitory**
  - **Serotonin**
  - **Glycine**
  - **Taurine**
  - **GABA**

Treble – Excitatory

Norepinephrine

Epinephrine

Dopamine

Glutamate

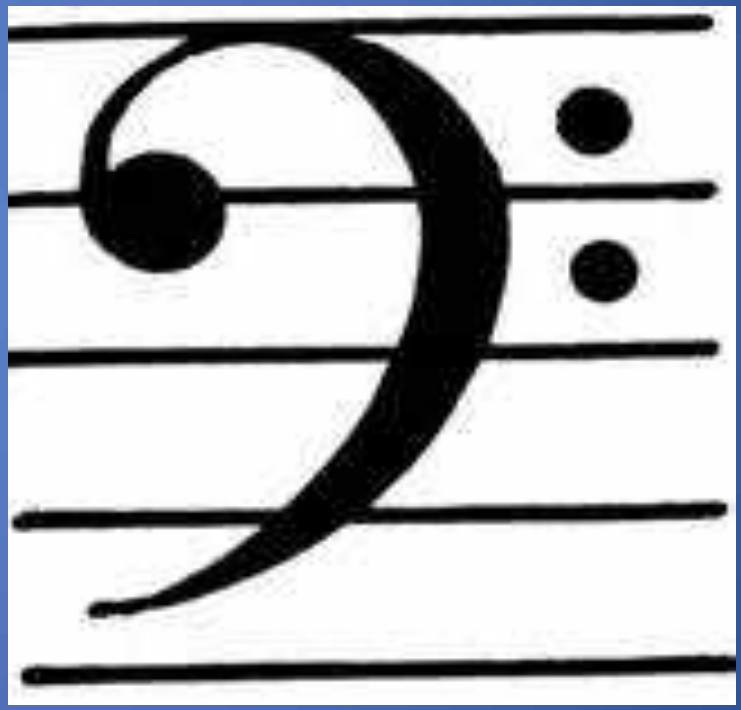
PEA

Histamine

Cortisol

BASE - Inhibitory - Calming

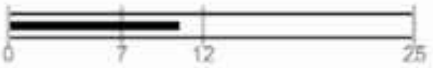
- GABA
- Serotonin
- Glycine



Epinephrine RO

Result

10.4 Normal



Norepinephrine RO

Result

106.6 Elevated

Dopamine RO

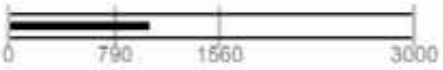
Result

441.2 Elevated

DOPAC RO

Result

1,024.1 Normal



Serotonin RO

Result

109.3 Low

5-HIAA RO

Result

3,896.0 Normal

Glycine RO

Result

1,068.0 Elevated

Taurine RO

Result

540.0 Normal

GABA RO

Result

5.9 Normal

Glutamate RO

Result

84.1 Elevated

PEA RO

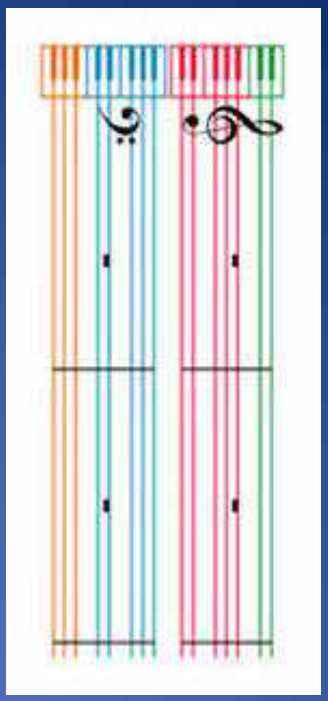
Result

78.9 Elevated

Histamine RO

Result

40.1 Elevated



Treble – Excitatory

BASE - Inhibitory - Calming

Anterior Cingulate

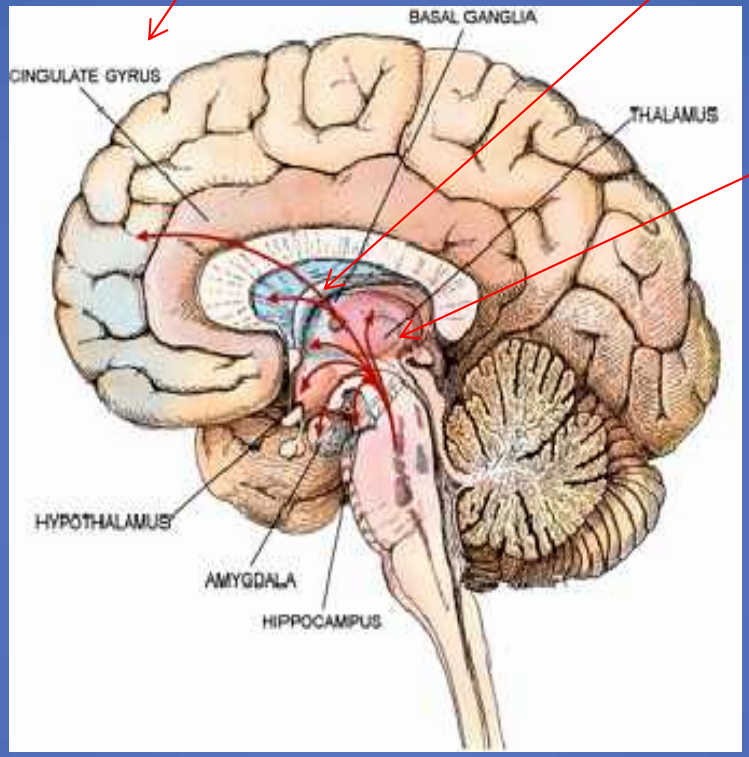
Serotonin

Basal Ganglia

GABA

Prefrontal Cortex

NE
Dopamine
PEA



Thalamic - Limbic

L-Tryptophan
5-HTP
Serotonin
Melatonin
SAMe

Temporal Lobe

Memory

Choline
Dopamine
Glutamate

Mood/Temper

GABA

Psychosis

Dopamine

Think of EPI/NE as stimulant

Irritability, Hostility

Epinephrine / Norepinephrine

Brain Fog , Fatigue

Sleep

GABA

Anxiety, Panic, Fear

Think of GABA as calming

- Alcohol metabolizes into GABA
- Progesterone metabolizes into GABA
- Divalproex sodium metabolizes into GABA

Irritability, Insomnia, Hypomania, Road Rage

SEROTONIN

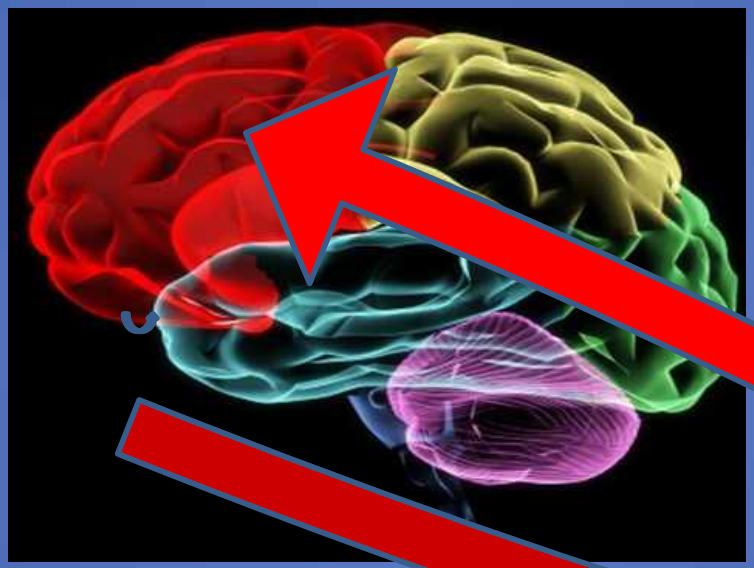
Depression, Anxiety, Sleep Disruption, Anhedonia, Lack of Joy, Amotivation,

Serotonin

Dopamine

Manipulating Neurotransmitters
The Food Industry

Serotonin



BREAD

Dopamine

Alcohol

Caffeine and Chocolate (PEA)

Why Metabolites ?

Serotonin

MAO – A

5HIAA

Serotonin		75.9 (L)
5-HIAA		6852.0 (H)

Agitation, Aggression, Paranoia, Psychosis

Dopamine

Anhedonia, Lack of Joy, Amotivation

Why Metabolites ?

Dopamine

MAO – B

DOPAC

Dopamine		339.5 (H)	03/19/2012 (7:00AM)	106 - 191	64 - 261	µg/gCr

Dopamine and Psychosis

Biomarkers guide treatment interventions

NE = Low

Dopamine = Low

Serotonin = Low

Intervention Choices:

SNRI

Amino Acid Substrates

(5-HTP, L-Tyrosine)

Likely Drug of Choice:

Cocaine, Meth

(NE and Dopamine)

NE = High

Dopamine = High

Serotonin = Low

Intervention Choices:

SSRI

Amino Acid Substrate

(5-HTP)

Likely Drug of Choice:

Ecstasy

(Serotonin)

Anterior Cingulate

SNRI

Serotonin SSRI

Prefrontal Cortex

NE
Dopamine
PEA

DNRI

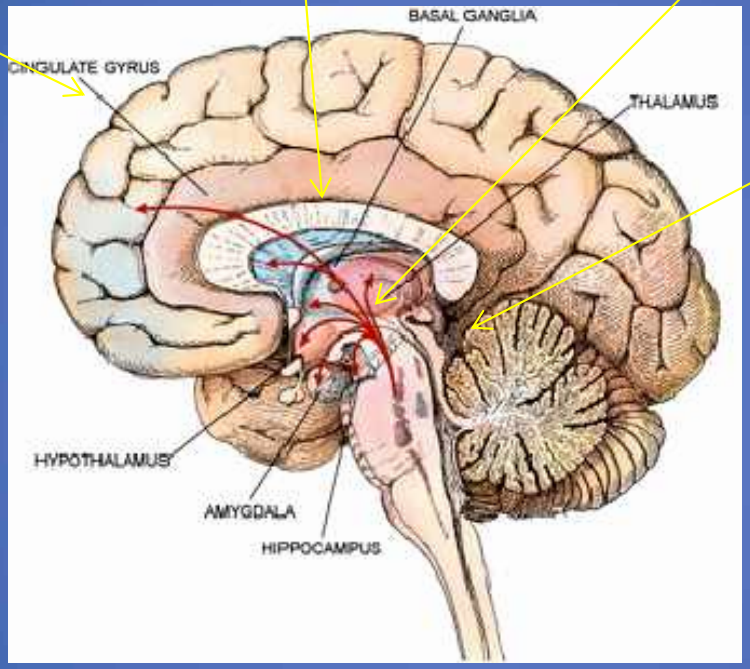
Basal Ganglia

GABA

Thalamic - Limbic

L-Tryptophan
5-HTP
Serotonin
Melatonin
SAMe

SSRI
Vitamin D-3



Temporal Lobe

Cholinergic
Glutamate Modulator

Memory

Choline
Dopamine
Glutamate

Mood/Temper

GABA
Mood Stabilizer

Psychosis

Dopamine

Antipsychotic

Observed clinical patterns

Low Serotonin – enjoys ecstasy

Low GABA – enjoys alcohol and benzodiazepines

Low PEA , NE, Dopamine– enjoys or abuses stimulants

High Dopamine – enjoys benzodiazepams

High Taurine – metabolic/detox/ CBS genetic issues

High Norepinephrine and Low Epinephrine – patient needs SAMe as cofactor

Low Serotonin and High 5-HIAA – patient will need 5HTP or SSRI repletion

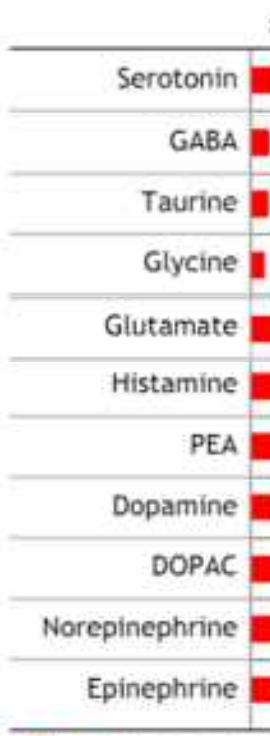
Very Low Serotonin – Start with L-tryptophan first to gently upregulate serotonin receptors then later change to 5HTP

High Dopamine and Low Serotonin – increasing Serotonin will lower Dopamine

High Dopamine and High Serotonin – must use antipsychotic to lower dopamine

Everything low…

Neurotransmitters



	Result	Collected	Inter-Quintile Range	Reference Range	Units
Serotonin	52.2 (L)	03/20/2012 (10:05AM)	99 - 203	57 - 306	µg/gCr
GABA	1.6 (L)	03/20/2012 (10:05AM)	3.9 - 7.9	2.4 - 12.7	µMol/gCr
Taurine	45.5 (L)	03/20/2012 (10:05AM)	156 - 535	52 - 1025	µMol/gCr
Glycine	159.0 (L)	03/20/2012 (10:05AM)	441 - 1258	182 - 2225	µMol/gCr
Glutamate	9.6 (L)	03/06/2012 (7:30AM)	13.5 - 36.8	6.9 - 71.8	µMol/gCr
Histamine	4.6 (L)	03/20/2012 (10:05AM)	10 - 32	4 - 71	µg/gCr
PEA	16.6 (L)	03/20/2012 (10:05AM)	29 - 83	15 - 167	nMol/gCr
Dopamine	54.0 (L)	03/20/2012 (10:05AM)	106 - 191	64 - 261	µg/gCr
DOPAC	260.0 (L)	03/20/2012 (10:05AM)	300 - 1000	100 - 2100	µg/gCr
Norepinephrine	22.5 (L)	03/20/2012 (10:05AM)	28 - 51	19 - 76	µg/gCr
Epinephrine	3.2 (L)	03/20/2012 (10:05AM)	7.1 - 13.6	4.7 - 20.8	µg/gCr

Red or light red bars indicate results out of Inter-Quintile Range.

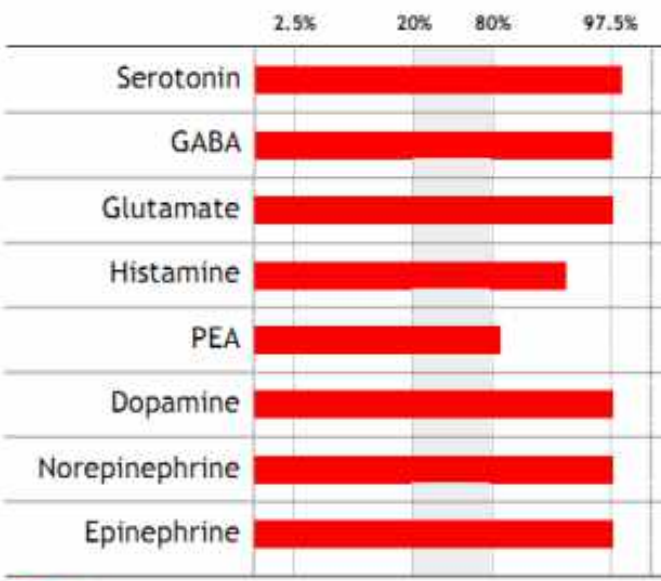
Inter-Quintile Range is defined as the 60th percentile, Reference Range as the 95th percentile.

… drug of choice – **Stimulants**

(Cocaine, Methamphetamines, Adderall)

Everything high…

Neurotransmitters



	Result	Collected	Inter-Quintile Range	Reference Range	Units
Serotonin	1,292.0 (H)	03/19/2012 (7:00AM)	99 - 203	57 - 306	µg/gCr
GABA	12.9 (H)	03/19/2012 (7:00AM)	3.9 - 7.9	2.4 - 12.7	µMol/gCr
Glutamate	79.7 (H)	03/19/2012 (7:00AM)	13.5 - 36.8	6.9 - 71.8	µMol/gCr
Histamine	56.0 (H)	03/19/2012 (7:00AM)	10 - 32	4 - 71	µg/gCr
PEA	89.0 (H)	03/19/2012 (7:00AM)	29 - 83	15 - 167	nMol/gCr
Dopamine	339.5 (H)	03/19/2012 (7:00AM)	106 - 191	64 - 261	µg/gCr
Norepinephrine	86.7 (H)	03/19/2012 (7:00AM)	28 - 51	19 - 76	µg/gCr
Epinephrine	22.3 (H)	03/19/2012 (7:00AM)	7.1 - 13.6	4.7 - 20.8	µg/gCr

Red or light red bars indicate results out of Inter-Quintile Range.

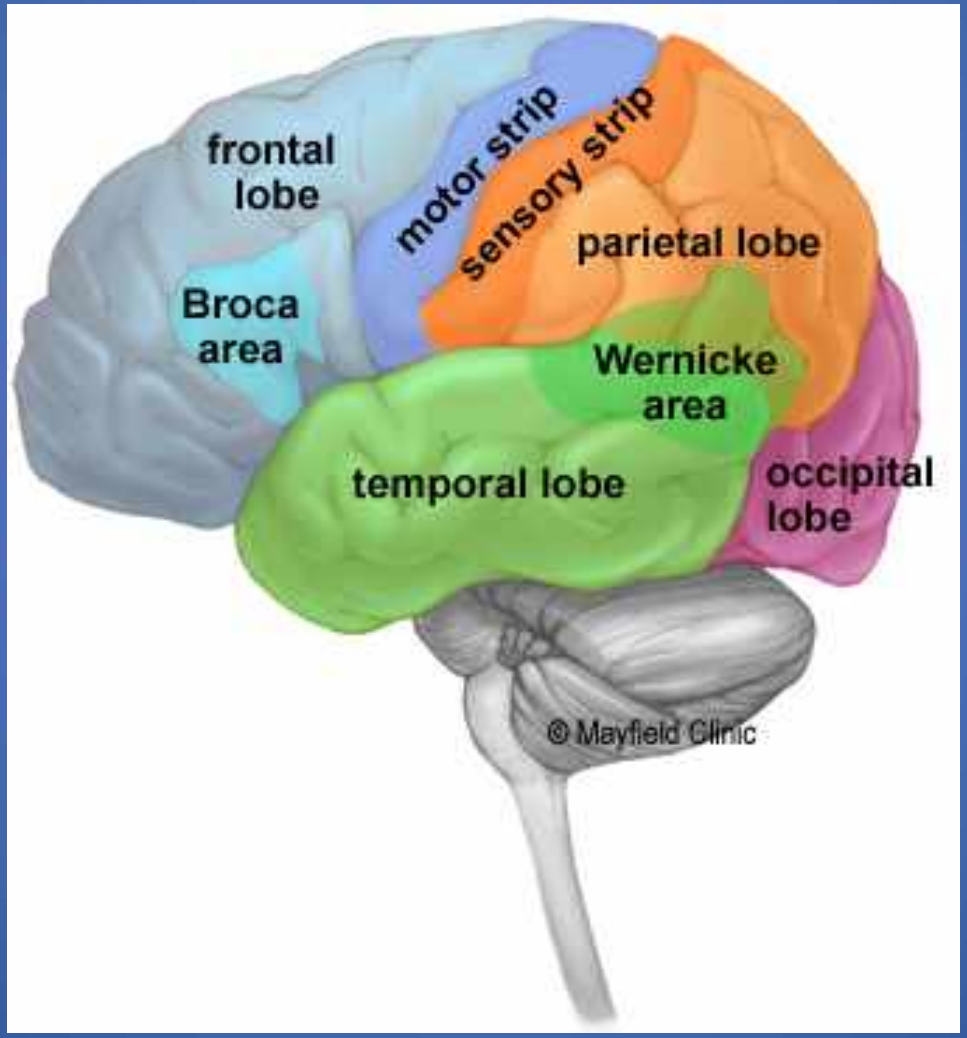
Inter-Quintile Range is defined as the 60th percentile.
Reference Range as the 95th percentile.

