A Brief History of Brain Function

Donald Stein, PhD
Professor Emeritus , Emergency Medicine
Emory University

Learning Objectives For The Course

- To get a better idea of where ideas concerning how the brain works came from in the first place.
- To appreciate that many current and popular ideas about brain functions have a very long history not always recognized by current researchers.
- To understand that the issue of "how the brain works" is still unresolved.

How Does Science (& Everything Else) Work? Some Basic Assumptions.

- ***"We know that people can maintain an unshakable faith in any proposition, however absurd, when they are sustained by a community of like-minded believers."***

- ***"You will often find that knowing little makes it easier to fit everything you know into a coherent pattern."***

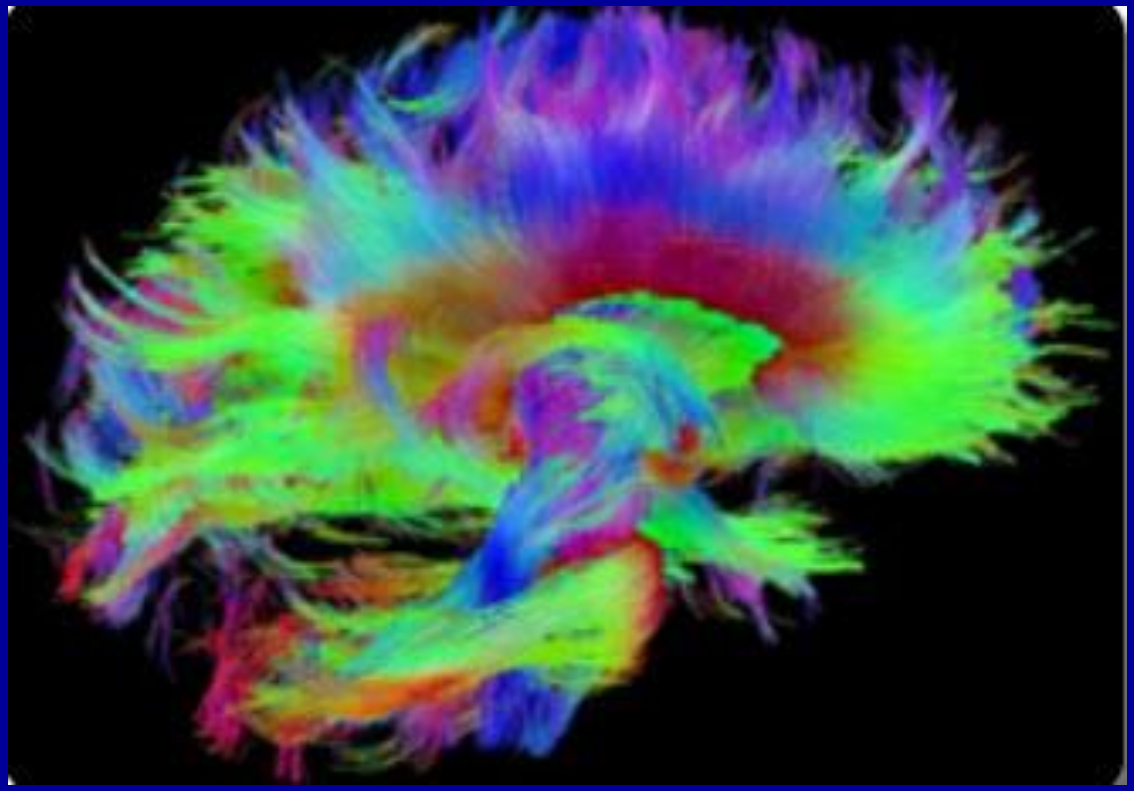
- ***D. Kahneman (Nobel Prize in Economic Sciences), Thinking, Fast and Slow,*** Farrar, Straus & Giro