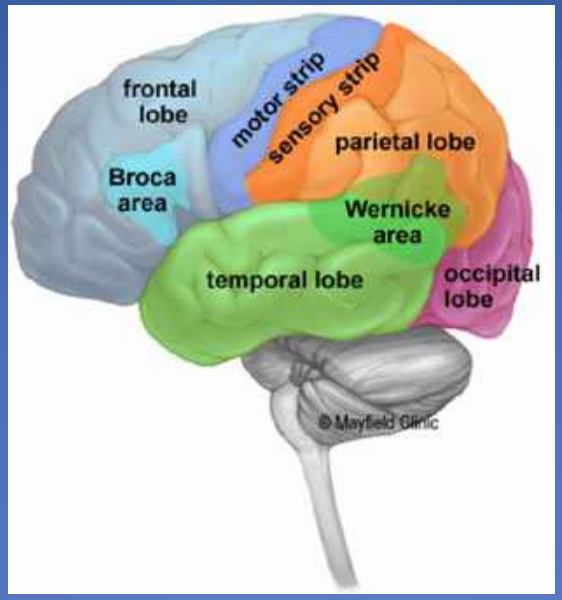
… drug of choice – Sedatives

(alcohol, benzodiazepams, opioids)

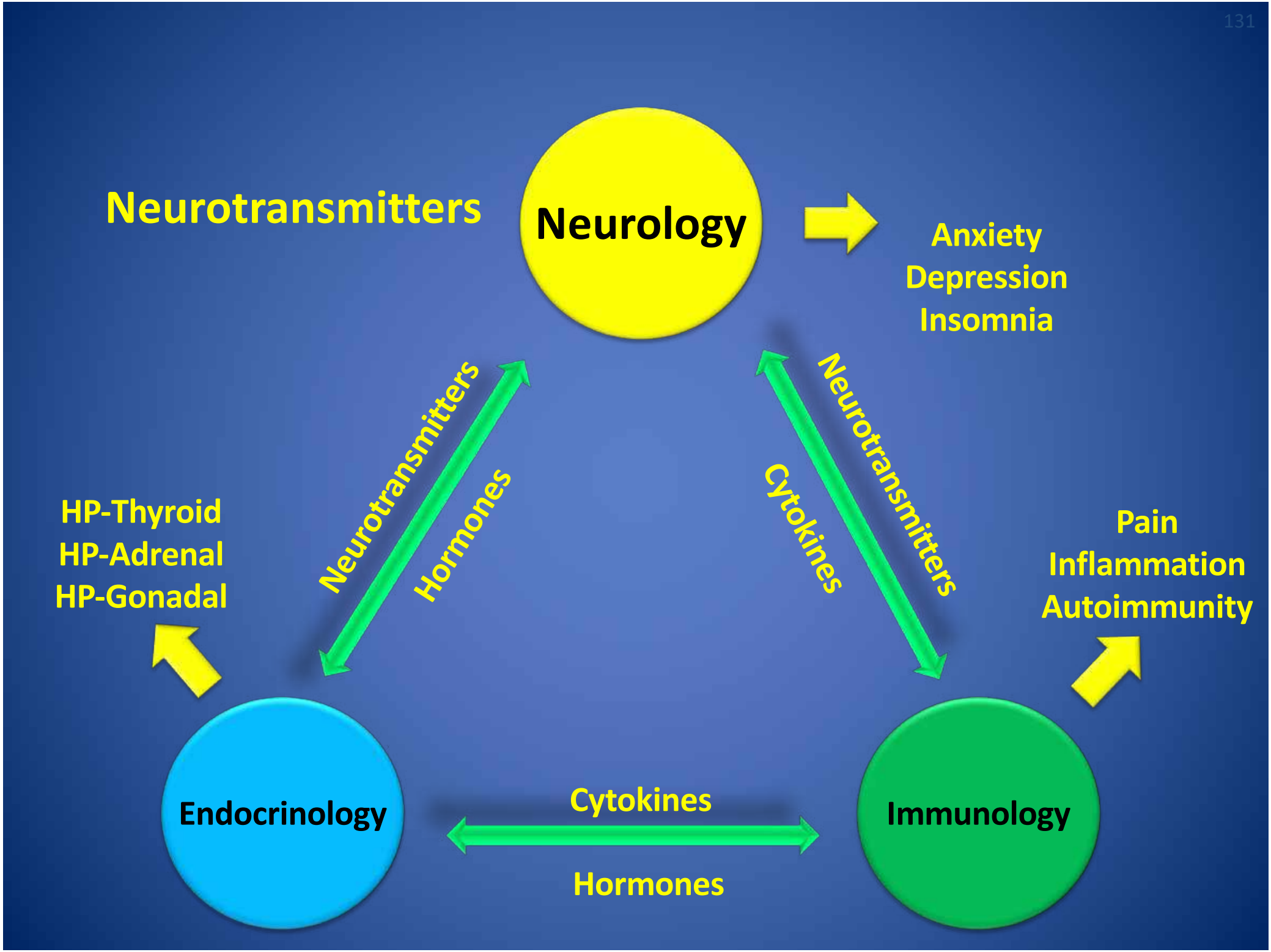

Surface Scan
Healthy Brain
Top Down view
Bottom Up view
Attention Deficit
Disorder (ADD)
BEFORE Treatment
AFTER Treatment
Active Scan
(Healthy)
Top Down view
Bottom Up view
Bipolar Disorder
BEFORE Treatment
AFTER Treatment
Substance Abuse
Brain Trauma
Alzheimer's
Alcohol
Methamphetamine
Relational
Problems
Autism
Obsessive Compulsive
OVERfocused
Wife
UNDERfocused
Husband

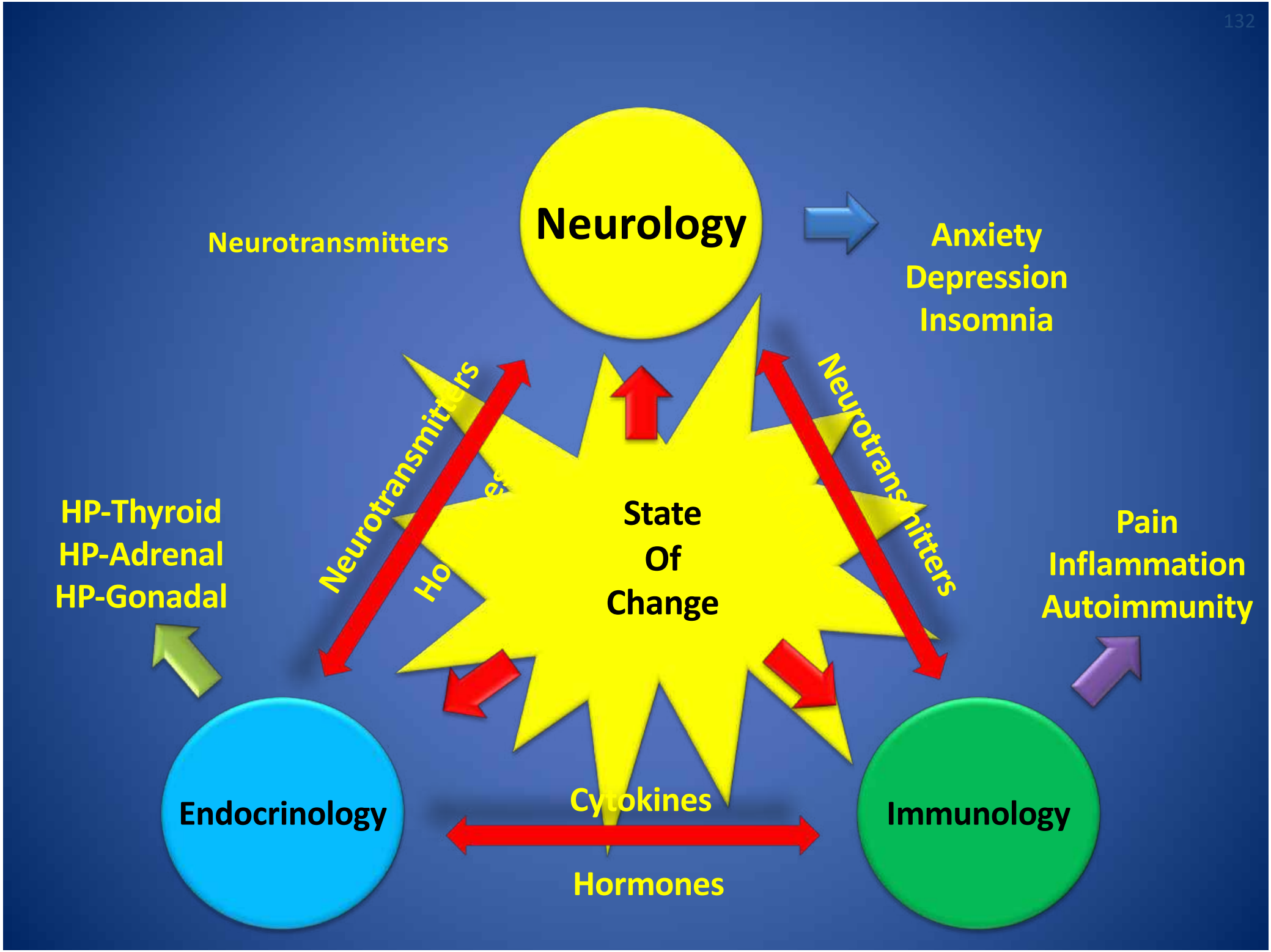
Neuro-immuno-endo-psychopharmacology



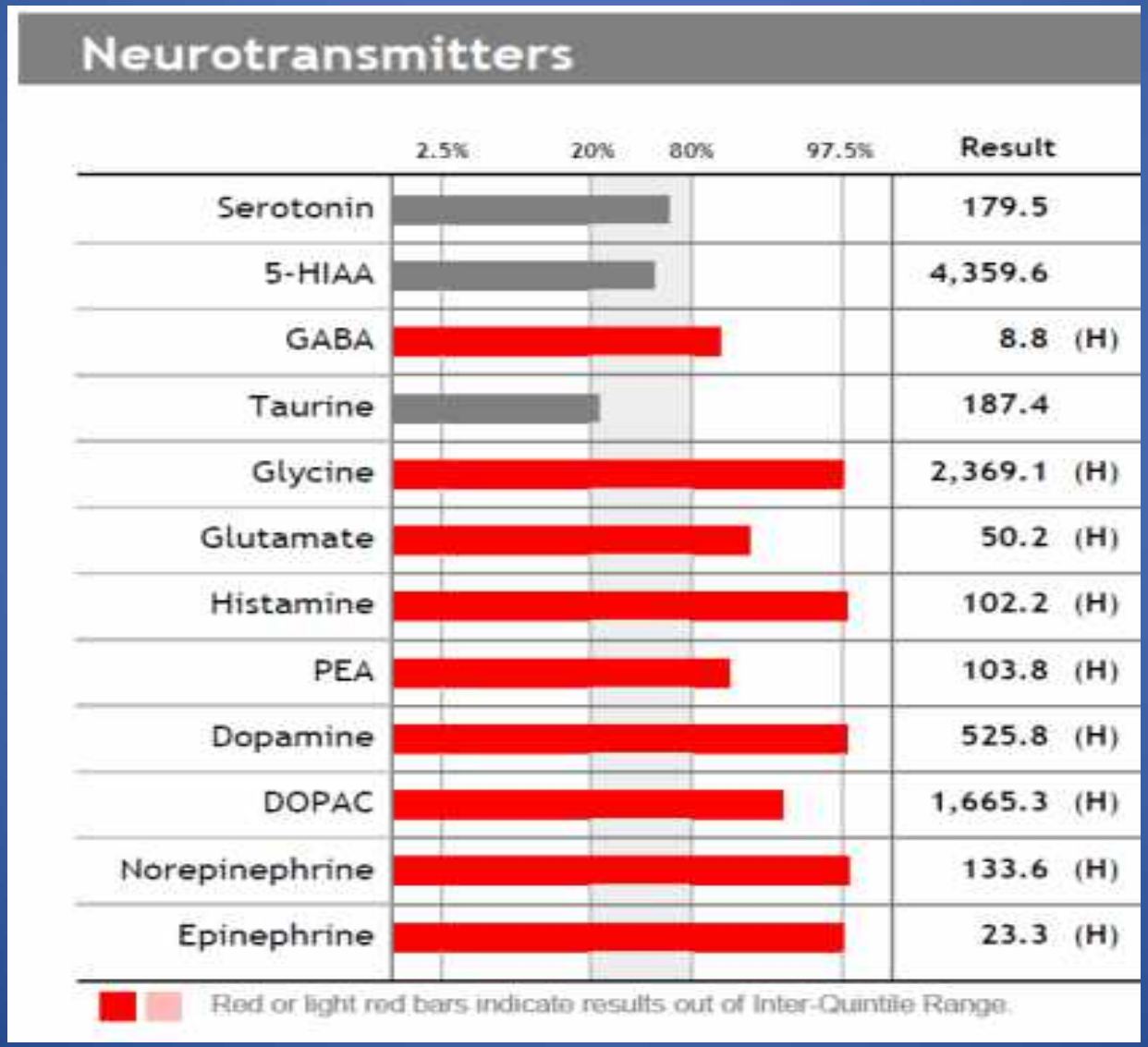


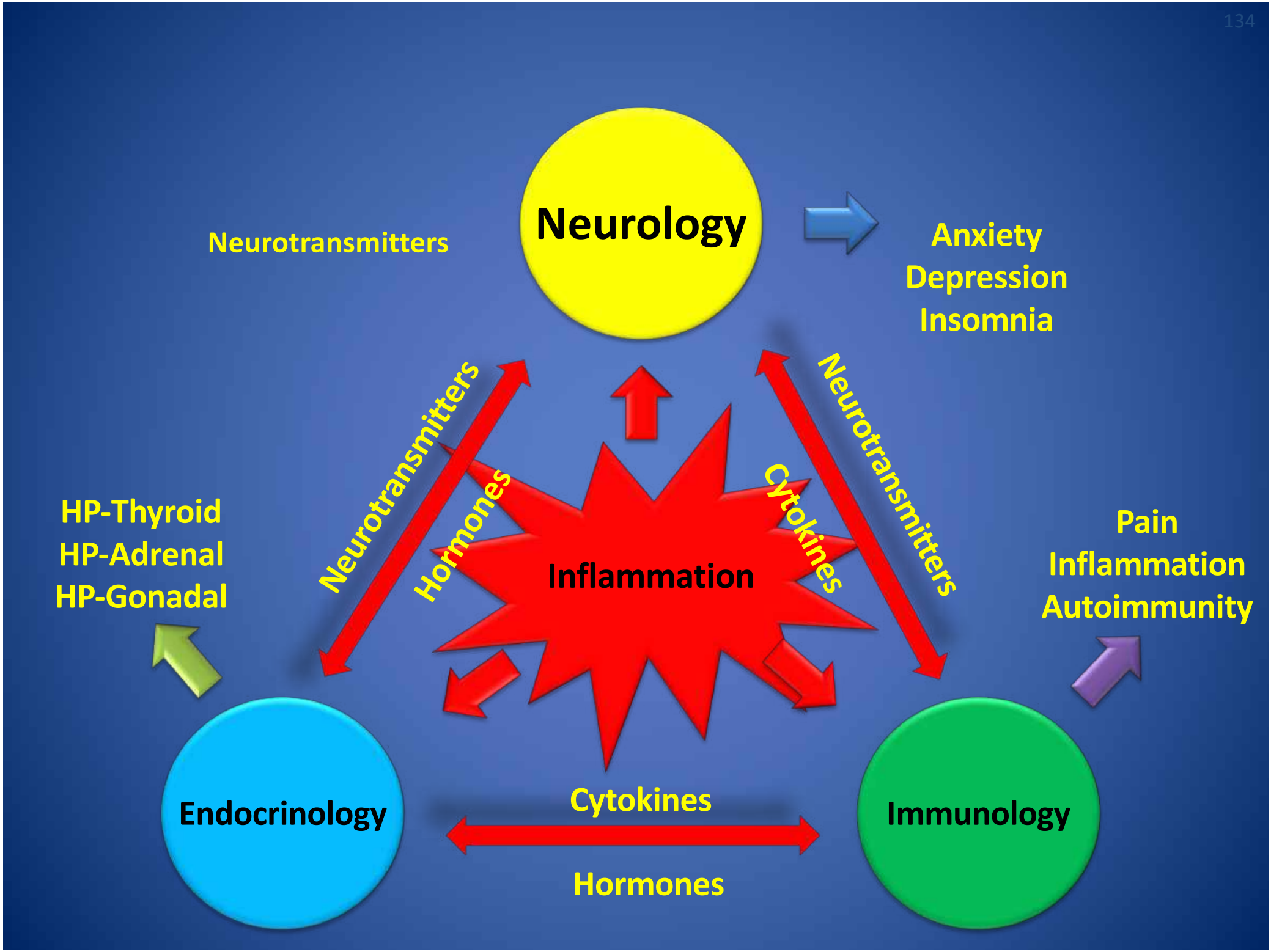
Neuropsychiatric conditions are *Spectrum Conditions* *that* can result from imbalances in multiple neuro-endo-immune messenger systems


Neurotransmitters
Neurology
Anxiety
Depression
Insomnia
Neurotransmitters
Hormones
Neurotransmitters
Cytokines
HP-Thyroid
HP-Adrenal
HP-Gonadal
Pain
Inflammation
Autoimmunity
Endocrinology
Cytokines
Hormones
Immunology

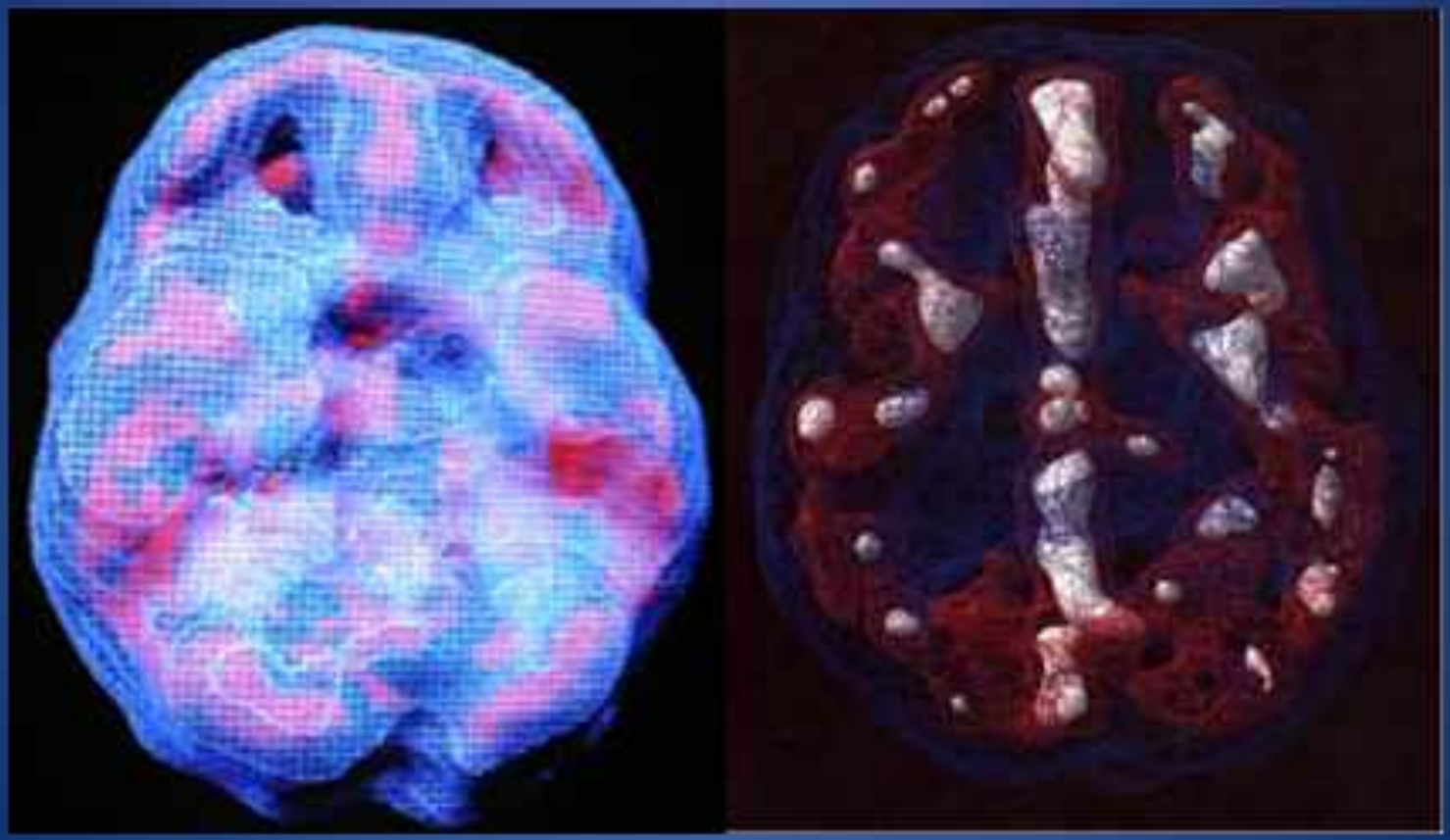

Neurotransmitters
Neurology
Anxiety
Depression
Insomnia
Neurotransmitters
Neurotransmitters
State
Of
Change
HP-Thyroid
HP-Adrenal
HP-Gonadal
Pain
Inflammation
Autoimmunity
Endocrinology
Cytokines
Hormones
Immunology

Recognizing Inflammation through NT testing: Elevated Histamine and the 3 - G's




Neurotransmitters
Neurology
Anxiety
Depression
Insomnia
Neurotransmitters
Hormones
Inflammation
Cytokines
Neurotransmitters
HP-Thyroid
HP-Adrenal
HP-Gonadal
Pain
Inflammation
Autoimmunity
Endocrinology
Cytokines
Hormones
Immunology