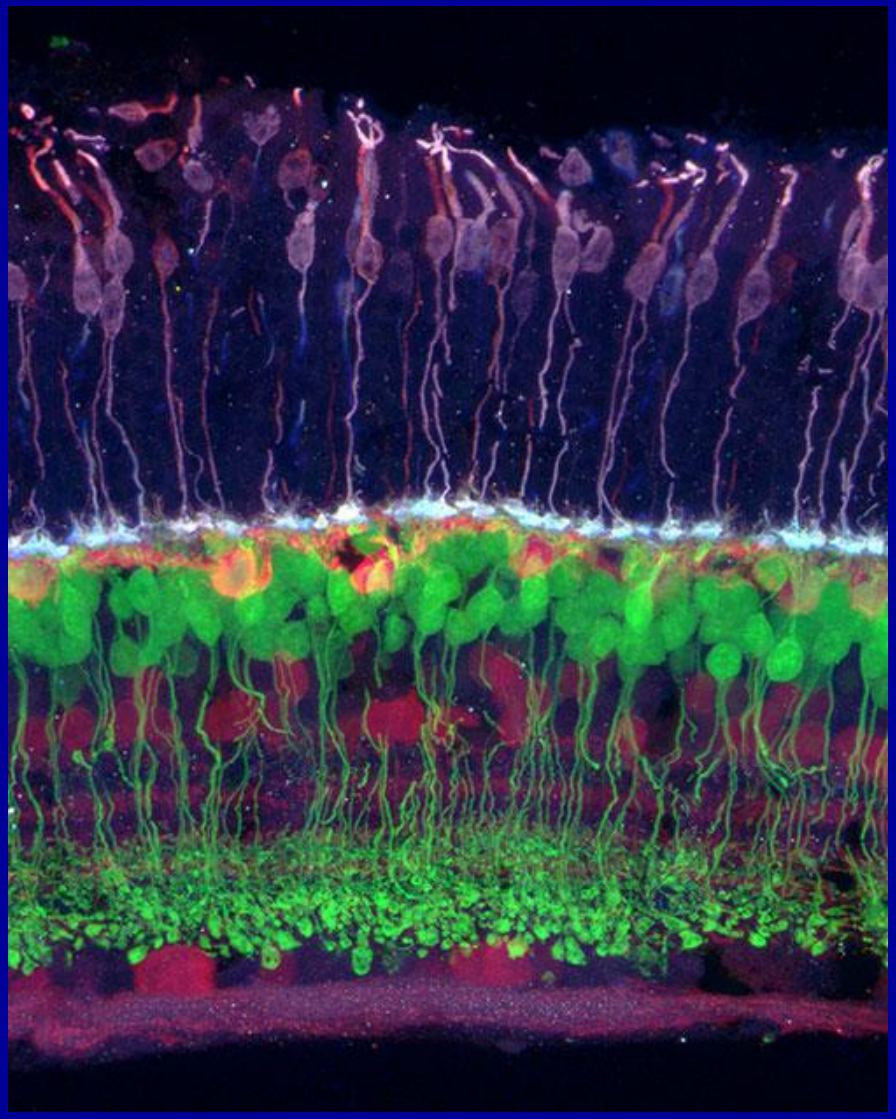
Why Is It Important To Gain Some Insight Into The Ideas/Concepts About How The Brain Works?

- Because "big" and costly decisions can be made that have important implications for how research proceeds and what results you look for.
- How you think things work will determine what techniques you use to measure brain 'functions'.
- But what if your ideas about how the brain works are wrong?
- Just because we have a sophisticated 'technology' to measure something—doesn't mean it's the right thing to measure.

A Highly Focused Direction: President Obama Sought to Boost Study Of Human Brain By Mapping *All* Of Its Connections

- Obama administration offered (and proposed to fund $454M) in a decade-long effort to determine the workings of the human brain and build a comprehensive map of its "activity"
- He sought to do for the brain what the Human Genome Project did for genetics (but what did it do for the treatment of diseases?).
- Sought $300M/year for a decade just for the mapping project.
- About a dozen scientists with ties to the Office of Science and Technology Policy lobbied successfully for this commitment.





Brain Research through *Advancing Innovative Neurotechnologies*® (BRAIN)

- With nearly 100 billion neurons and 100 trillion connections, the human brain remains one of the greatest mysteries in science and one of the greatest challenges in medicine.

- Despite the many advances in neuroscience in recent years, the underlying causes of most of neurological and psychiatric conditions remain largely unknown, due to the vast complexity of the human brain.

- If we are ever to develop effective ways of helping people suffering neurological diseases, researchers will first need a *more complete arsenal of tools* and information for understanding how the brain functions both in health and disease.

- ***The goal of the BRAIN Mapping Initiative is to help researchers map out complete wiring diagrams of all neural circuits.***

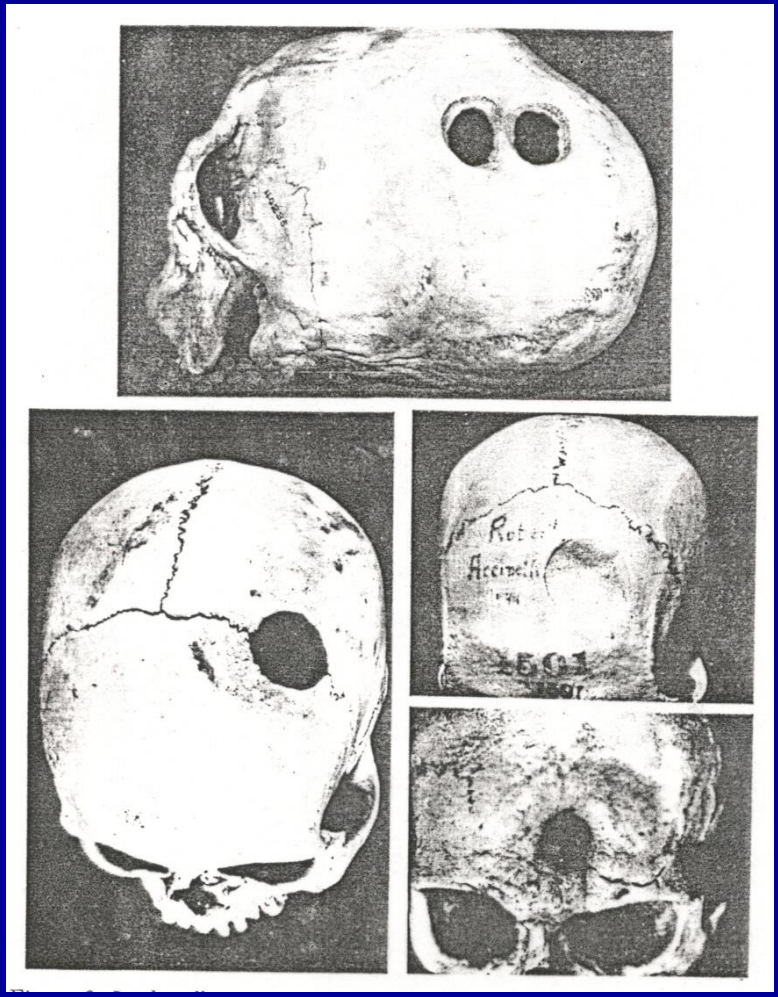
What's Being Done Right Now?

The brain initiative aims to *develop and apply cutting-edge technologies* to create a dynamic picture of the brain in action

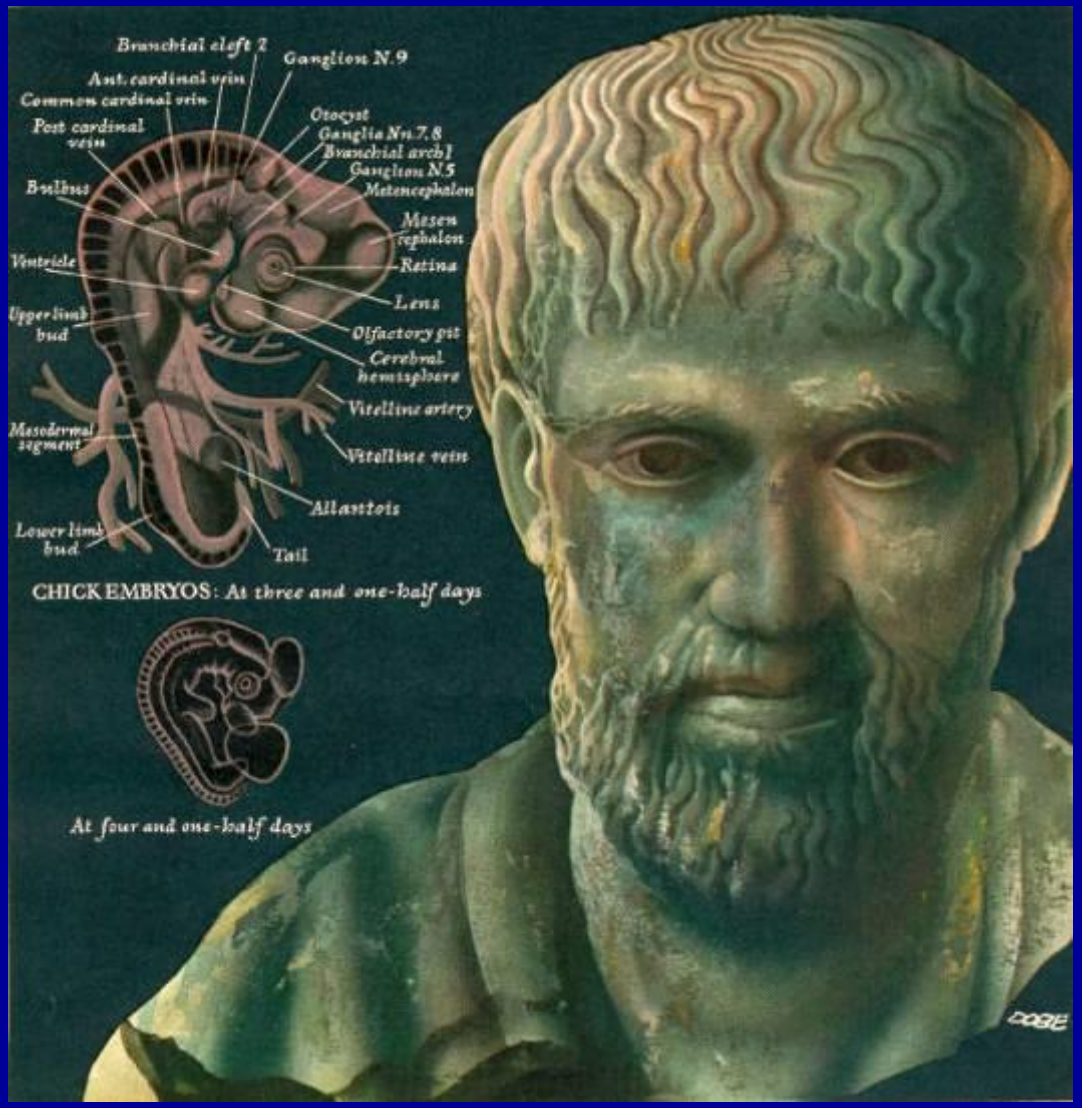
- ***From The NIH Website:***
- **Research Opportunities Using Invasive Neural Recording and Stimulating Technologies in the Human Brain.**
- ***Next-Generation Invasive Devices for Recording and Modulation in the Human CNS.***
- **Clinical Studies to Advance Next-Generation Invasive Devices for Recording and Modulation in the Human CNS.**
- **Development of Next Generation Human Brain Imaging Tools and Technologies.**
- **Non-Invasive Neuromodulation – New Tools and Techniques for Spatiotemporal Precision.**

When Did Brain ”Technology” Get Started?