The Inflamed Brain

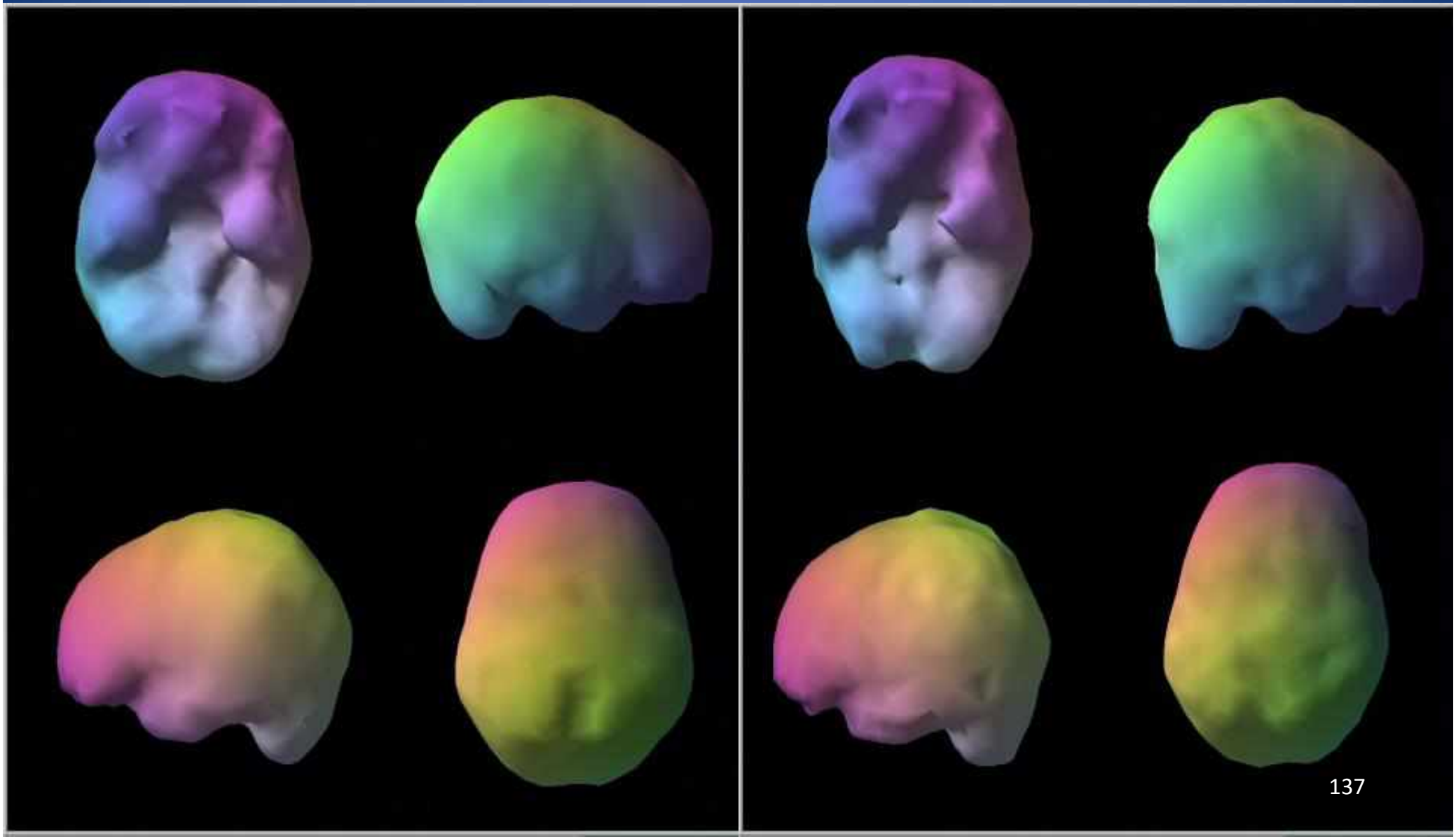



TIME
BUSH'S MILITARY RECORDS IS DISNEY MOUSETRAPPED?
THE SECRET KILLER
The surprising link between INFLAMMATION and HEART ATTACKS, CANCER, ALZHEIMER'S and other diseases
What you can do to fight it

Surface SPECT

At Rest

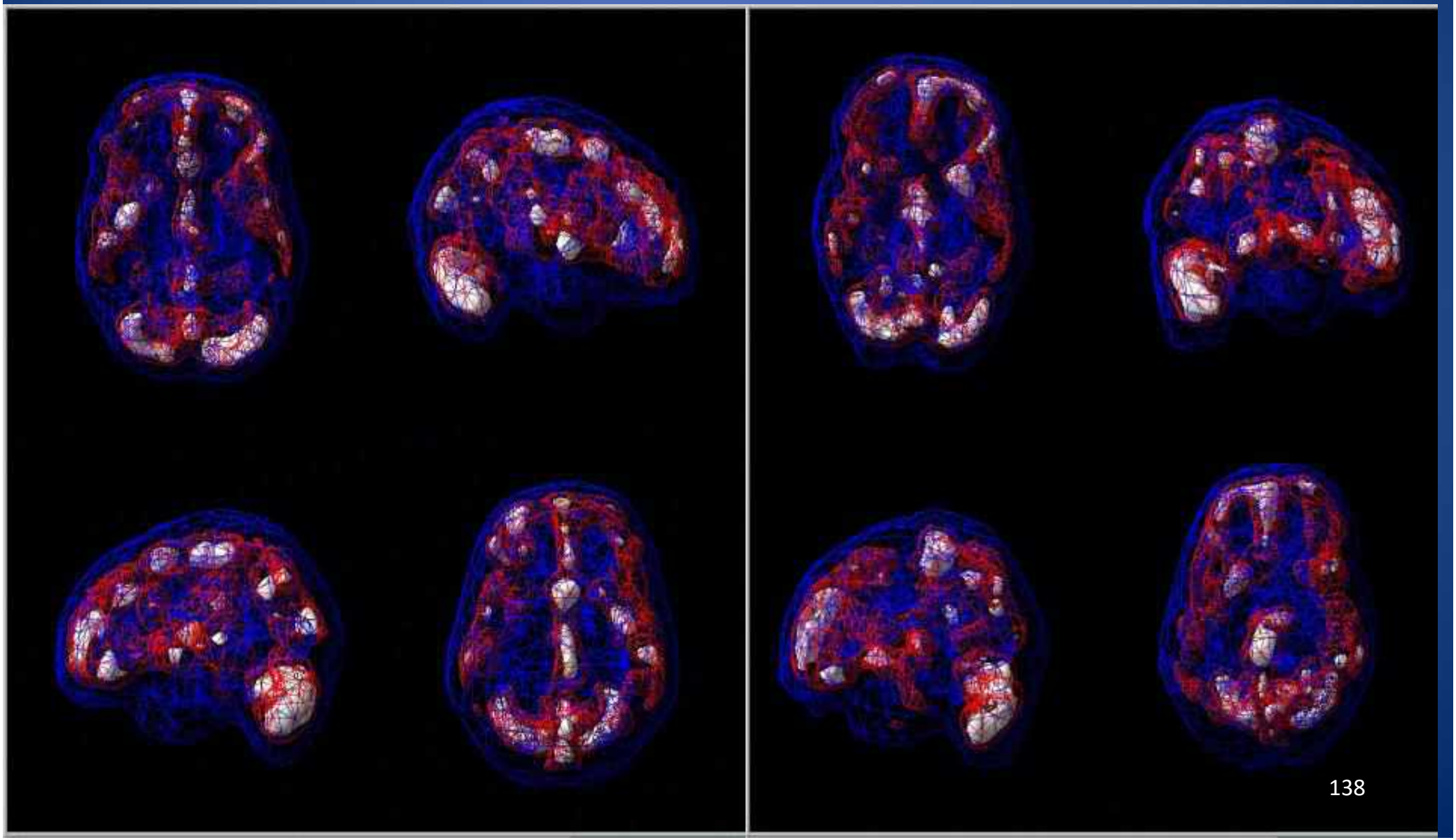
Concentration



SUB CORTICOL SPECT IMAGING

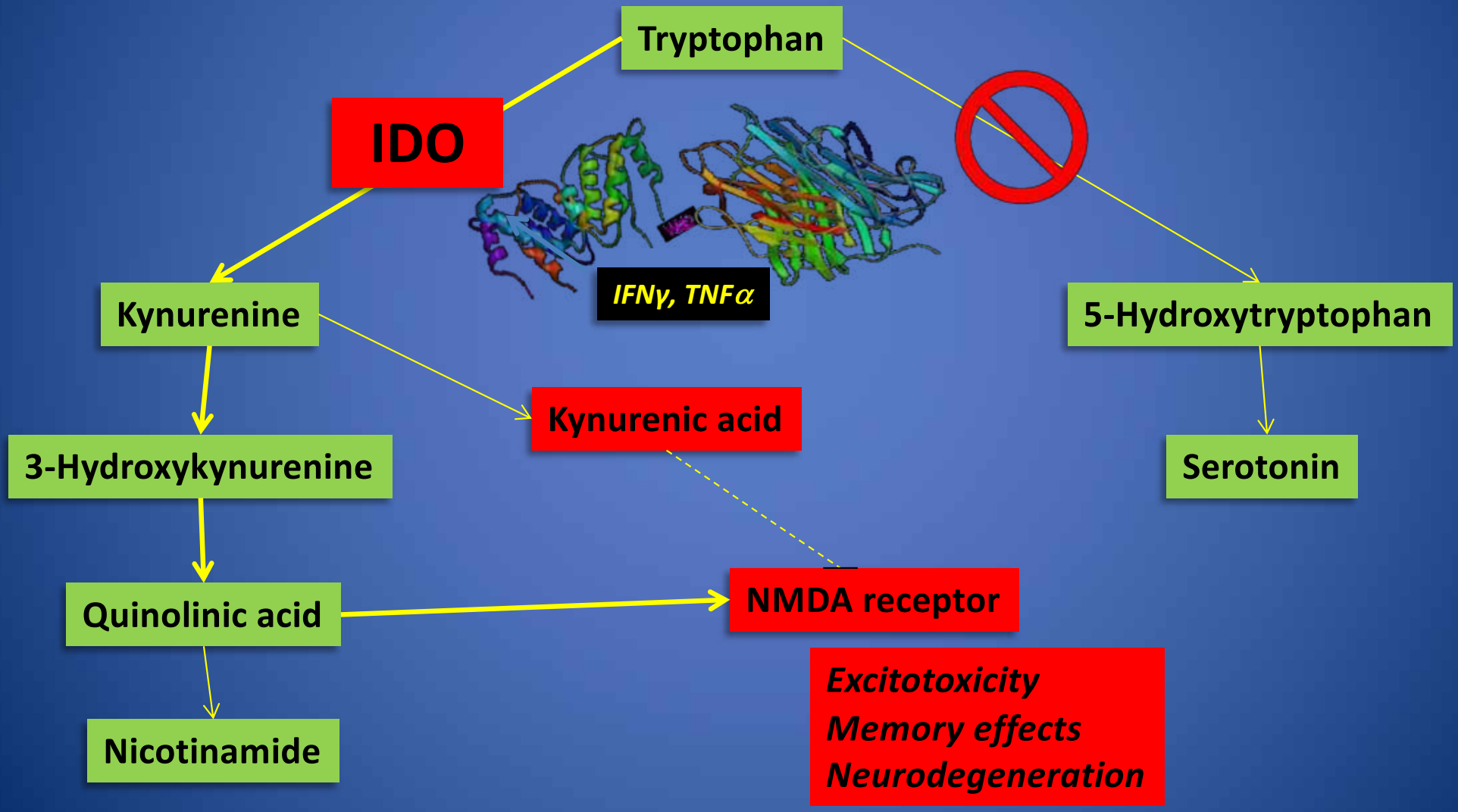
at rest

concentration



Glutamate & Increased Histamine In Excess = Neuroexcitotoxic

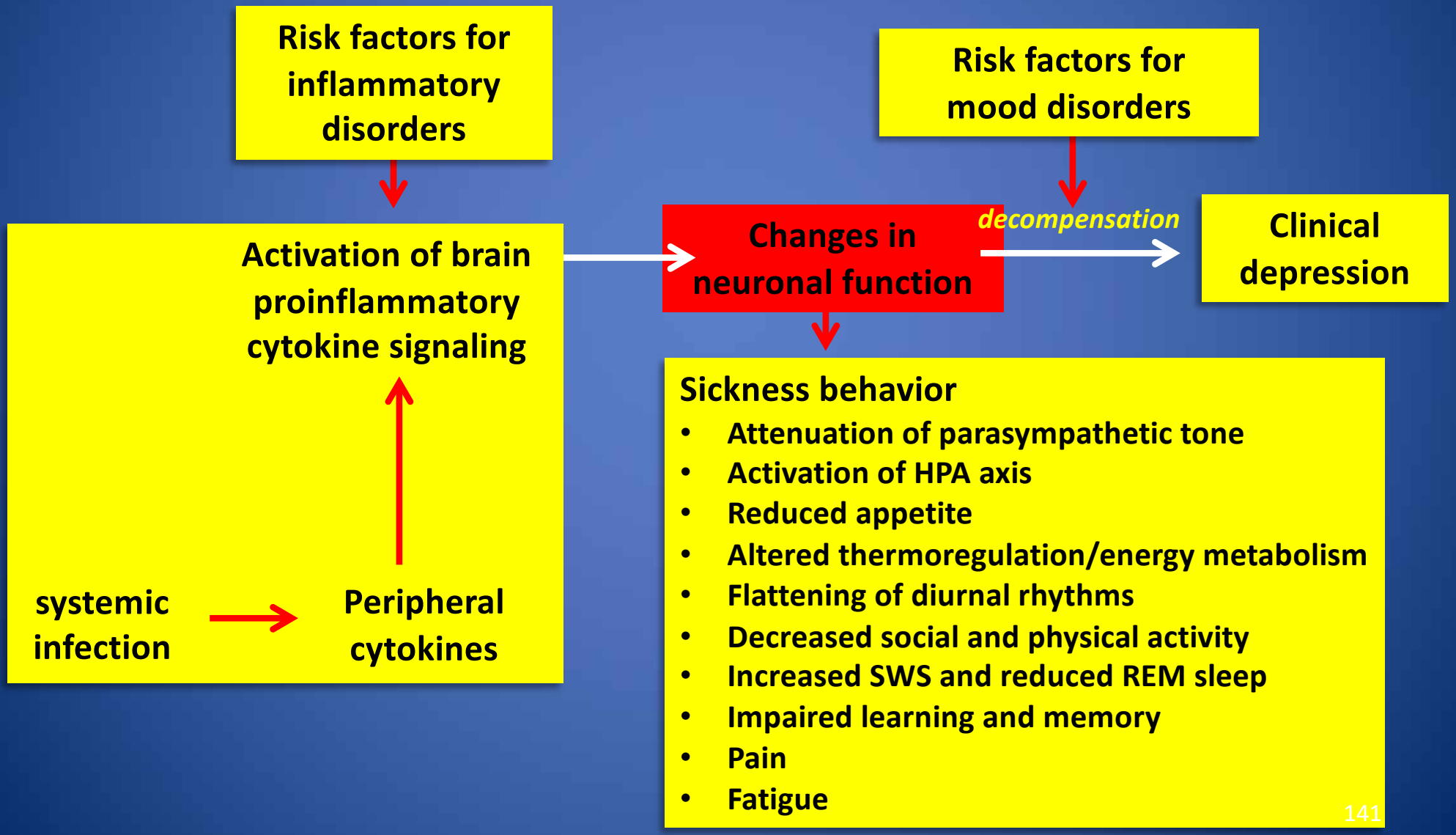
Depression: the Inflammation-Serotonin link



IDO: indoleamine 2,3-dihydroxyoxygenase

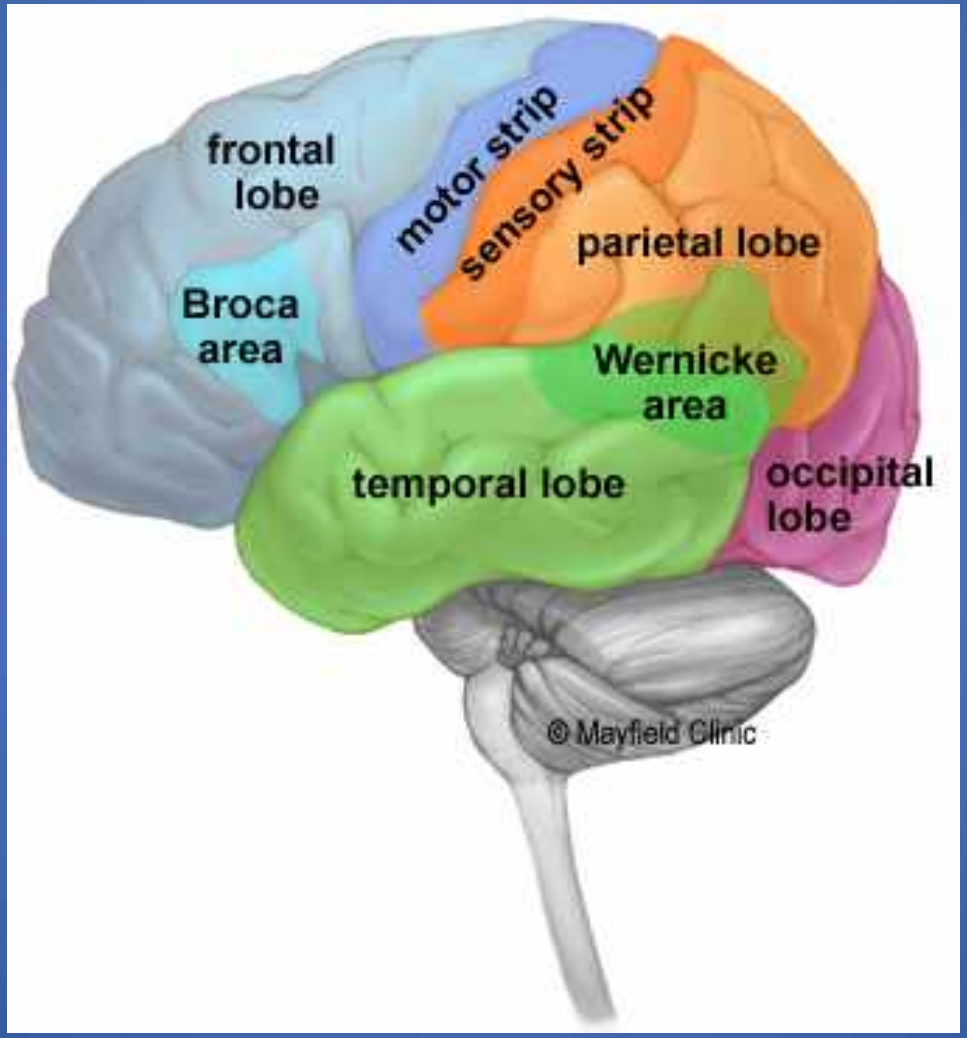
Adapted from Dantzer R et al. (2008). *Nat Rev Neurosci.* 9(1):46-569:46-57.

How can inflammation lead to clinical symptoms?

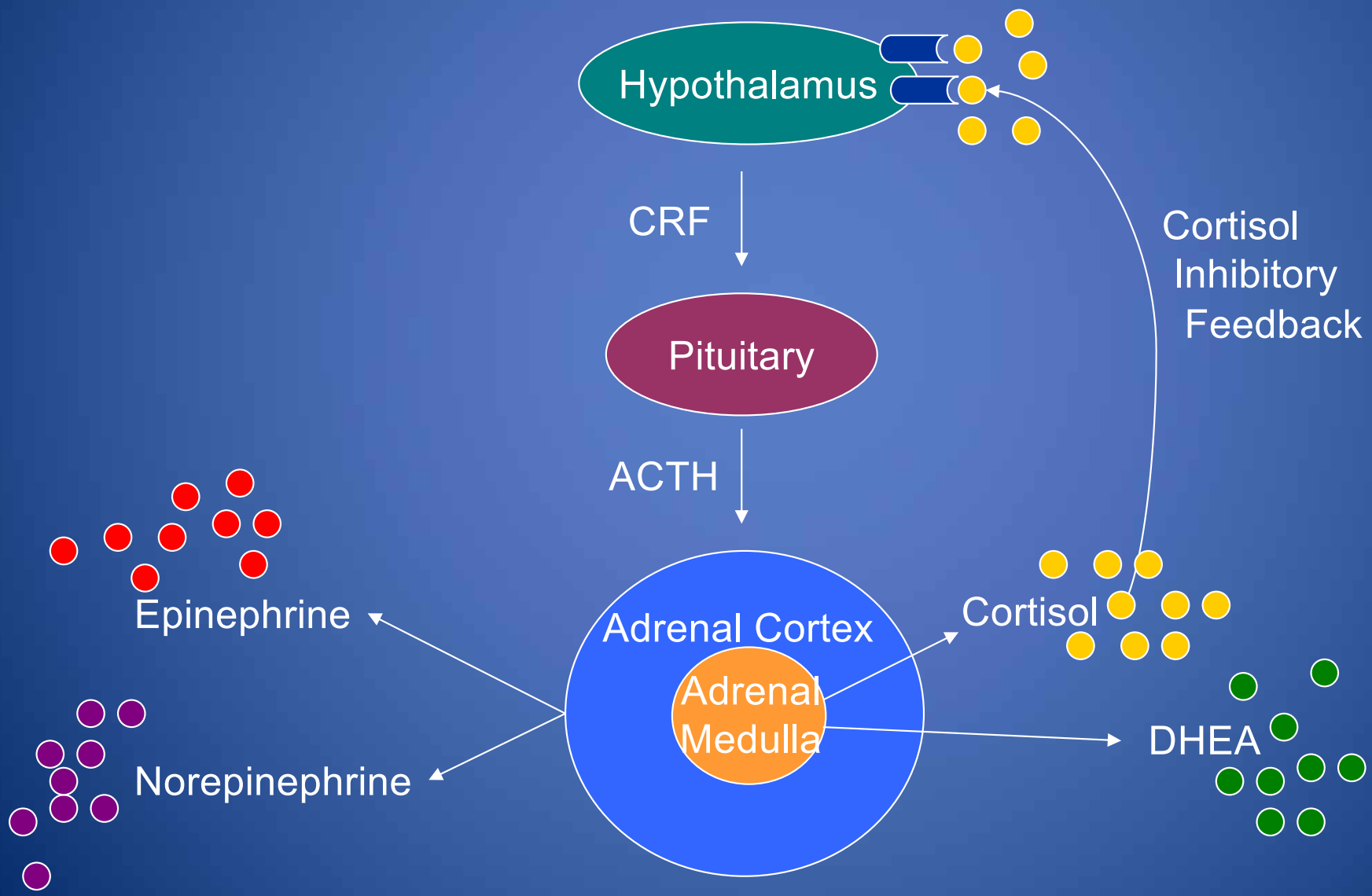


Adapted from Dantzer R et al. (2008). *Nat Rev Neuroscience* 9:46-57.

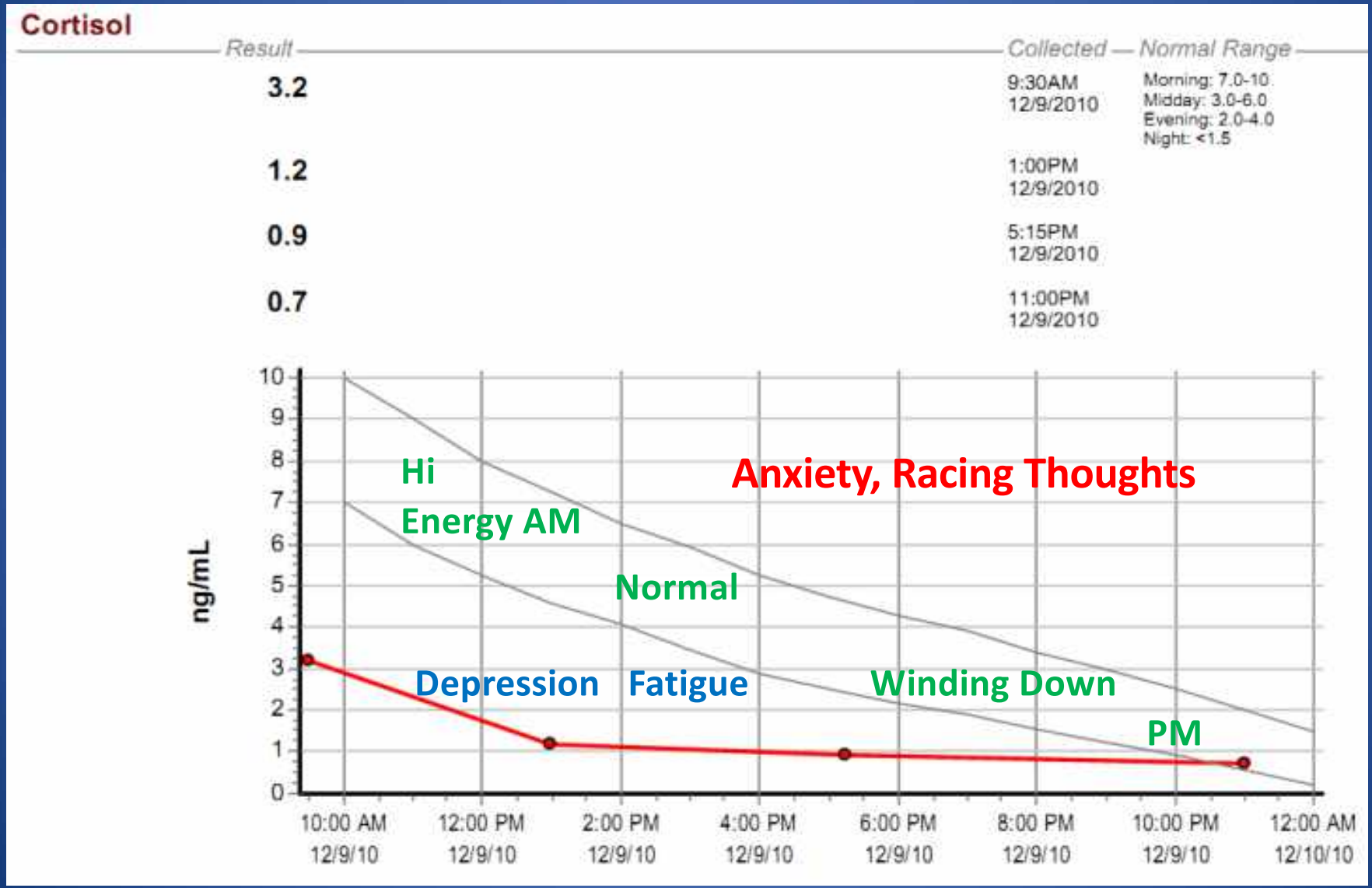
Neuro-immuno-endo-psychopharmacology



HPA Stress Response



Cortisol Graph

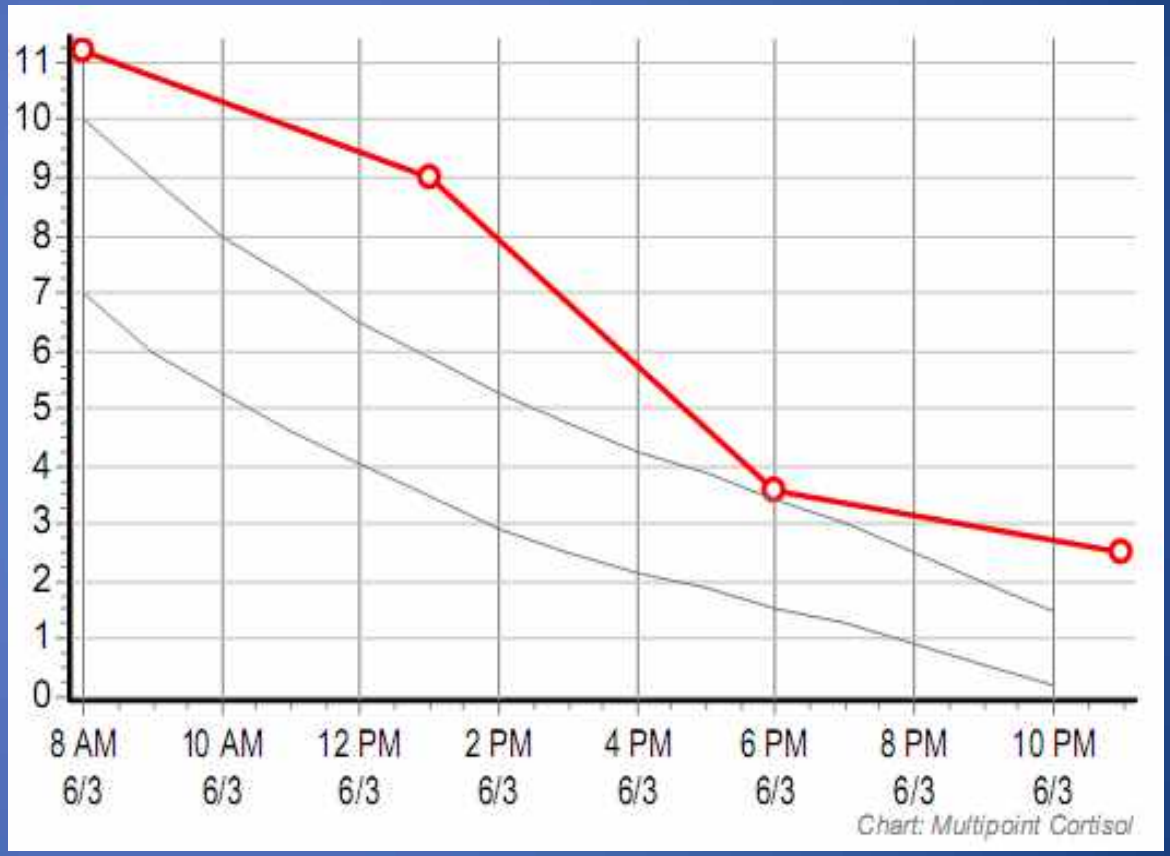


Acute Inflammation
Histamine and the 3 G's

Neurotransmitters

	2.5% 20% 80% 97.5%	Result
Serotonin		179.5
5-HIAA		4,359.6
GABA		8.8 (H)
Taurine		187.4
Glycine		2,369.1 (H)
Glutamate		50.2 (H)
Histamine		102.2 (H)
PEA		103.8 (H)
Dopamine		525.8 (H)
DOPAC		1,665.3 (H)
Norepinephrine		133.6 (H)
Epinephrine		23.3 (H)

Red or light red bars indicate results out of Inter-Quintile Range.

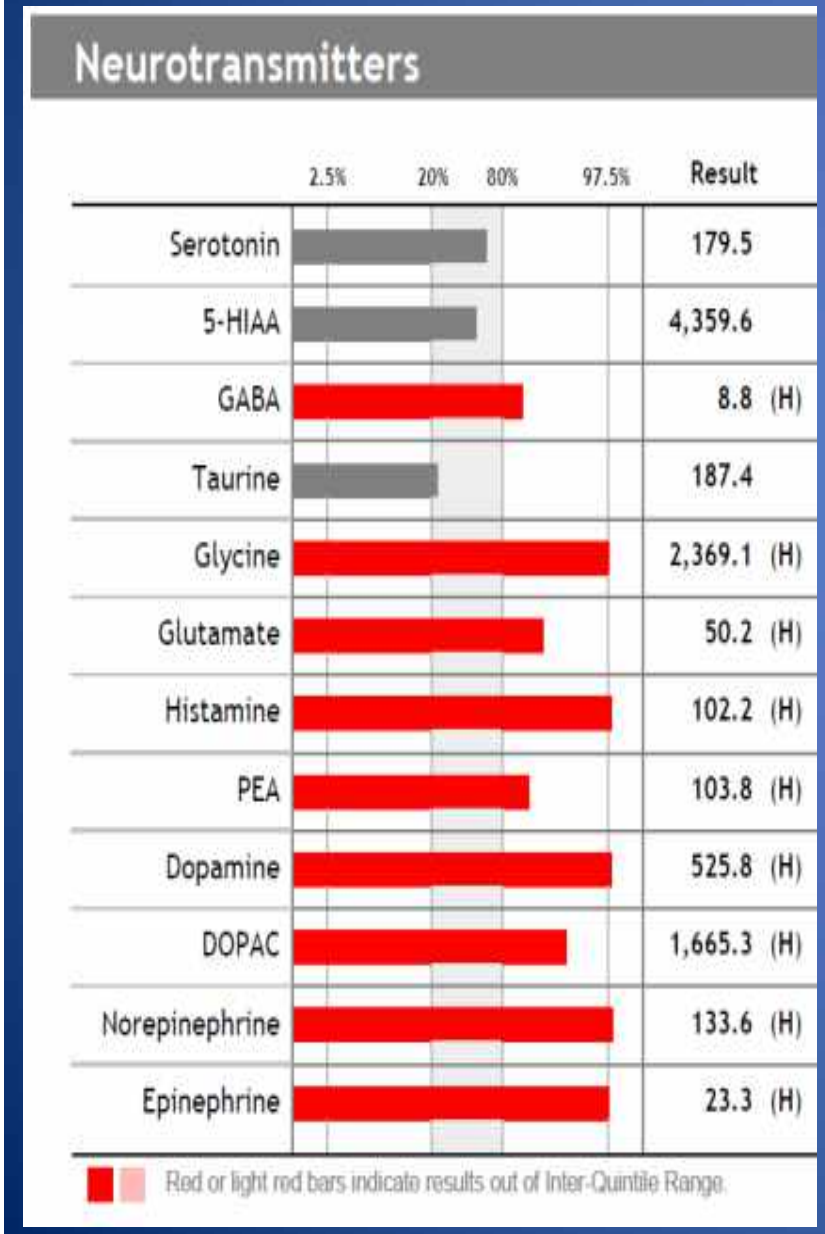


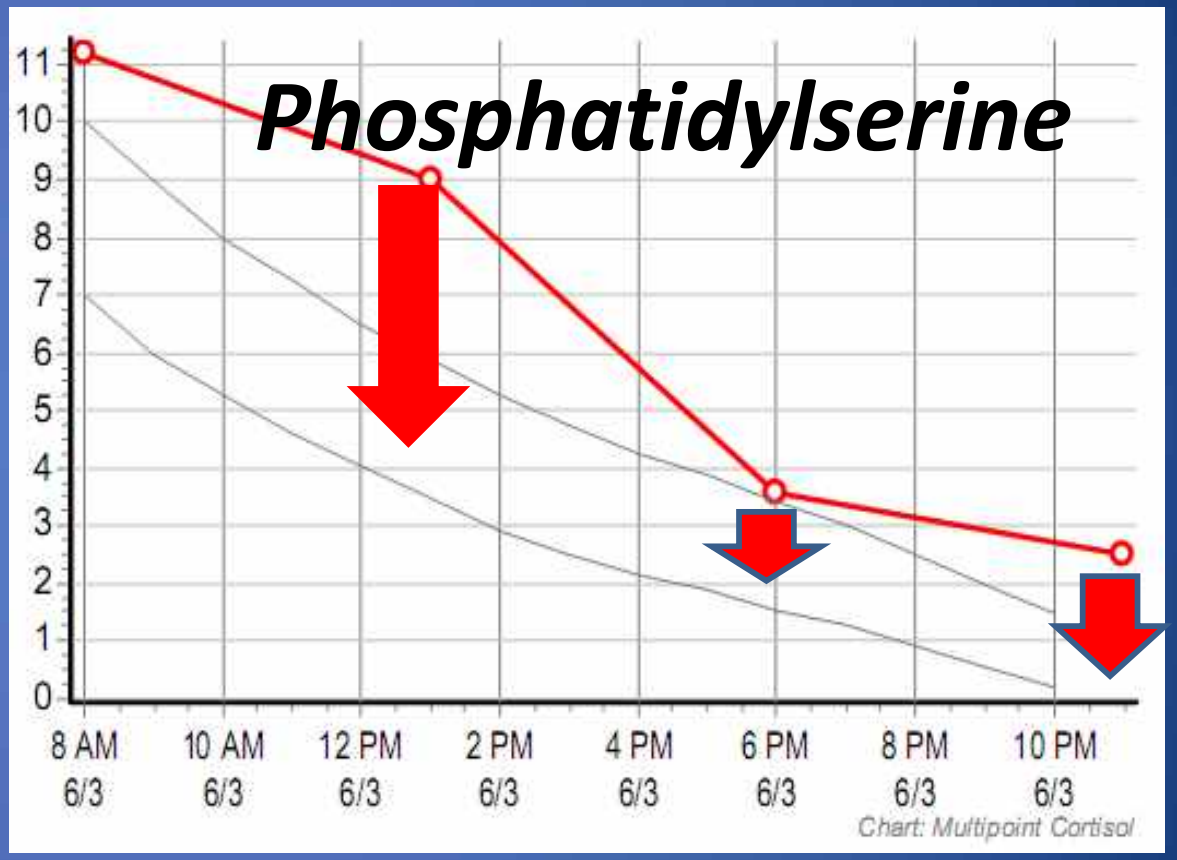
Cortisol and PTSD

October 16, 2012 | By: Khalil A. Cassimally

Fukushima Dogs Had Symptoms Comparable To Post-traumatic Stress Disorder

Lowering High Cortisol Levels



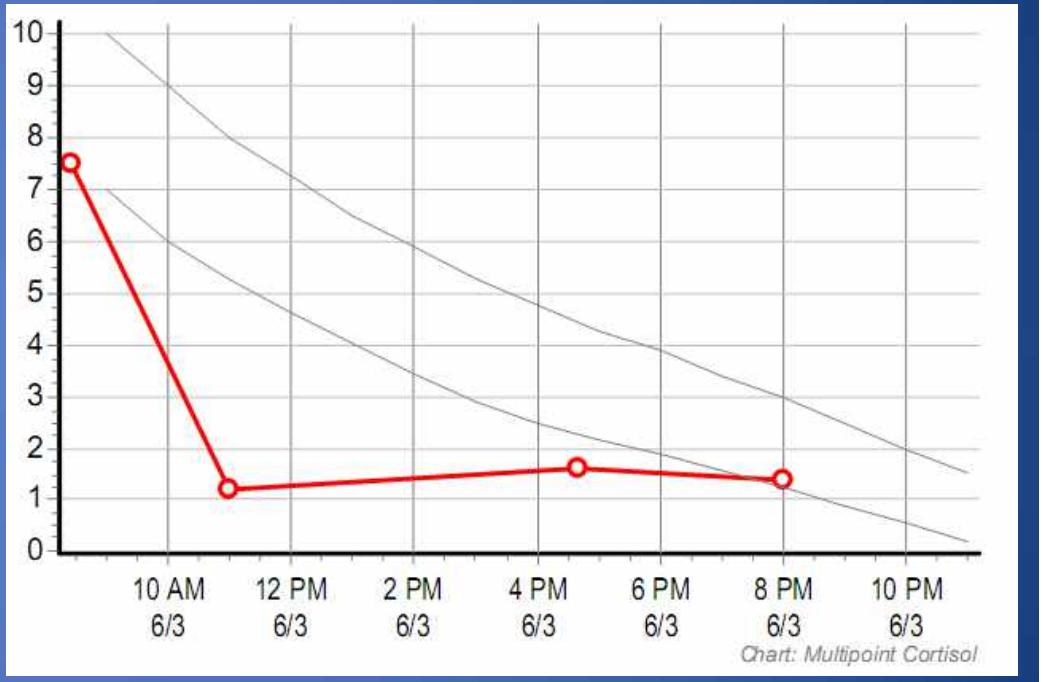


Biomarkers for transitional inflammation

Neurotransmitters

	2.5% 20% 80% 97.5%	Result
Serotonin		238.0 (H)
5-HIAA		5,426.4
GABA		5.9
Taurine		494.0
Glycine		1,284.7 (H)
Glutamate		42.2 (H)
Histamine		24.5
PEA		65.2
Dopamine		286.2 (H)
DOPAC		573.4
Norepinephrine		58.9 (H)
Epinephrine		7.9

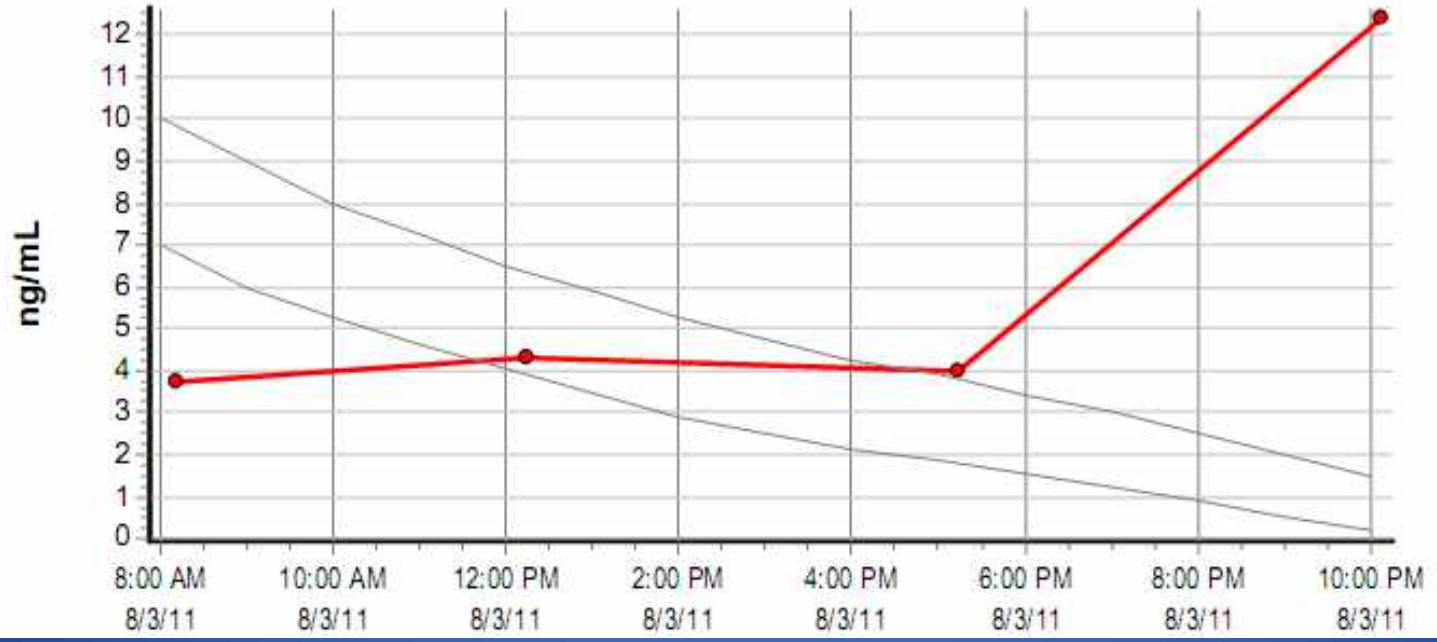
Red or light red bars indicate results out of Inter-Quintile Range.



The Vampires VS The Humans

Cortisol — Saliva - ng/mL

Result	Collected	Normal Range	Observed Range
3.7	8:12AM 8/3/2011	Morning: 7.0-10 Midday: 3.0-6.0 Evening: 2.0-4.0 Night: <1.5	Morning: 8.0-15.0 Midday: 3.0-7.0 Evening: 2.0-4.0 Night: <1.5
4.3	12:15PM 8/3/2011		
4.0	5:15PM 8/3/2011		
12.4	10:08PM 8/3/2011		



Elevating Low Cortisol Levels

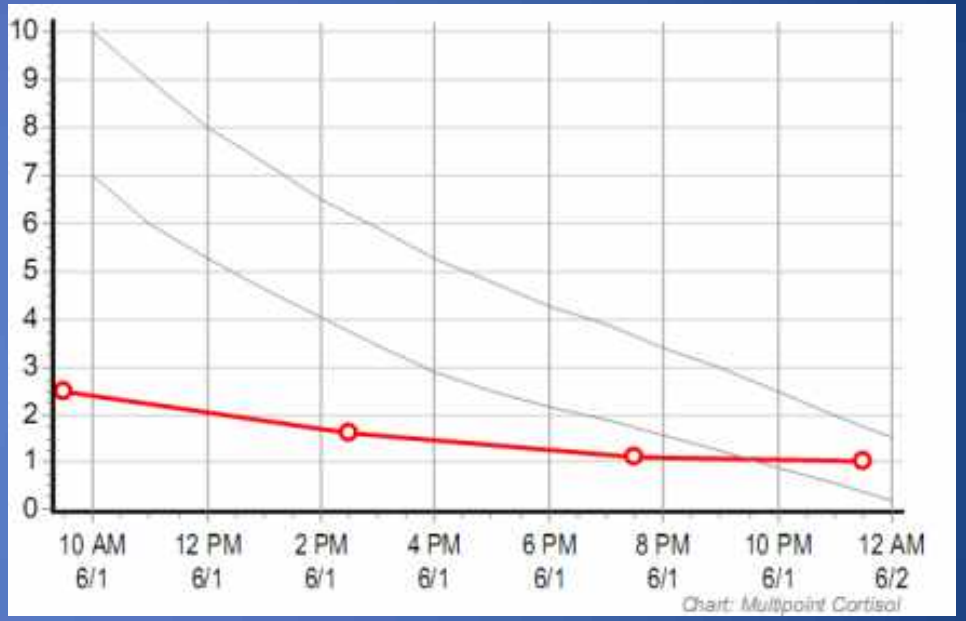
Rhodiola Rosea
Ashwagandha
Licorice Root
Holy Basil

Biomarkers for chronic inflammation

Neurotransmitters

	2.5% 20% 80% 97.5%	Result
Serotonin		61.3 (L)
5-HIAA		3,116.4
GABA		3.3 (L)
Taurine		41.9 (L)
Glycine		434.6 (L)
Glutamate		10.3 (L)
Histamine		4.0 (L)
PEA		25.6 (L)
Dopamine		122.4
DOPAC		481.9
Norepinephrine		23.3 (L)
Epinephrine		4.2 (L)

Red or light red bars indicate results out of Inter-Quintile Range.