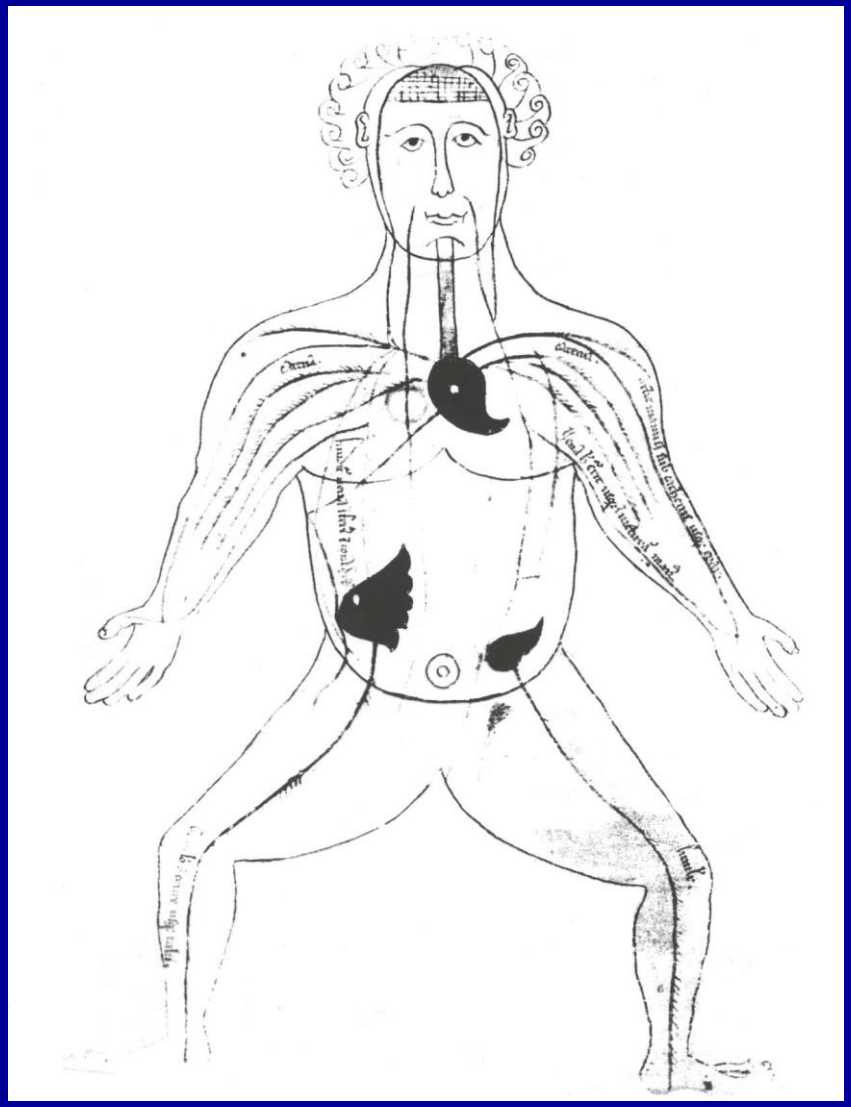
Trephination



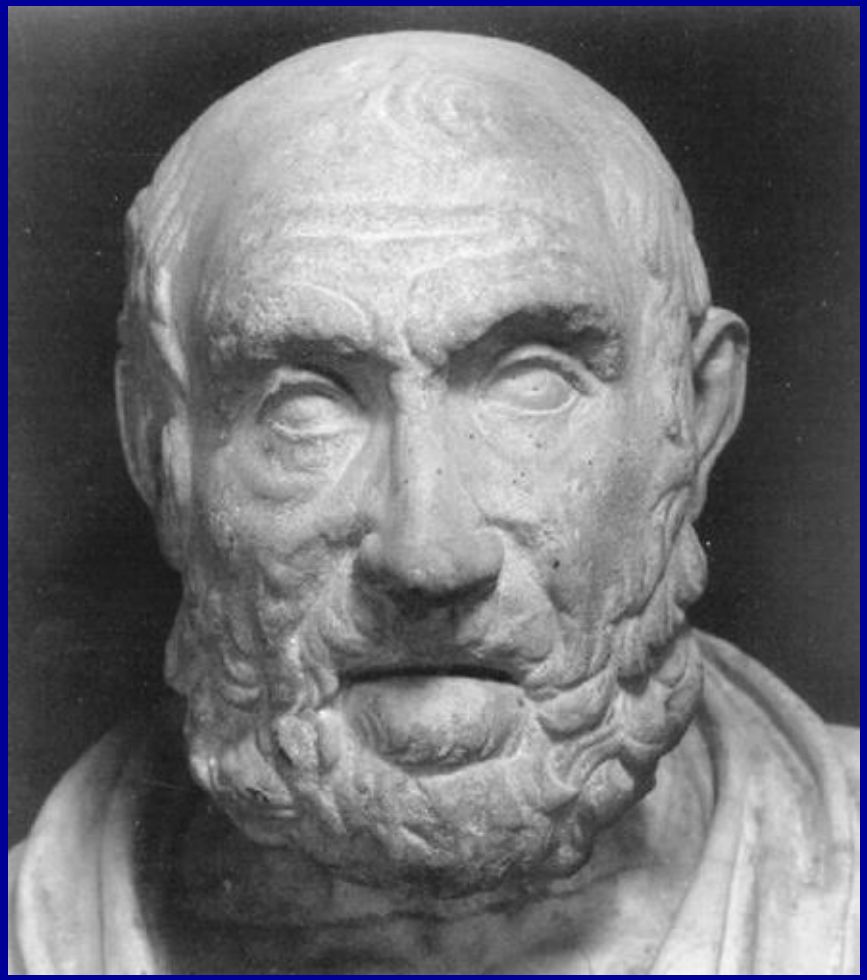
Aristotle (400 b.c.) & Cardiocentric Doctrine



Ventricular & Cardiac Localization of Function



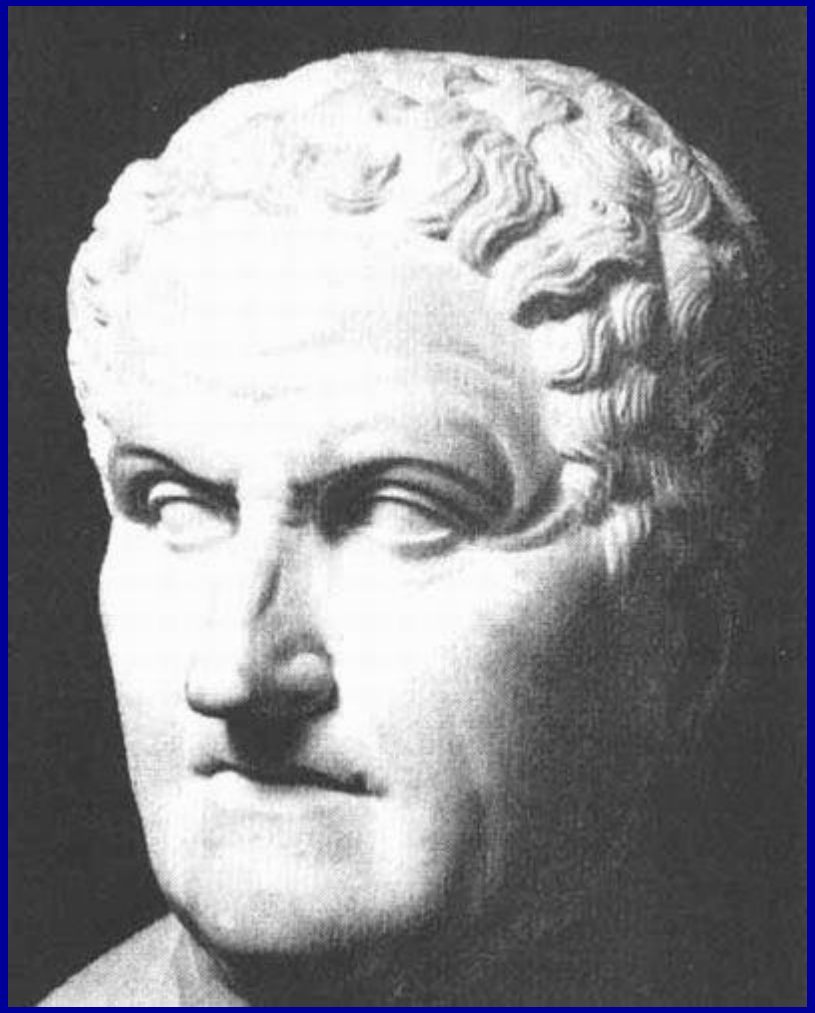
Hippocrates & Brain (ca 400 b.c.)



The Hippocratic School: The Rise Of The Brain Over the Heart

- "Men ought to know that from nothing else but the brain come joys, delights, laughter, sports and sorrows, grifes despondency and lamentations. And by this we aquire wisdom and knowledge and see and hear and know…."

Galen (c 200AD): Experimentalist and Physician- Humoral Doctrine



Galenic Teachings

- A strong experimentalist only believed what he could see and evaluate—did many dissections in animals and people.
- Strongly argued against cardicentric dogma of Aristotle.
- Carefully described structure of the eye and described sensory and motor nerves.
- Strongly pushed ‘humoral theory’ which endured about 1500 years!

Mapping the Brain in Medieval Medicine

MacLeose: Prog Brain Res, v243,2018

- Still heavily influenced by Galen, late 13th century normal Brain divided into 3 main *ventricular* structures (cells): phantasy (imagination), intellect and memory. All 3 working together were collectively called the 'mind'.
- Medieval physicians thought there were 3 levels of injury: diminution (diminution) alteration (permutatio) and complete loss of rationality(ablatio).
- They saw a direct correlation between mental diseases and cognitive impairments which they then mapped onto one of the 3 brain ventricular structures being dysfunctional.

Leonardo da Vinci Was Also A Believer In Humoral Theory (1500?)