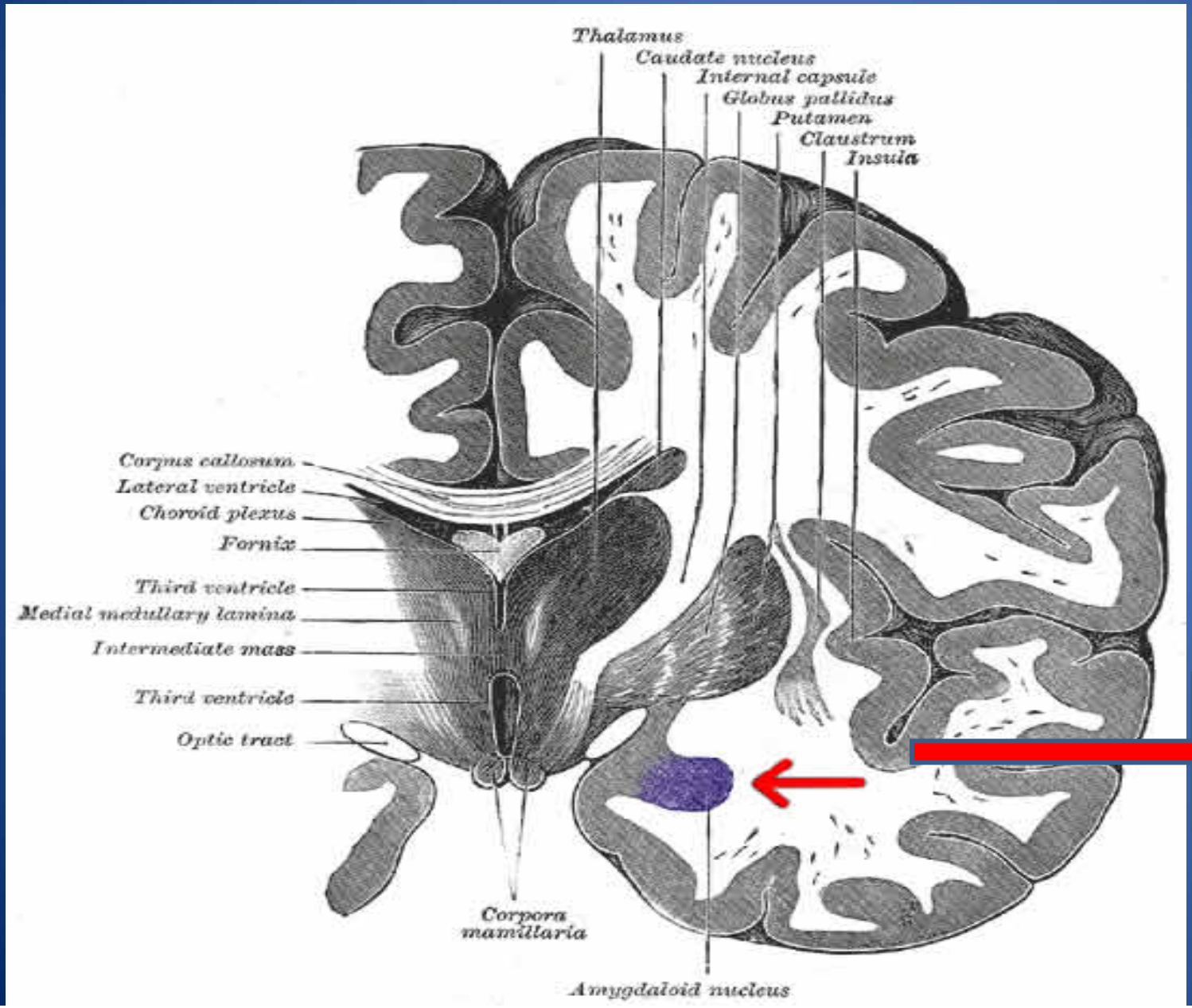


DHEA Saliva	34.1	pg/mL

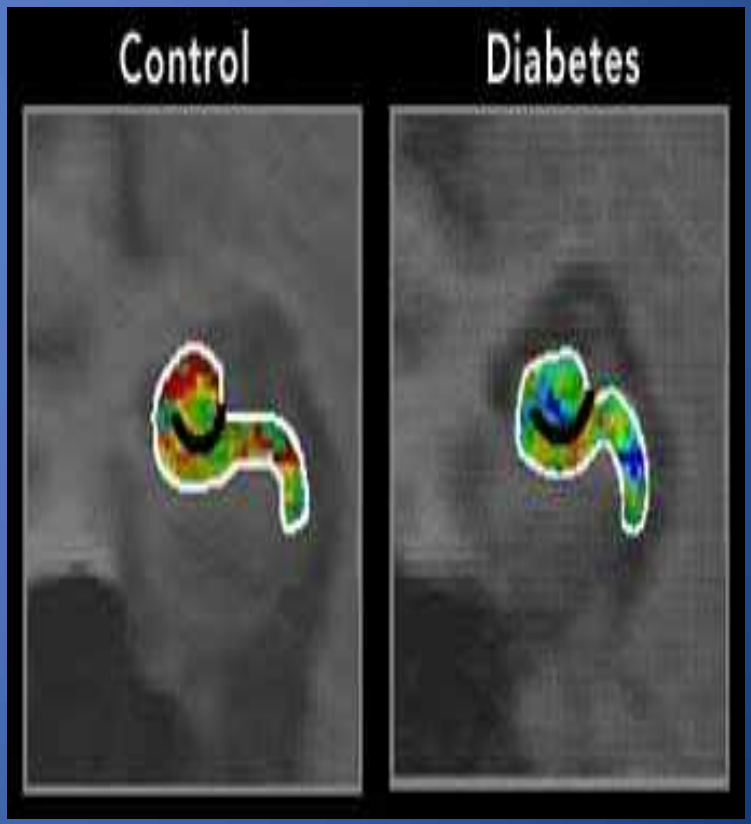

WORK
FREE TIME

Two "Weak" Vacation

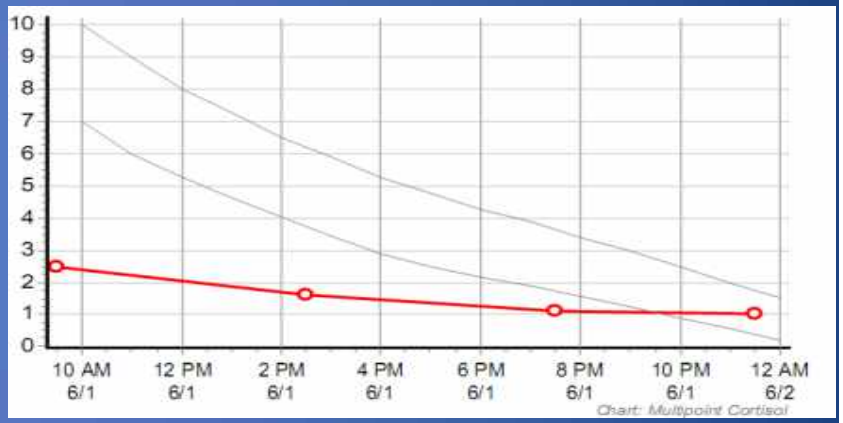
Hippocampus – learning and memory



Untreated Depression , Addiction , Diabetes , PTSD, Alzheimer's disease can Decrease Hippocampal Volume (↓ Memory and Learning)



	Result	Collected	Normal Range
Epinephrine RO	5.8 Low (0 7 12 25)	3:10PM 6/2/2011	Day: 7-12 Night: 4-6
Norepinephrine RO	17.2 Low (0 30 45 100)	3:10PM 6/2/2011	Day: 30-45 Night: 15-23
Dopamine RO	58.7 Low (0 115 175 460)	3:10PM 6/2/2011	Day: 115-175 Night: 75-120
DOPAC RO	719.2 Low (0 790 1560 3000)	3:10PM 6/2/2011	Day: 790-1,560 Night: 530-930
Serotonin RO	70.6 Low (0 120 185 450)	3:10PM 6/2/2011	Day: 120-185 Night: 100-150
5-HIAA RO	1,305.0 Low (0 2100 5000 7500)	3:10PM 6/2/2011	Day: 2,100-5,000 Night: 2,000-3,300
Glycine RO	348.8 Low (0 455 980 2500)	3:10PM 6/2/2011	Day: 455-980 Night: 390-750
Taurine RO	98.0 Low (100 540 2400)	3:10PM 6/2/2011	Day: 100-540 Night: 65-360
GABA RO	3.9 Low (0 4.7 7 18)	3:10PM 6/2/2011	Day: 4.7-7.0 Night: 3.8-5.7
Glutamate RO	10.2 Low (0 15 32 100)	3:10PM 6/2/2011	Day: 15-32 Night: 12-22
PEA RO	12.5 Low (0 30 70 200)	3:10PM 6/2/2011	Day: 30-70 Night: 20-40
Histamine RO	6.5 Low (0 14 24 75)	3:10PM 6/2/2011	Day: 14-24 Night: 8-14



Did you know...

An estimated

300-400

physicians die by suicide each year in the U.S.

The suicide rate among male physicians is

1.41

times higher than the general male population.

The suicide rate among female physicians is

2.27

times higher than the general female population.

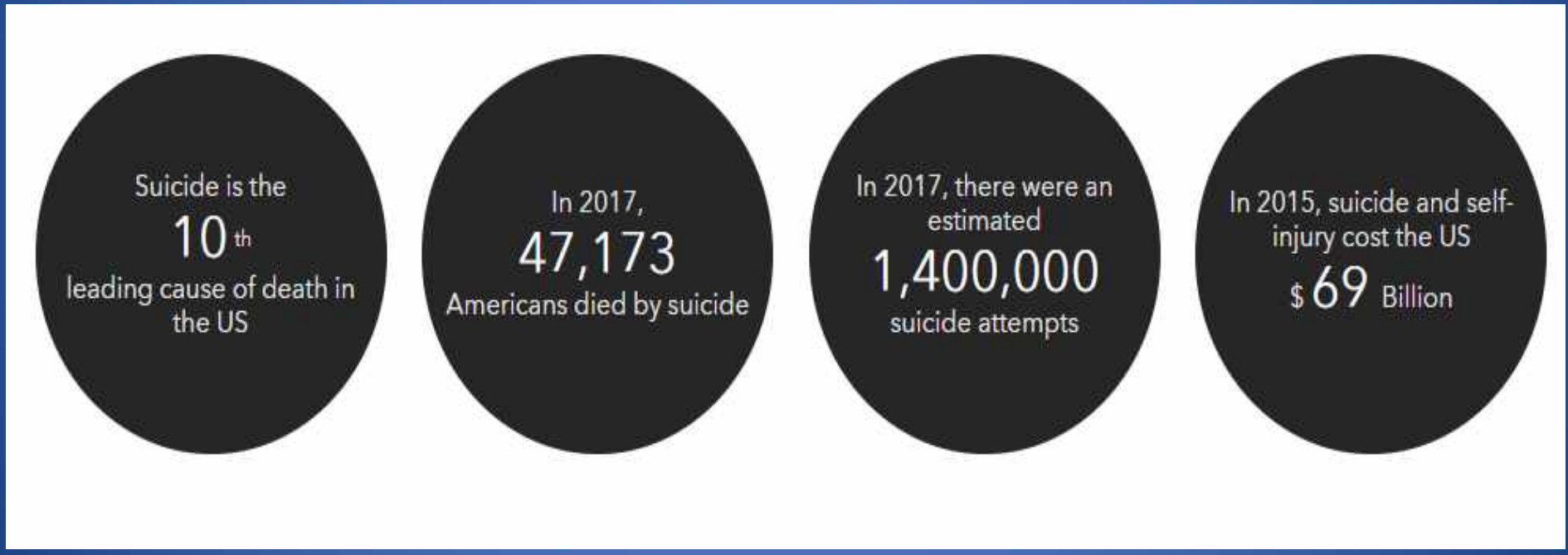
Physician Suicide

- Suicide generally is caused by the convergence of multiple risk factors — the most common being untreated or inadequately managed mental health conditions.

- Among physicians, risk for suicide increases when mental health conditions go unaddressed, and self-medication occurs as a way to address anxiety, insomnia or other distressing symptoms. Although self-medicating, mainly with prescription medications, may reduce some symptoms, the underlying health problem is not effectively treated. This can lead to a tragic outcome.

- Drivers of burnout include workload, work inefficiency, lack of autonomy and meaning in work, and work-home conflict.

American Foundation for Suicide Prevention



On average, there are 129 suicides per day.

2017

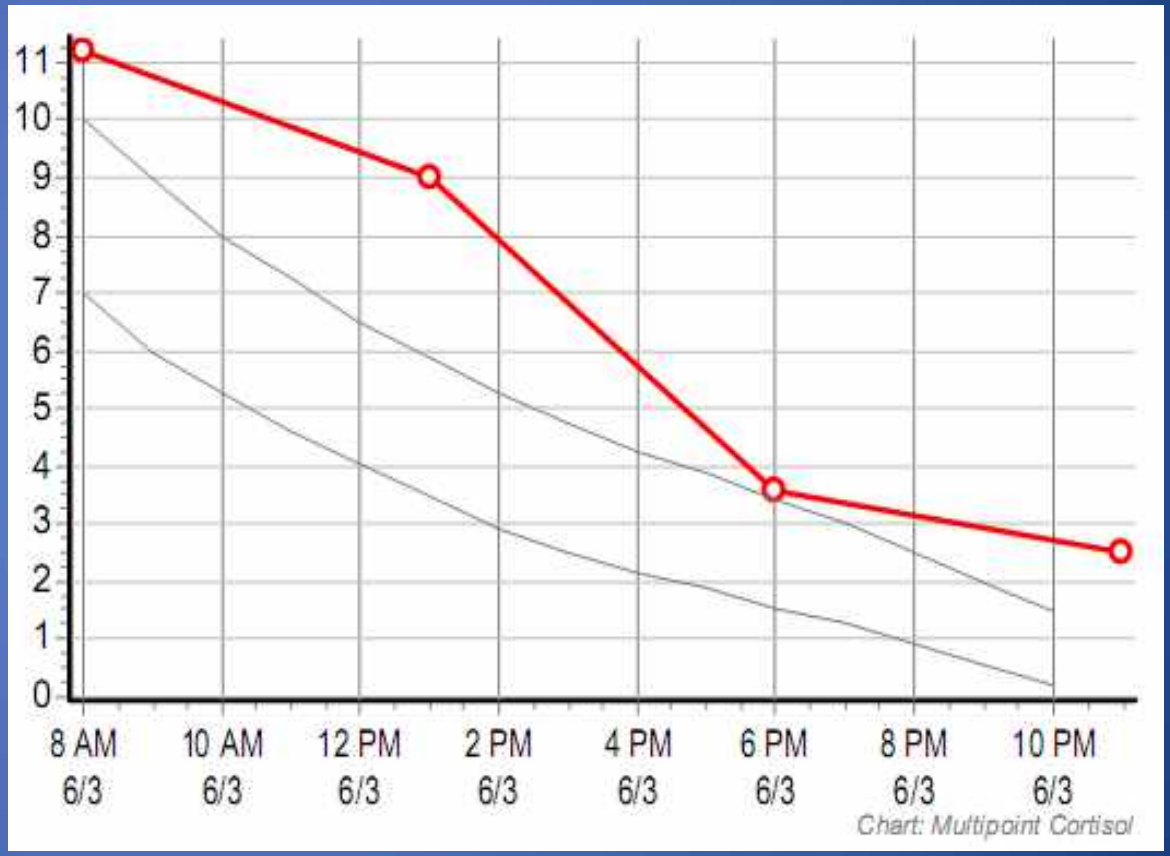
- **USA Homicide 2017 – 17, 284**
- **USA Suicides 2017 – 47,173**

Acute Inflammation
Histamine and the 3 G's

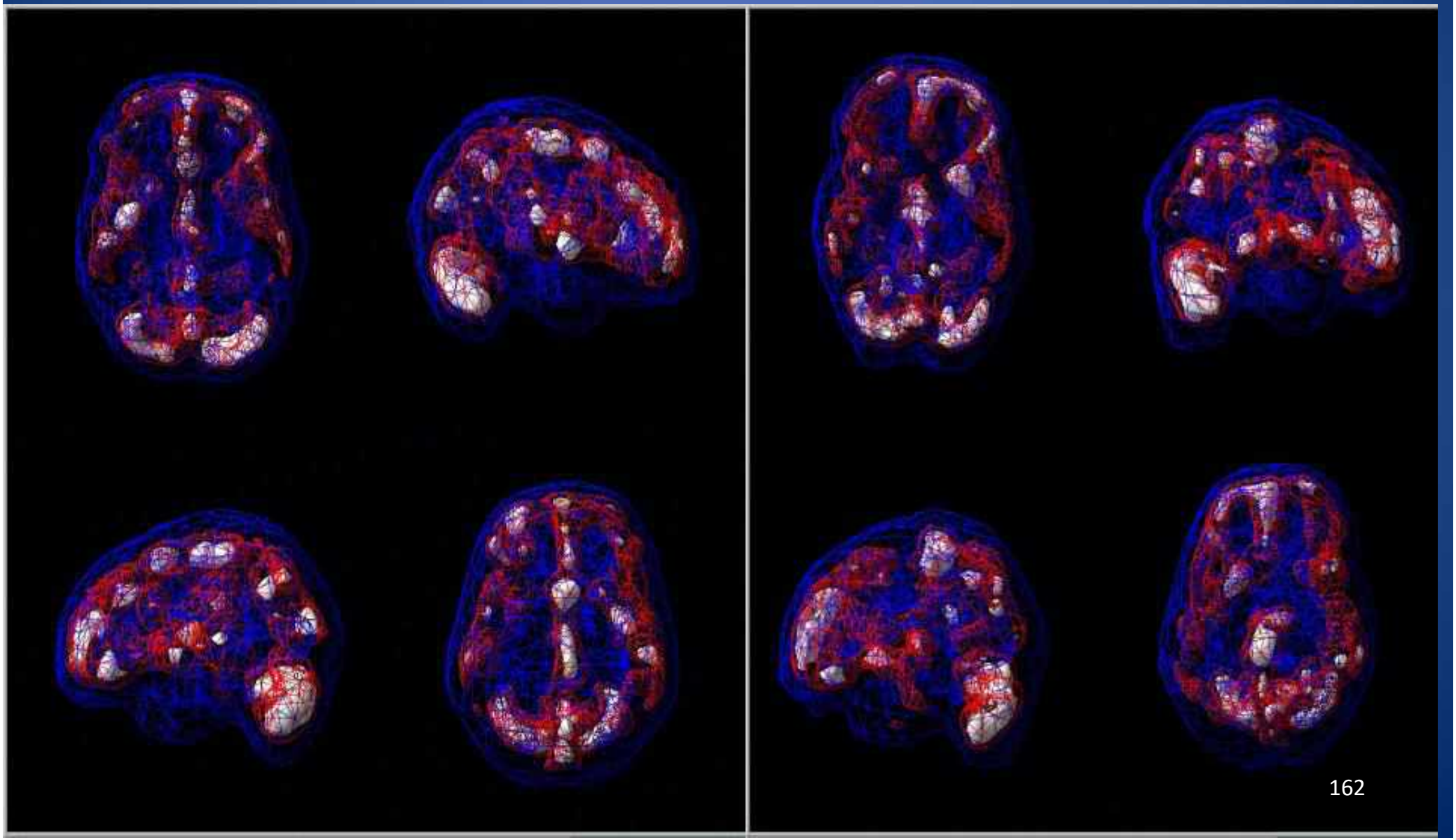
Neurotransmitters

	2.5% 20% 80% 97.5%	Result
Serotonin		179.5
5-HIAA		4,359.6
GABA		8.8 (H)
Taurine		187.4
Glycine		2,369.1 (H)
Glutamate		50.2 (H)
Histamine		102.2 (H)
PEA		103.8 (H)
Dopamine		525.8 (H)
DOPAC		1,665.3 (H)
Norepinephrine		133.6 (H)
Epinephrine		23.3 (H)

Red or light red bars indicate results out of Inter-Quintile Range.