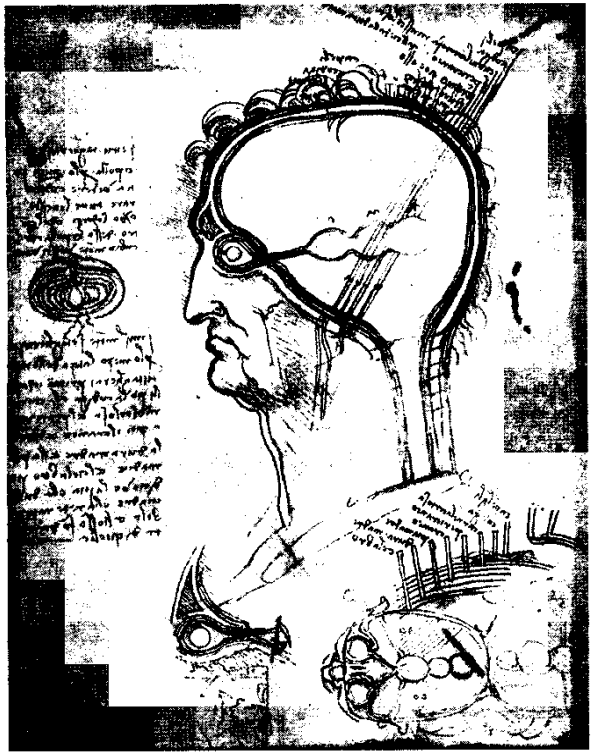
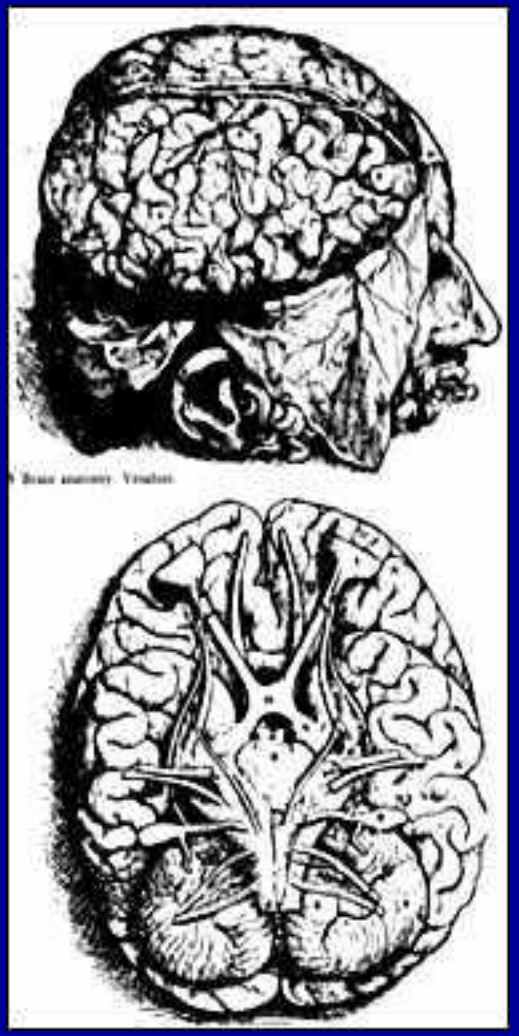


Figure 2.3 An early (ca. 1490) drawing of the eye and cerebral ventricles of the brain that uncritically combines Greek, Arab, and medieval views. W12603r