Therefore Treat Early



Find the Root Cause of Inflammation

MTHFR

Genetics

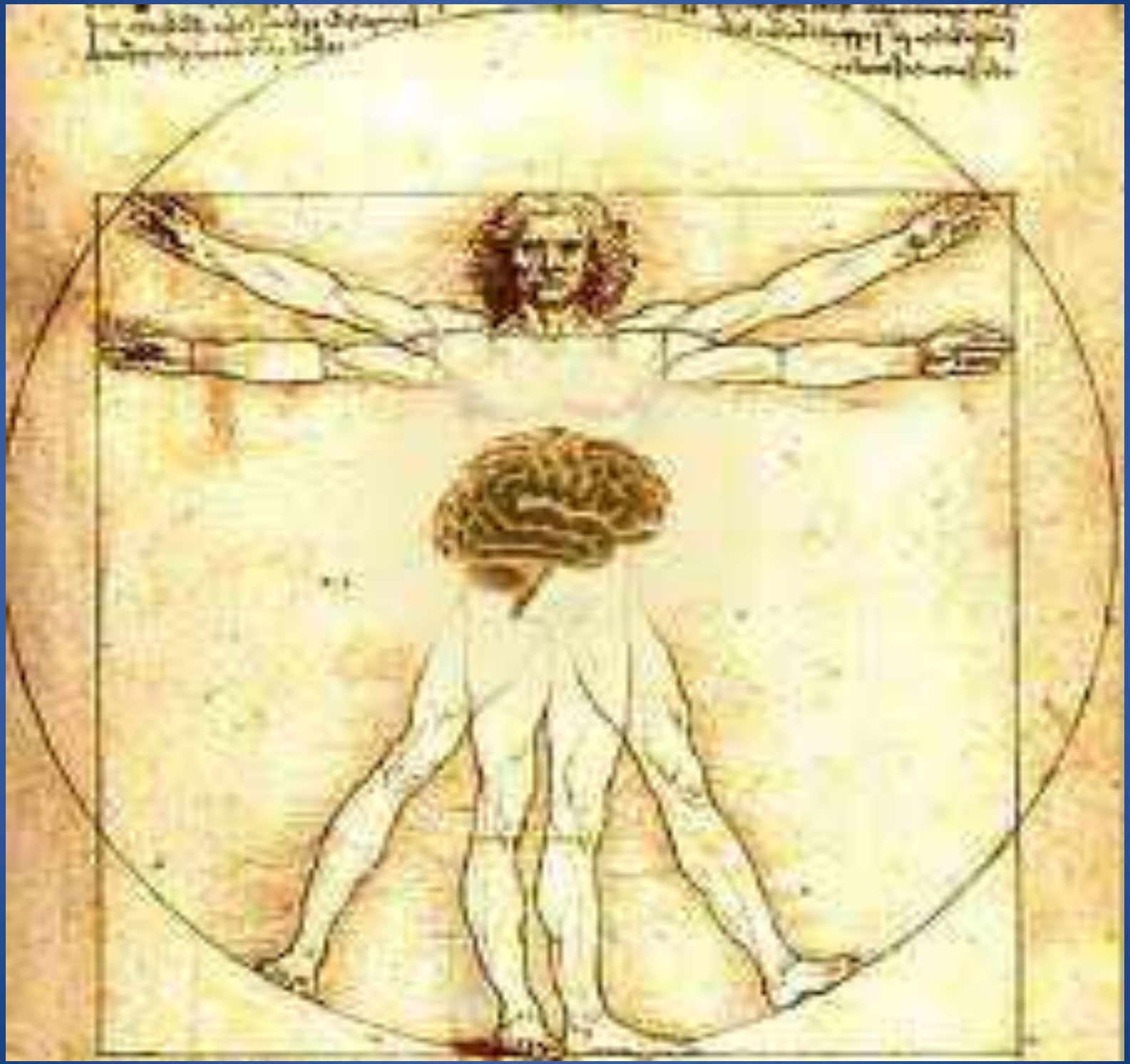
22 Y/O Male with Food Sensitivities and Chronic Drug Use

Neurotransmitters

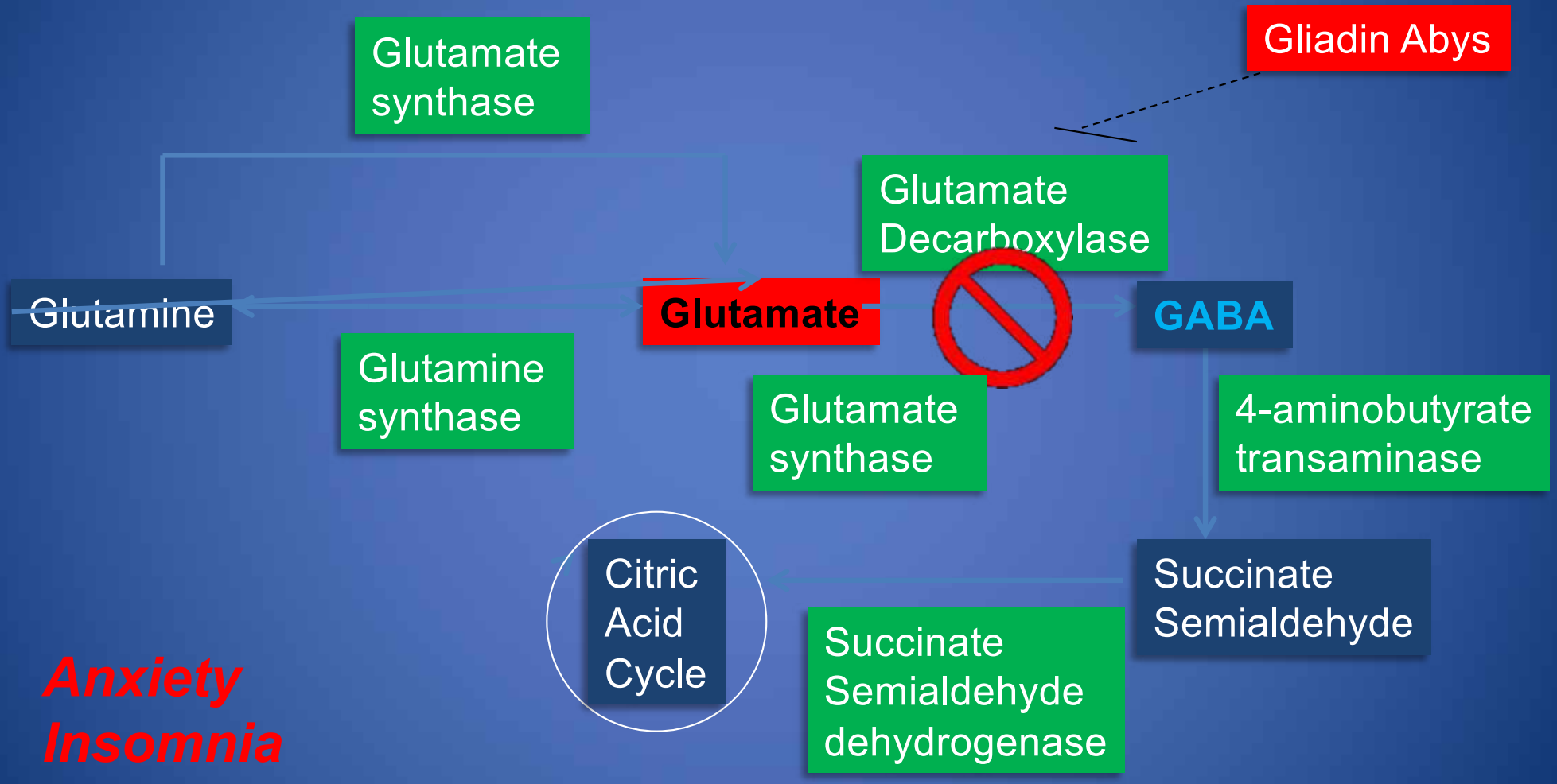
	Result	Collected	Inter-Quintile Range	Reference Range	Units
Serotonin	382.2 (H)	04/06/2012 (7:40AM)	99 - 203	57 - 306	µg/gCr
GABA	6.7	04/06/2012 (7:40AM)	3.9 - 7.9	2.4 - 12.7	µMol/gCr
Glycine	1,599.4 (H)	04/06/2012 (7:40AM)	441 - 1258	182 - 2225	µMol/gCr
Glutamate	107.4 (H)	04/06/2012 (7:40AM)	13.5 - 36.8	6.9 - 71.8	µMol/gCr
Histamine	75.3 (H)	04/06/2012 (7:40AM)	10 - 32	4 - 71	µg/gCr
PEA	153.2 (H)	04/06/2012 (7:40AM)	29 - 83	15 - 167	nMol/gCr
Dopamine	441.6 (H)	04/06/2012 (7:40AM)	106 - 191	64 - 261	µg/gCr
Norepinephrine	110.5 (H)	04/06/2012 (7:40AM)	28 - 51	19 - 76	µg/gCr
Epinephrine	27.4 (H)	04/06/2012 (7:40AM)	7.1 - 13.6	4.7 - 20.8	µg/gCr

Red or light red bars indicate results out of Inter-Quintile Range.

Inter-Quintile Range is defined as the 60th percentile, Reference Range as the 95th percentile.



Excitation: the inflammation-glutamate link



Anxiety
Insomnia
Trouble focusing
Anger or aggression

Hadjivassi R et al. (2004). *Trends in Immunology* 11:578-582.

The Brain in Your Gut

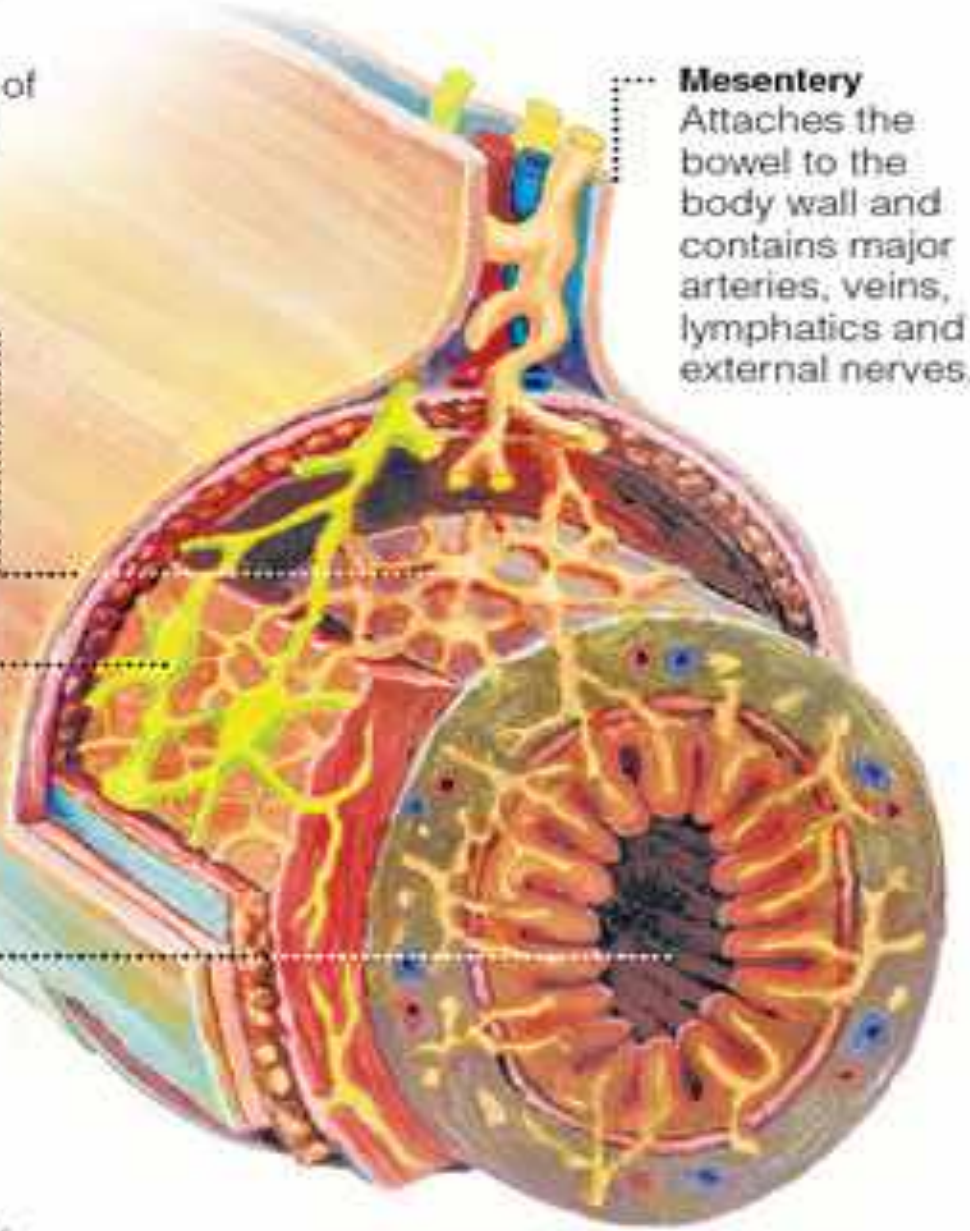
The gut's brain, known as the enteric nervous system, is located in sheaths of tissue lining the esophagus, stomach, small intestine and colon.

SMALL INTESTINE CROSS SECTION

Submucosal plexus Layer contains sensory cells that communicate with the myenteric plexus and motor fibers that stimulate the secretion of fluids into the lumen.

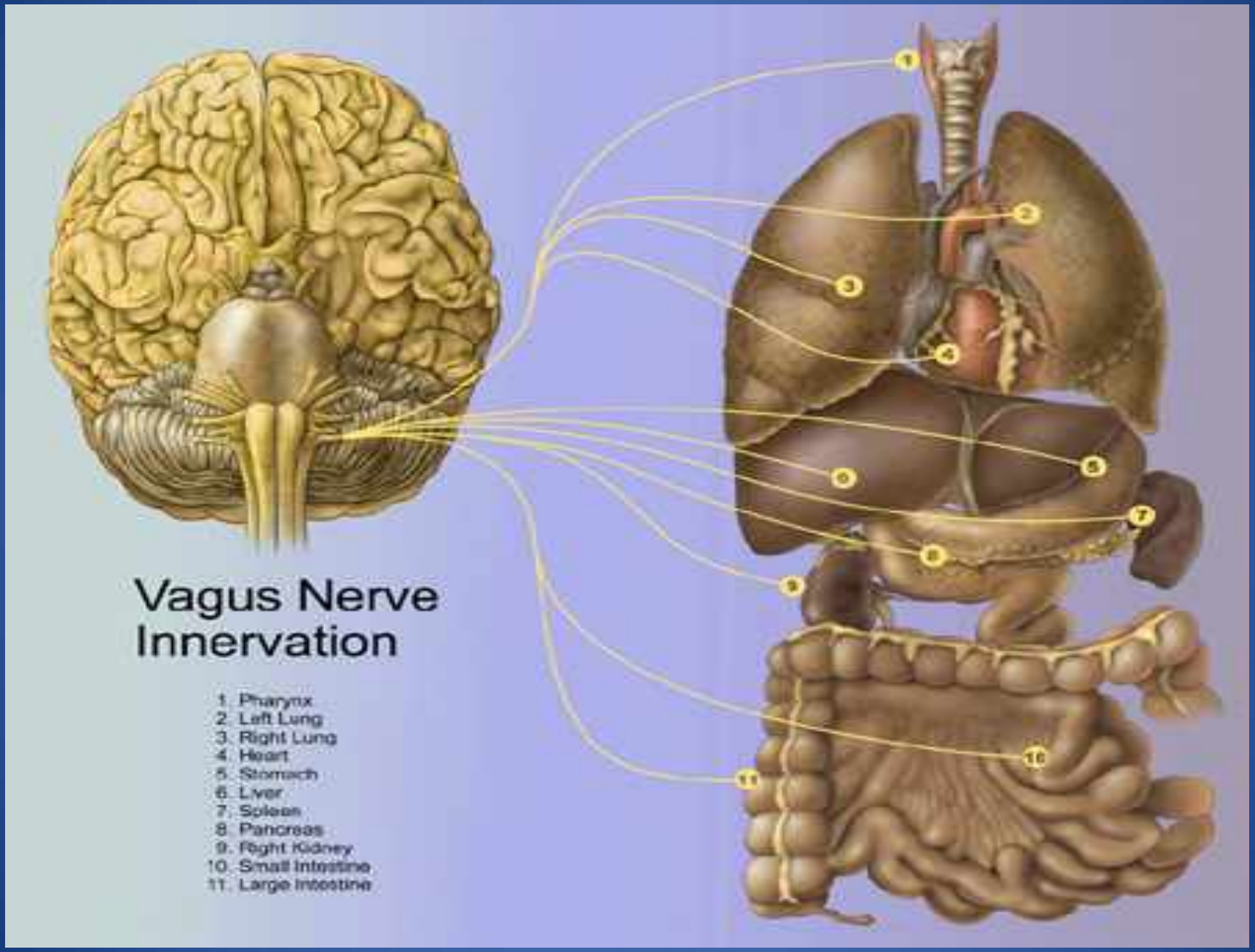
Myenteric plexus Layer contains the neurons responsible for regulating the enzyme output of adjacent organs.

Lumen No nerves actually enter this area, where digestion occurs. The brains in the head and gut have to monitor conditions in the lumen across the lining of the bowel.

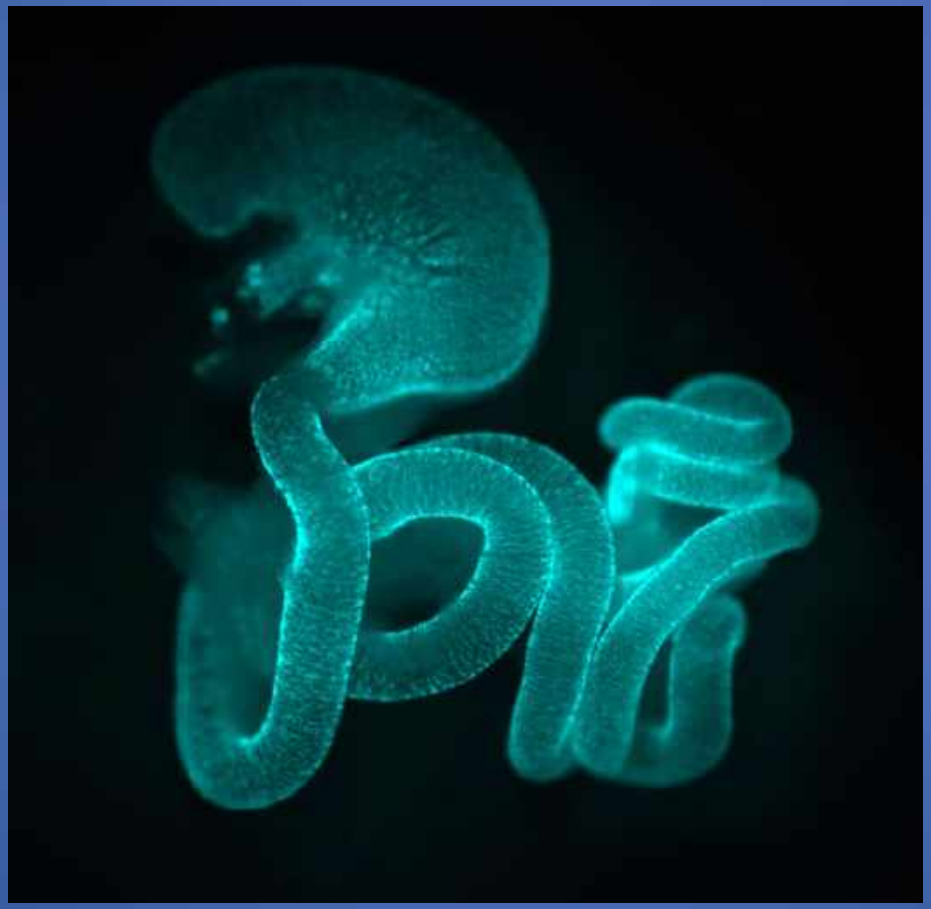


Mesentery Attaches the bowel to the body wall and contains major arteries, veins, lymphatics and external nerves.