Vesalius Rejected Ventricular Dogma Around 1550

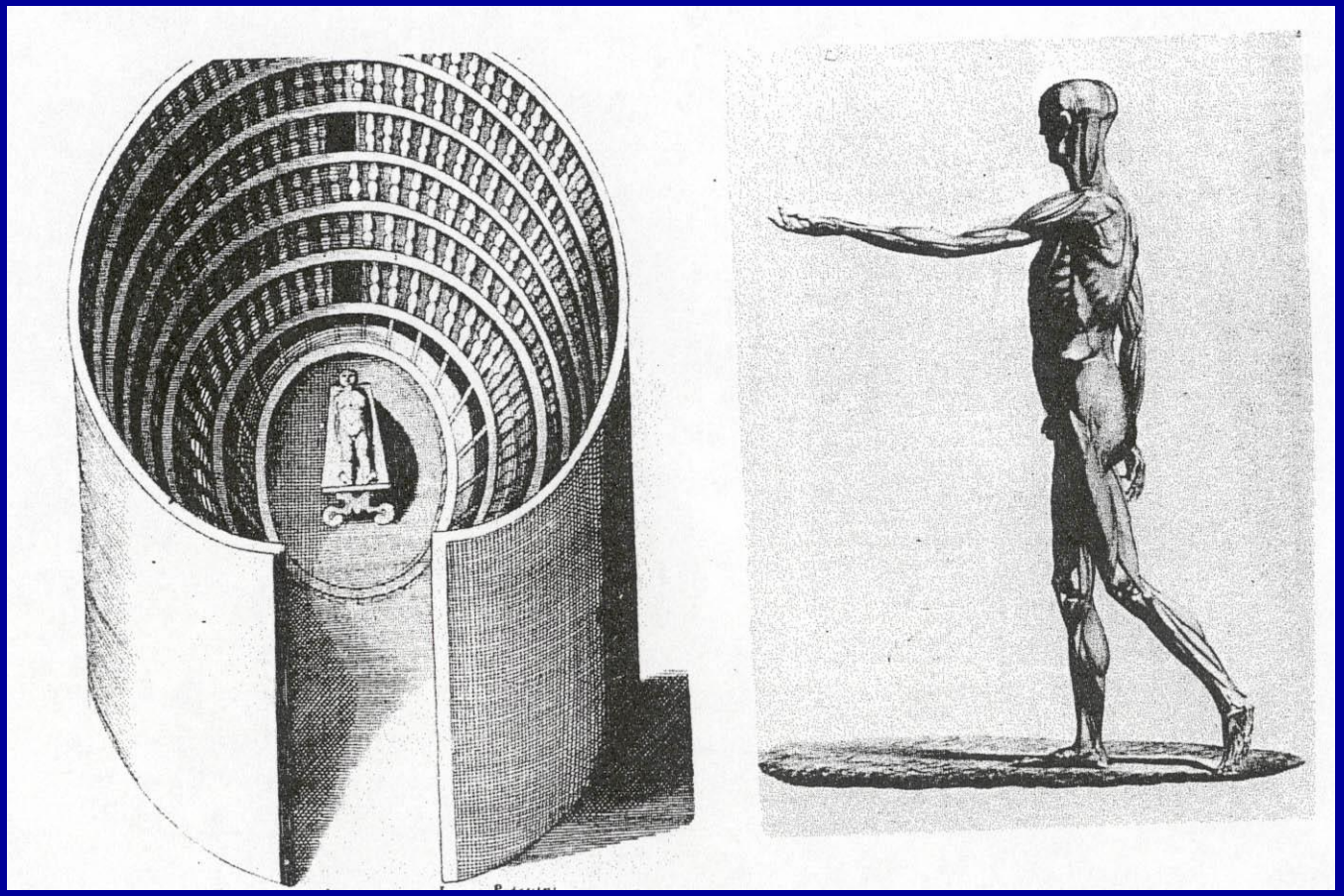




Vesalius' Contributions

- One of first to perform careful *human* dissections illegally) and rejected ventricular theory.
- Rejected the idea that nerves are 'hollow tubes' filled with humors and spirits.
- Forced more attention on brain 'substance'.
- Really ticked off his professors: "Honest reader, I urge you to pay no attention to a certain ridiculous madman, one utterly lacking in talent who curses and inveighs impiously against his teachers" (Jacobus Sylvius).