Source: Dr. Michael D. Gershon, Columbia University


Vagus Nerve Innervation
1. Pharynx
2. Left Lung
3. Right Lung
4. Heart
5. Stomach
6. Liver
7. Spleen
8. Pancreas
9. Right Kidney
10. Small Intestine
11. Large Intestine

The Gut - Brain Relationship



Converging Scientific Discoveries

Enteric Neuroscience

Neuroimaging

Intestinal Microbiology

Host Microbial Interactions

Microbial Gut Brain Signaling

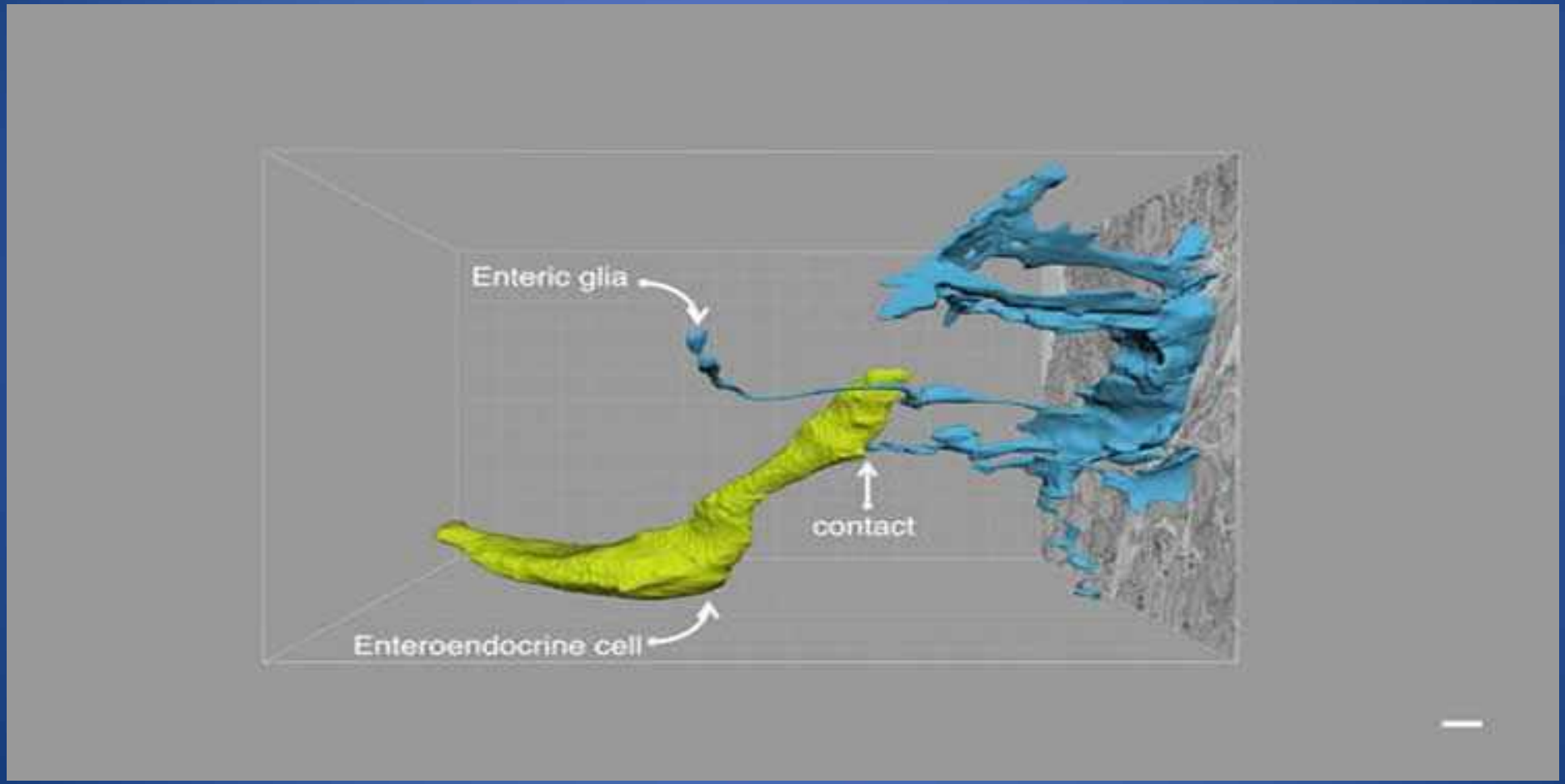
Enteric Neuroscience

“The study supports the idea that there could be a real biology of gut feelings……. as soon as food contacts the wall of the gut, the brain will know in real time what’s going on in the gut”

-Diego Bohórquez, Assistant Professor of medicine at Duke,
Postdoctoral Researcher in the lab of Dr. Rodger Liddle,
a professor of gastroenterology.

An image taken from 3-D electron microscopy reveals the structure of a Neuropod — a cell in the gut that senses nutrient levels and sends signals that govern appetite, but isn't a neuron.

Credit Diego Bohorquez, Duke University.



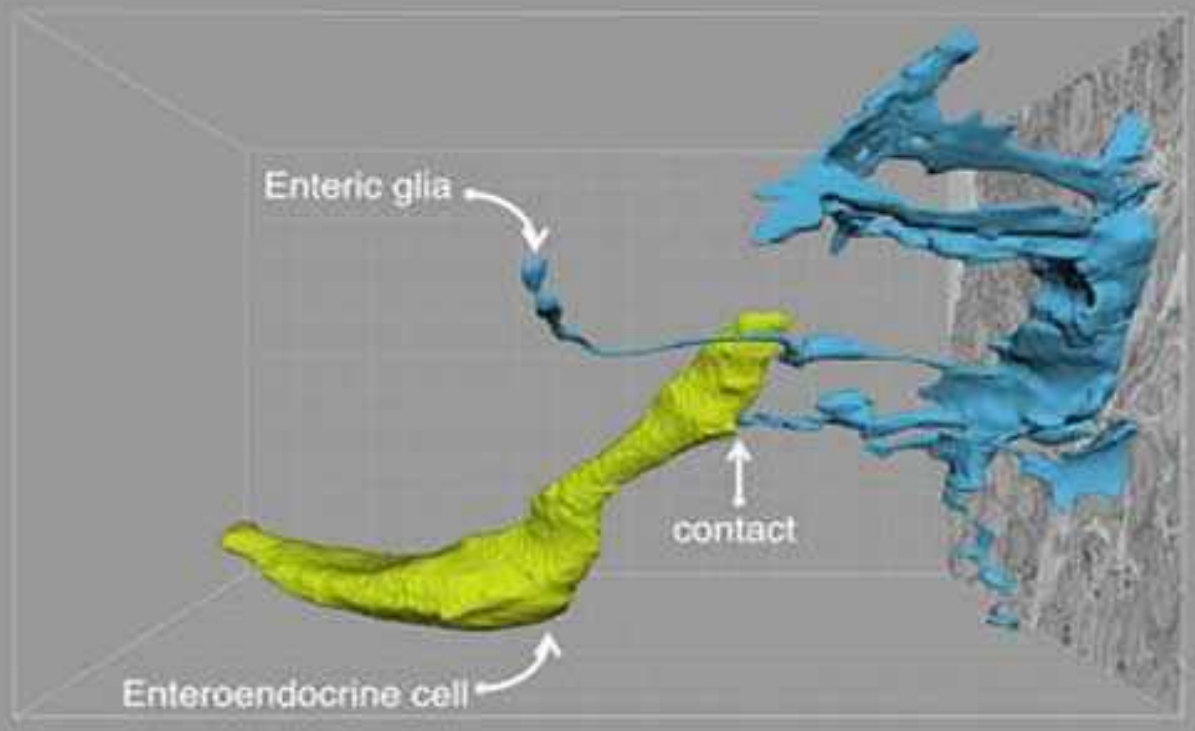
"Neuroepithelial circuit formed by innervation of sensory enteroendocrine cells"

by Diego V. Bohórquez, Rafiq A. Shahid, Alan Erdmann,
Alex M. Kreger, Yu Wang, Nicole Calakos, Fan Wang and Rodger A. Liddle
in *Journal of Clinical Investigation*. Published online January 2 2015 doi:10.1172/JCI78361

- Several years ago, **Liddle's team developed methods to visualize a type of cell found scattered throughout the lining of the mouse gut that is remarkably similar to a neuron.** Although the cells have a normal shape on the gut's surface, their underside bears a long arm.

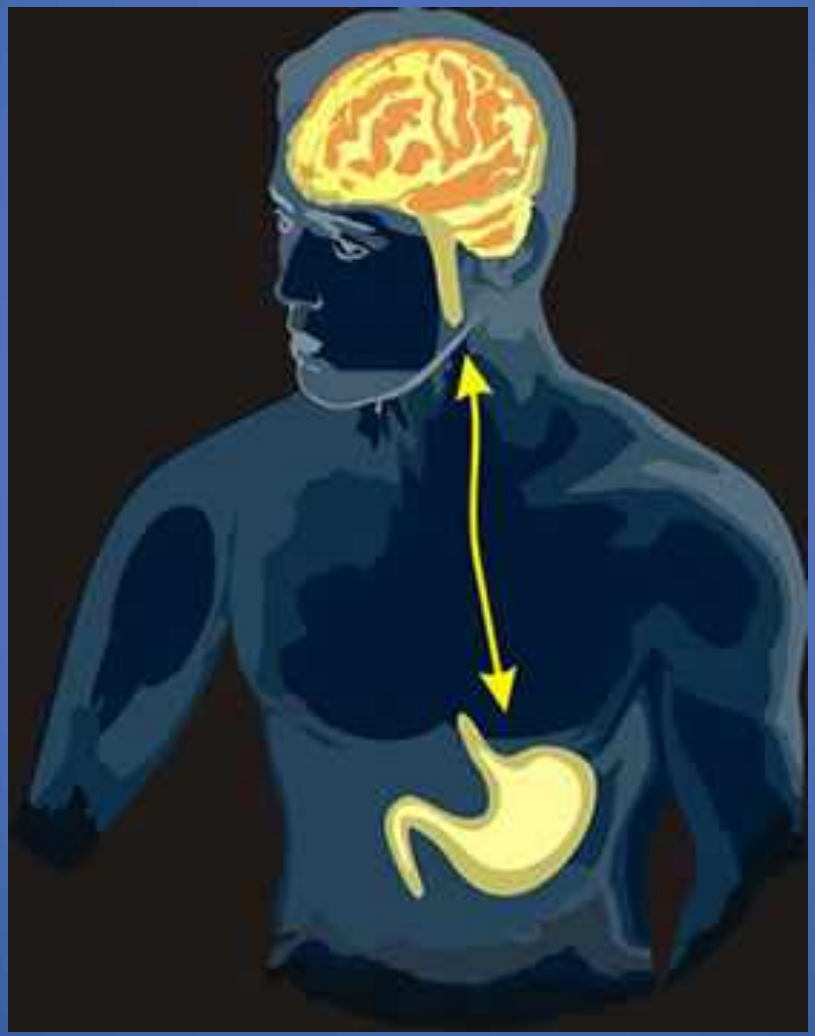
- **Dubbed 'Neuropods,' these special arms are nurtured by support cells known as glia that work with neurons, which suggested at the time that they could be involved in a neuronal circuit.**

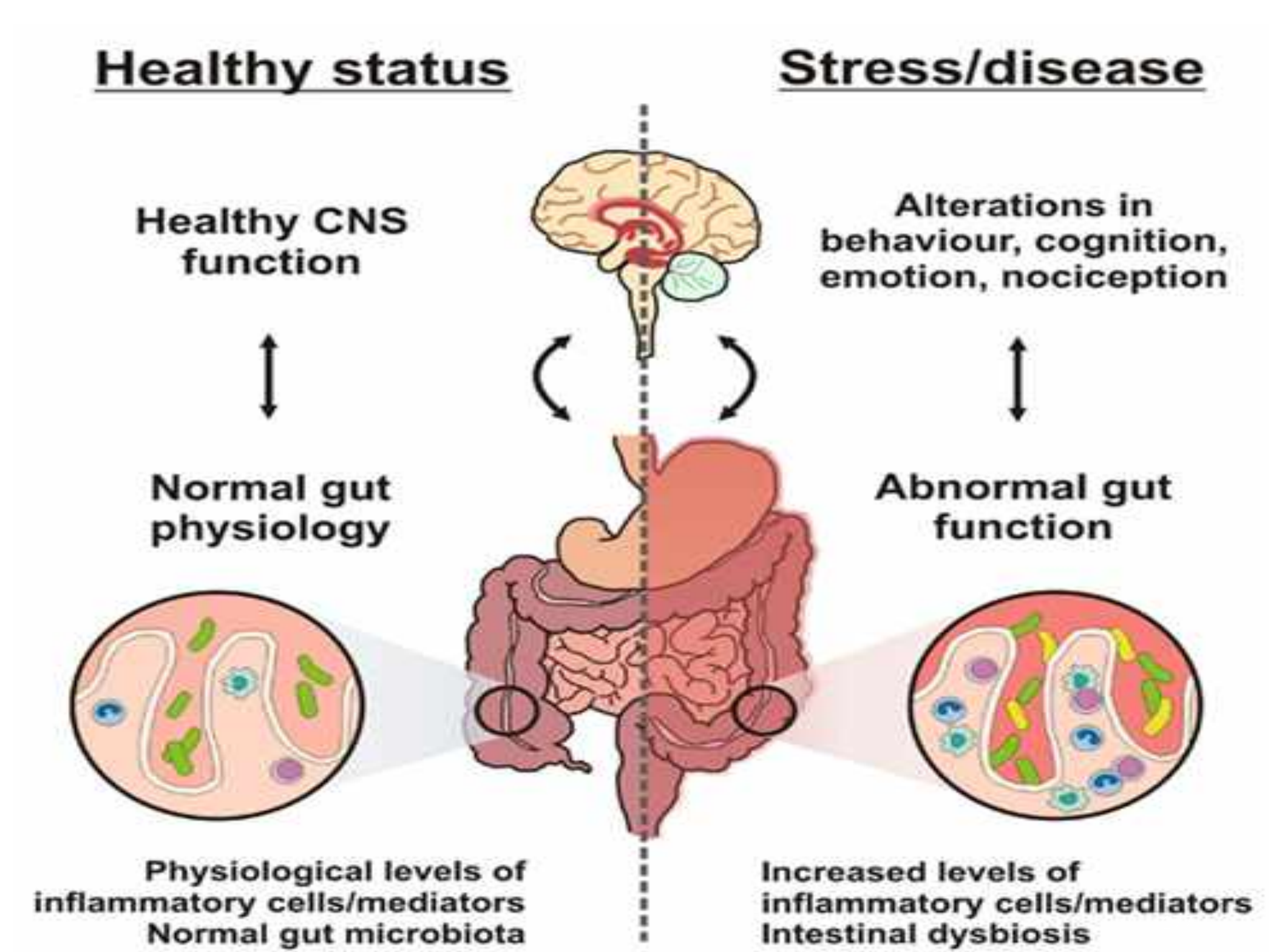
Meet the "Neuropod"
"Neuroepithelial circuit formed by innervation of sensory enteroendocrine cells"

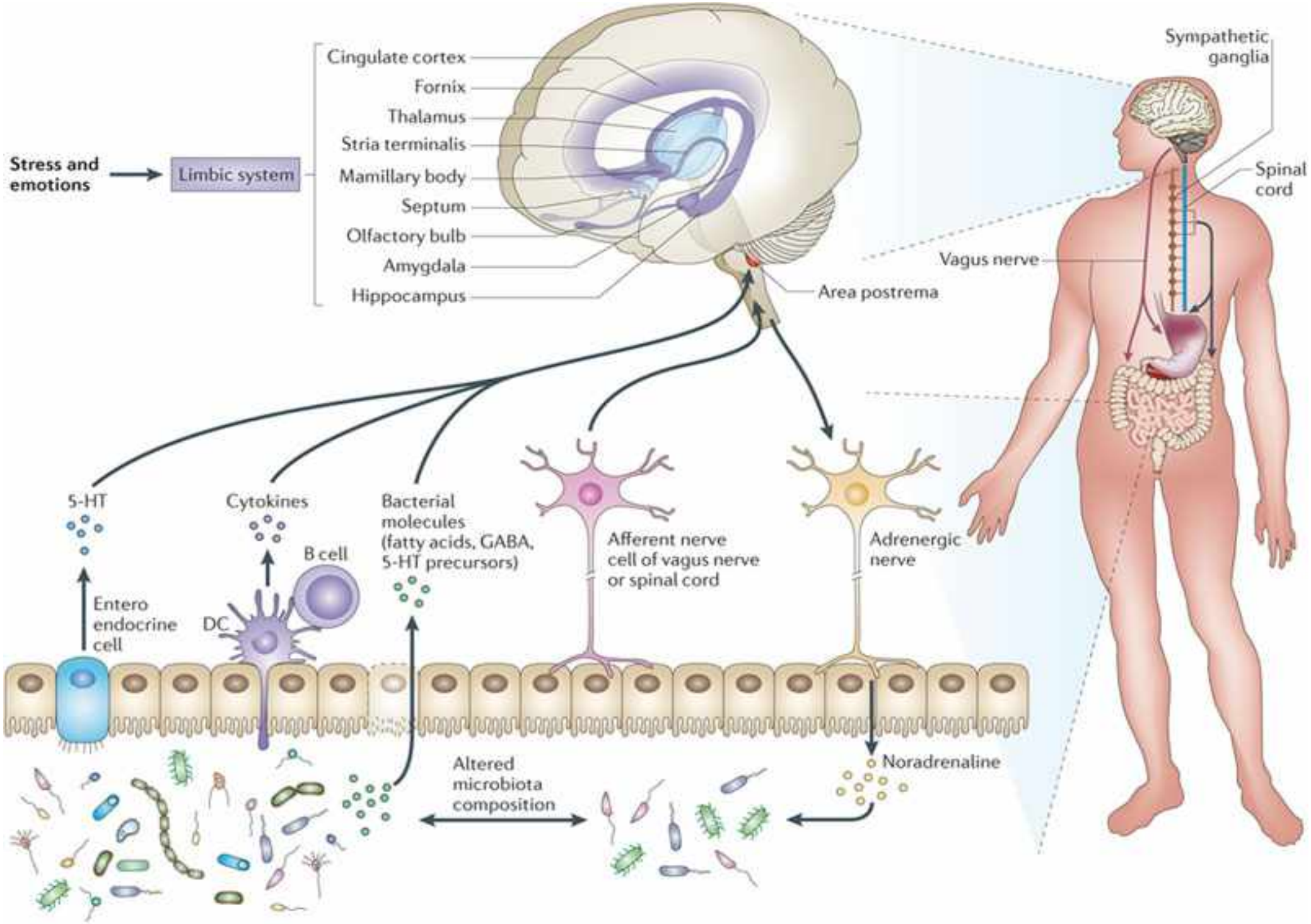


"Neuroepithelial circuit formed by innervation of sensory enteroendocrine cells" by Diego V. Bohórquez, Rafiq A. Shahid, Alan Erdmann, Alex M. Kreger, Yu Wang, Nicole Calakos, Fan Wang and Rodger A. Liddle In *Journal of Clinical Investigation*. Published online January 2 2015 doi:10.1172/JCI78361

Bidirectionality




Healthy status
Stress/disease
Healthy CNS function
Alterations in behaviour, cognition, emotion, nociception
Normal gut physiology
Abnormal gut function
Physiological levels of inflammatory cells/mediators
Normal gut microbiota
Increased levels of inflammatory cells/mediators
Intestinal dysbiosis


Stress and emotions
Limbic system
Cingulate cortex
Fornix
Thalamus
Stria terminalis
Mamillary body
Septum
Olfactory bulb
Amygdala
Hippocampus
Area postrema
Sympathetic ganglia
Spinal cord
Vagus nerve
5-HT
Cytokines
Bacterial molecules (fatty acids, GABA, 5-HT precursors)
Afferent nerve cell of vagus nerve or spinal cord
Adrenergic nerve
Entero endocrine cell
DC
B cell
Noradrenaline
Altered microbiota composition

The "Gut" Feeling

How our GI tract can influence the CNS

Stress, dietary or environmental triggers

Microbiota changes

Gut epithelial breakdown – "leaky gut"

Neural, behavioral and mood changes

Immune activation by endotoxemia (LPS stimulation)

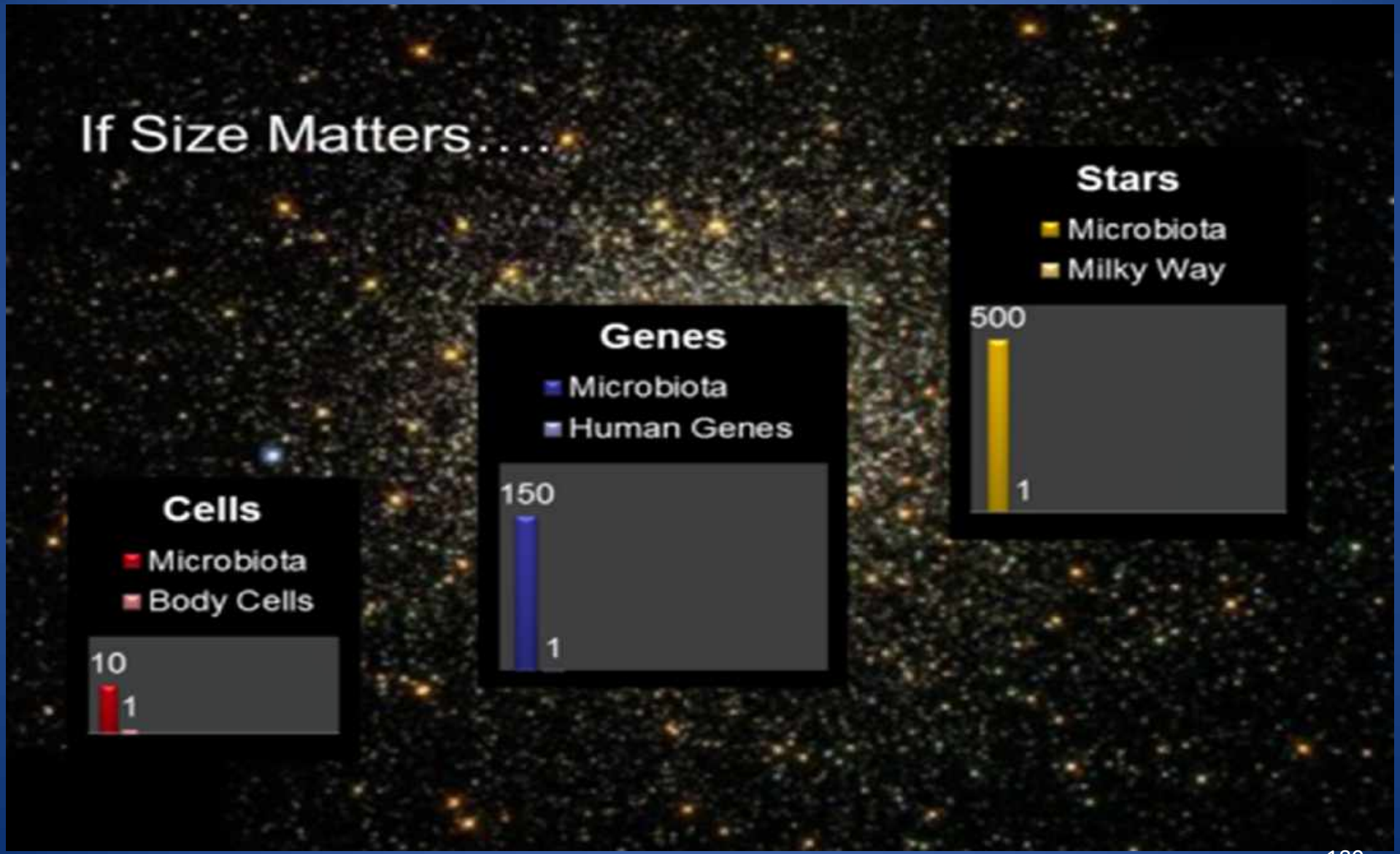
Changes in synaptic plasticity

Inflammatory cytokine production

Alterations in neurotransmitter levels

Blood brain barrier breakdown

Scratching the Surface of the Microbiome



INTESTINAL MICROFLORA

10^{14} micro-organisms, >500 differentes species

Stomach 10^2 to 10^3

Lactobacilli

Duodenum $<10^{4-5}$

Streptococci
Lactobacilli

Jejunum

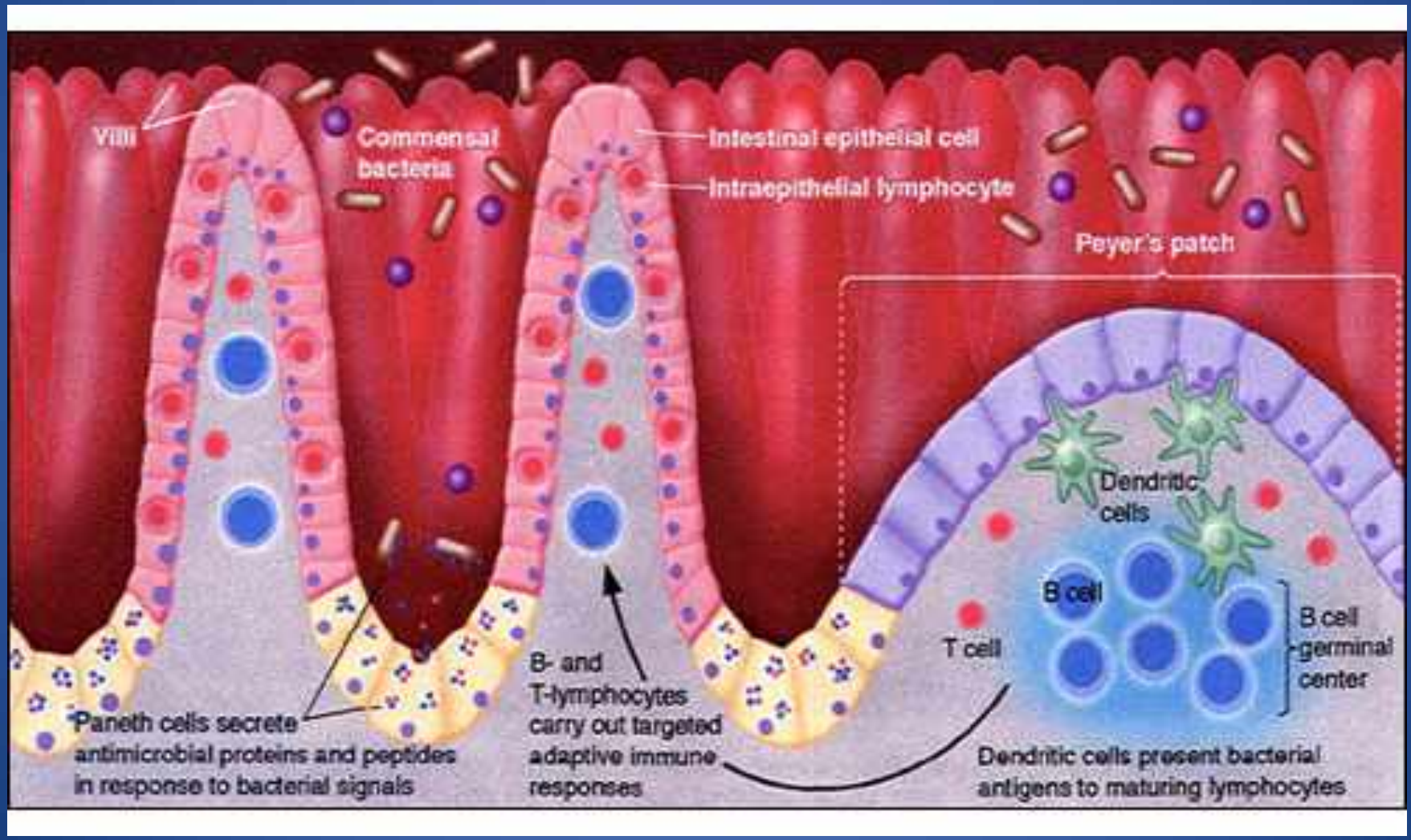
Enterobacteria
Enterococcus
Faecalis
Bacteroides
Bifidobacteria
Peptococcus
Peptostreptococc
Ruminococcus
Clostridia
Lactobacilli

Ileum 10^3 to 10^7

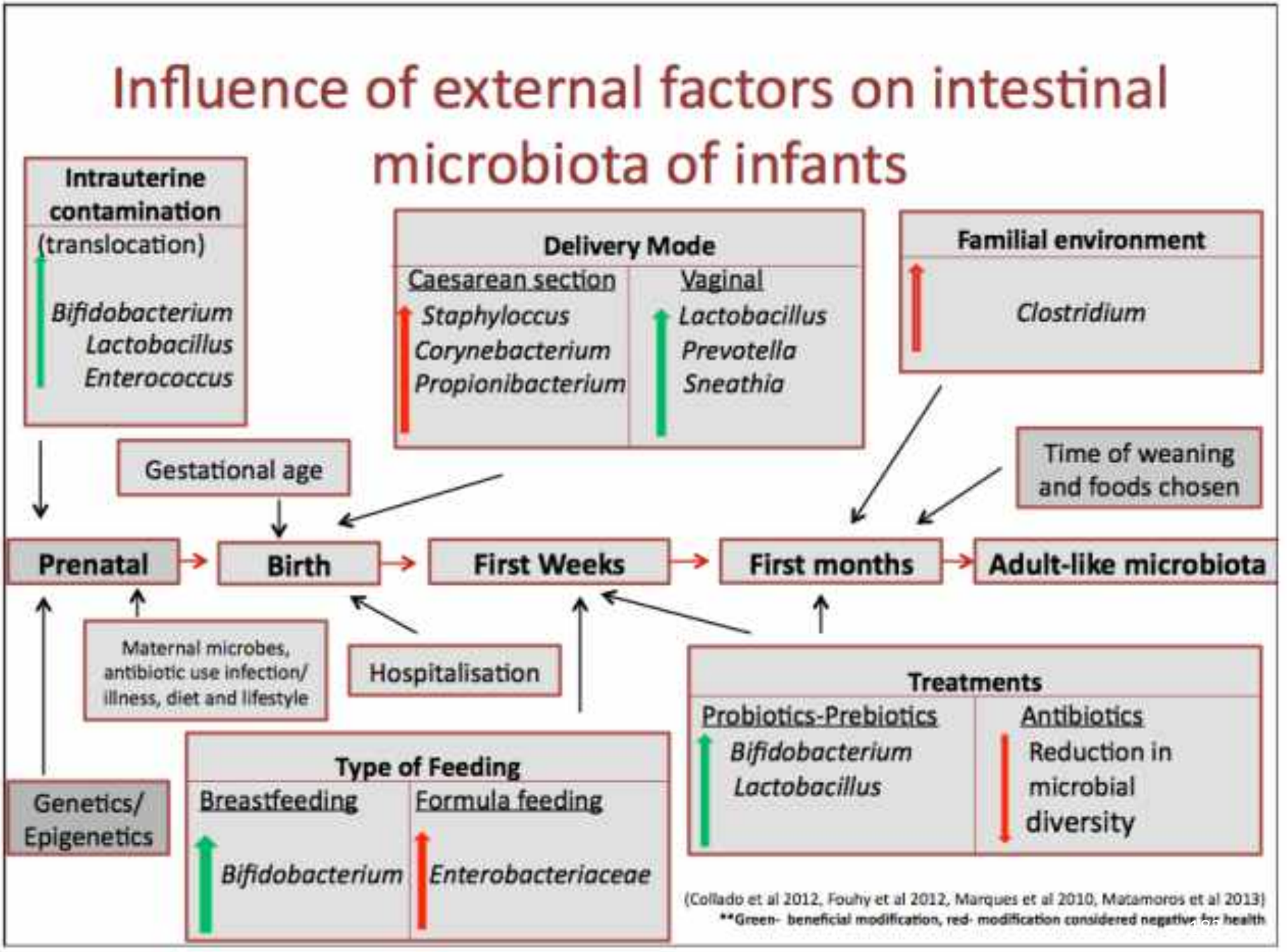
Colon with appendix 10^9 to 10^{12}

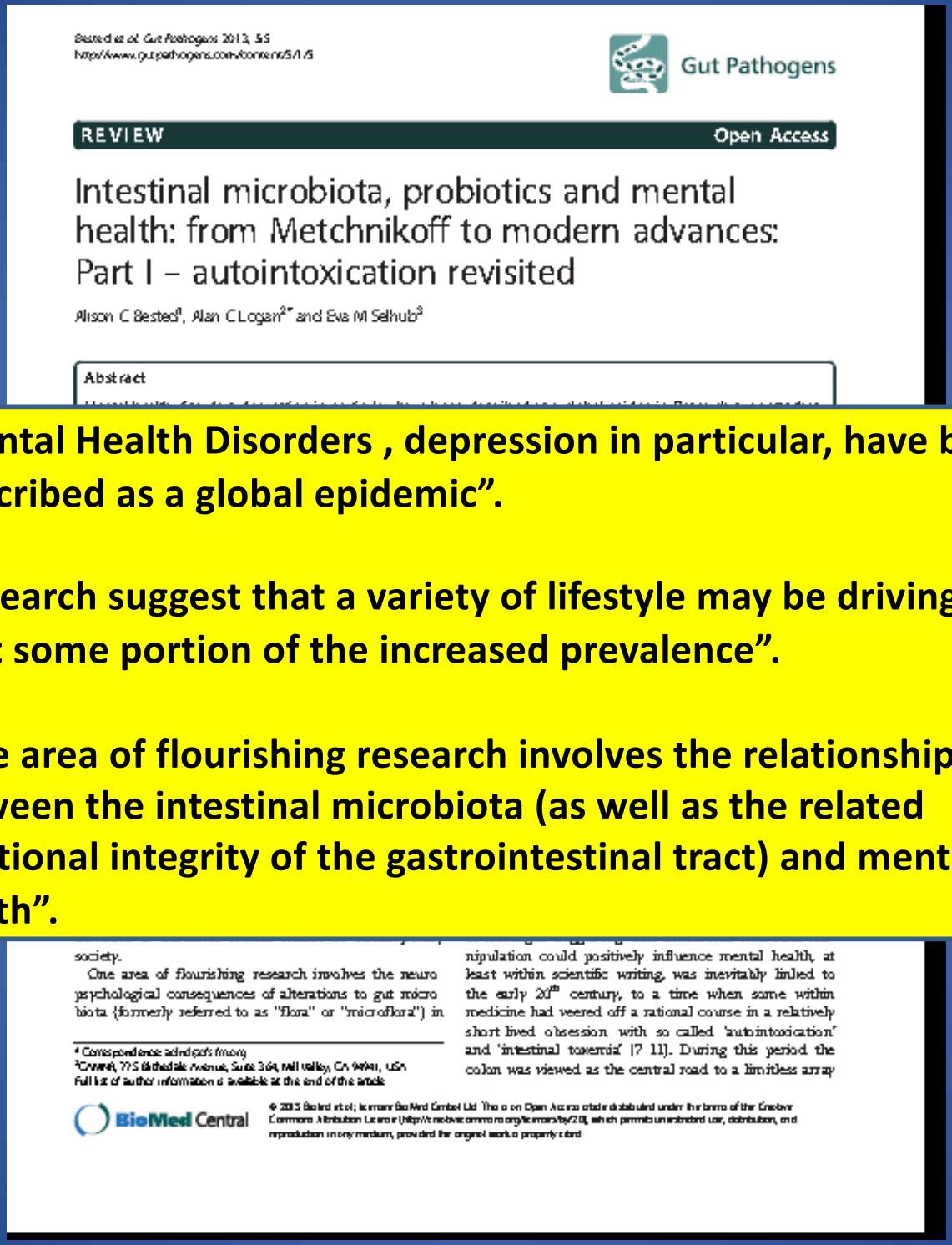
and....

The main functional compartment of the small intestine. Most people are not aware that the intestine is the largest part of the body's immune system.



Influence of external factors on intestinal microbiota of infants





Gut Pathogens

REVIEW Open Access

Intestinal microbiota, probiotics and mental health: from Metchnikoff to modern advances: Part I – autointoxication revisited

Alison C Bested[1], Alan C Logan[2*] and Eva M Selhub[3]

Abstract

society.

One area of flourishing research involves the neuro psychological consequences of alterations to gut micro biota (formerly referred to as "flora" or "microflora") in

nipulation could positively influence mental health, at least within scientific writing, was inevitably linked to the early 20th century, to a time when some within medicine had veered off a rational course in a relatively short lived obsession with so called 'autointoxication' and 'intestinal toxemia' [7 11]. During this period the colon was viewed as the central road to a limitless array

BioMed Central

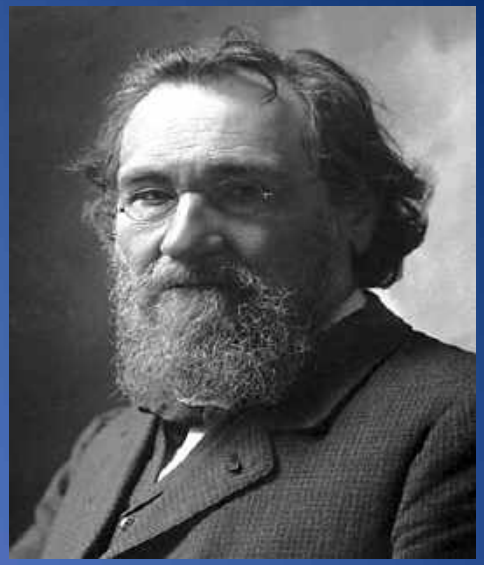
"Mental Health Disorders , depression in particular, have been prescribed as a global epidemic".

"Research suggest that a variety of lifestyle may be driving at least some portion of the increased prevalence".

"One area of flourishing research involves the relationship between the intestinal microbiota (as well as the related functional integrity of the gastrointestinal tract) and mental health".

Élie Metchnikoff

1845 – 1916



- Mechnikov's work on phagocytes won him the Nobel Prize in 1908.
- Immunology (specialist is microbes)
- Credited by some sources with coining the term gerontology in 1903, for the emerging study of aging and longevity.
- Mechnikov also developed a theory that aging is caused by toxic bacteria in the gut and that lactic acid could prolong life. Based on this theory, he drank sour milk every day (Lactobacillus Bulgaricus)

ARTICLE IN PRESS

Brain, Behavior, and Immunity xxx (2009) xxx–xxx

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Review

Mood and gut feelings

Paul Forsythe[a,b], Nobuyuki Sudo[c], Timothy Dinan[d], Valerie H. Taylor[e], John Bienenstock[a,b,f,*]

[a] McMaster Brain-Body Institute, St. Joseph's Healthcare, Hamilton, Ont., Canada
[b] Department of Medicine, McMaster University, Hamilton, Ont., Canada
[c] Department of Psychosomatic Medicine, Graduate School of Medical Sciences, Kyushu University, Japan
[d] Department of Psychiatry and Alimentary Pharmacology Centre, University College Cork, Ireland
[e] Department of Psychiatry and Behavioural Neuroscience, McMaster University, Hamilton, Ont., Canada

"GABA is made by many bacteria, especially Lactobacilli, and this property may well serve to protect the organism from the acid environment encountered in the stomach, since it synthesis involves proton exchange for the uptake of glutamate."

Higuchi et al.,1997

there is extensive epidemiological evidence to support the view that significant co morbidity exists between many chronic medical and psychiatric diseases, especially mood disorders (Moussavi et al., 2007; Van Lieshout et al., 2008). The severity and prognosis of medical illness are substantially affected by the presence or absence of co morbid depression. For example, depression is a significant risk factor for myocardial infarction (Rosengren et al., 2004) and its presence at the time of infarction predicts a greater than

their application to the study of the human genome have produced much evidence to support the genetic basis of a number of chronic diseases. However, the results are fraught with difficulty of interpretation as well as the knowledge that most of these diseases are polygenic in origin. Indeed the solution to some of the conundra of causation of chronic diseases may lie in greater understanding of the consequences of gene environment interactions (Cooper, 2008). As a result, the field of epigenetics is expanding explosively and is being applied to psychiatric disorders (Mill and Petronis, 2007; Tsankova et al., 2007).

We believe that one of the most significant areas that need to be investigated in terms of potential environmental factors contributing to both mood disorders and chronic diseases is the external

* Corresponding author. Address: McMaster Brain-Body Institute, St. Joseph Healthcare, 50 Charlton Avenue East, T3304, Hamilton, Ont., Canada L8N 4A6. Fax: +1 905 540 8593.
E-mail address: bienens@mcmaster.ca (J. Bienenstock).

Fermented Milk

- A UCLA study tested how fermented milk affected the brains of women. The women were split into three different groups: one that didn't receive probiotics, one that received non-fermented milk, and one that got fermented milk. Fermented milk can be a great source for probiotics, and some of the strains that are found in fermented milk include:

- Lactobacillus Bulgaricus
- Bifidobacterium Animalis
- Lactococcus Lactis
- Streptococcus Thermophiles

- Consumption of Fermented Milk Product With Probiotic Modulates Brain Activity

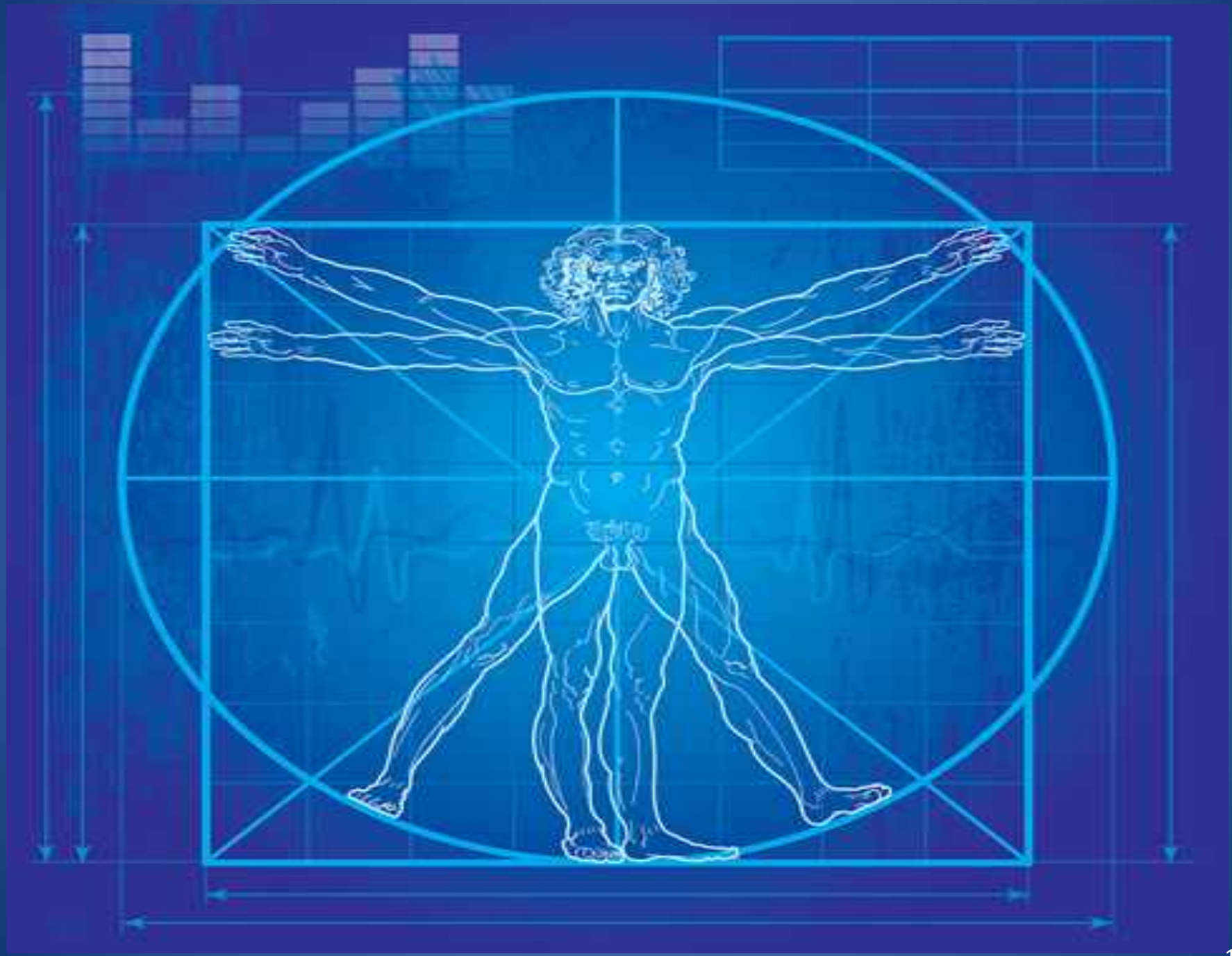
- The research showed that the group that received the fermented milk showed better brain function by MRI analaysis.

Kirsten Tillisch et al **Gastroenterology**
Volume 144, Issue 7 , Pages 1394-1401.e4, June 2013

Invisible Ink – “Inky”

Robert W. Copelan, DVM

Photo Credit: Anne M. Eberhardt/BloodHorse



Thank You!

Elizabeth A. Stuller, MD
ABPN Board Certified
Adult and Addiction Psychiatry
Fellow – American Psychiatric Association
Fellow – American Society of Addiction Medicine

Stuller Resettings, LLC
Catonsville, Maryland

stullerresettings@gmail.com