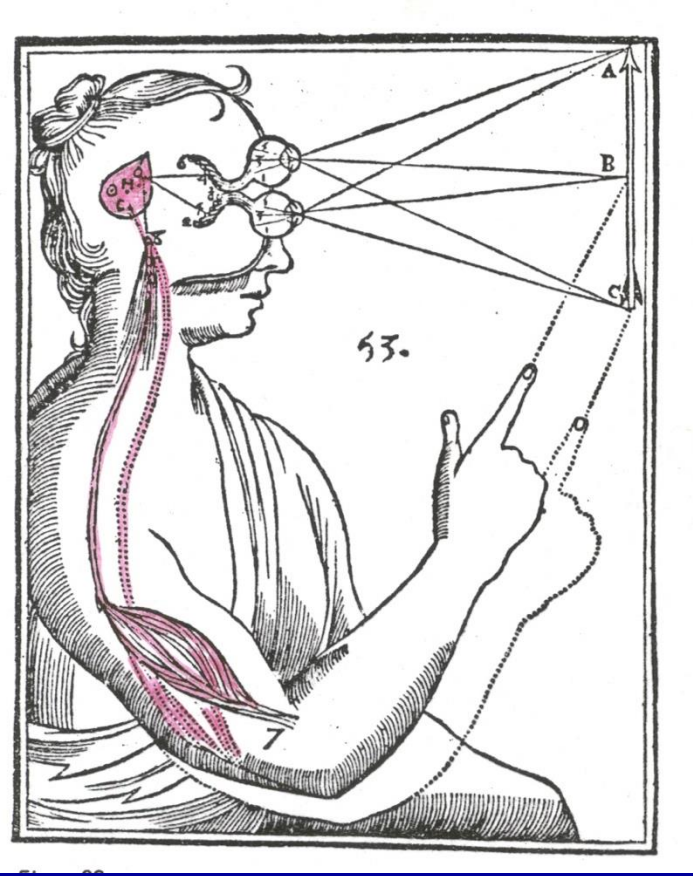
The AnatomyAmphitheater at Padua

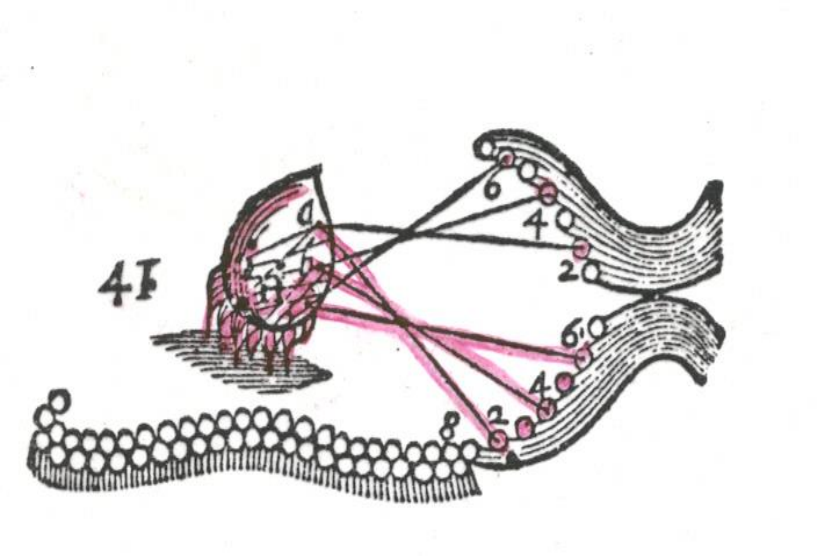


One Of The First To 'Localize Function' In Brain Tissue Itself: Rene Descartes



Descartes, the Pineal Gland & Mind-Body Dualism





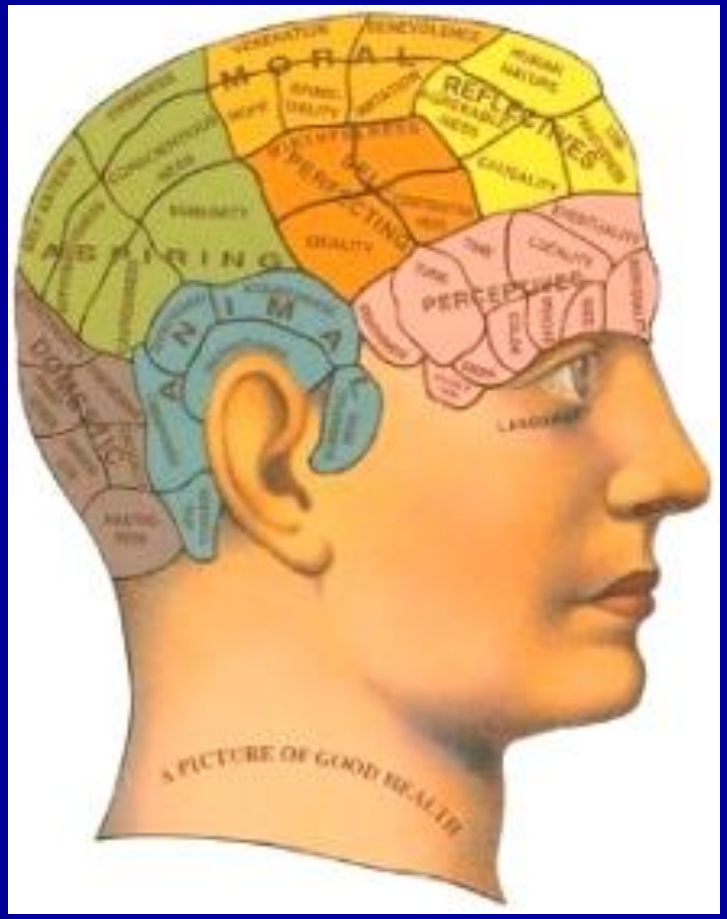
The Beginning of Modern, Scientific Neurology and Neuroscience

Franz Gall and Cortical Localization



Figure 13
Franz Josef Gall (1758-1828)

The Science of Phrenology



Modern Advances in Technology for *Objective* Phrenological Assessment!



Phrenology died a slow death. The Lavery Electric Phrenometer of 1907 was intended to lend twentieth-century accuracy to the measurement of bumps. As late as 1938 there was an Ohio State Phrenological Society, which published its own journal, and the British Phrenological Society was not disbanded until 1967.

The Contributions of Franz Gall
1790-2024!

- The brain is the organ of the mind.
- The mind is composed of multiple distinct, innate faculties.
- Because they are distinct, each faculty must have a separate seat or "organ" in the brain.
- The size of an organ, other things being equal, is a measure of its power.
- The shape of the brain is determined by the development of the various organs.
- As the skull takes its shape from the brain, the surface of the skull can be read as an accurate index of psychological aptitudes and tendencies.

Localization Doctrine In the 19th , 20th And 21st Centuries

"The more things change the more they stay the same"

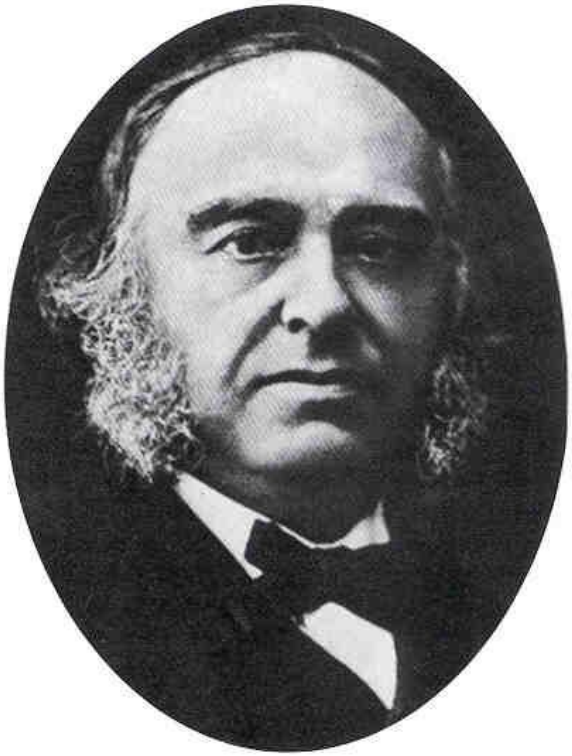
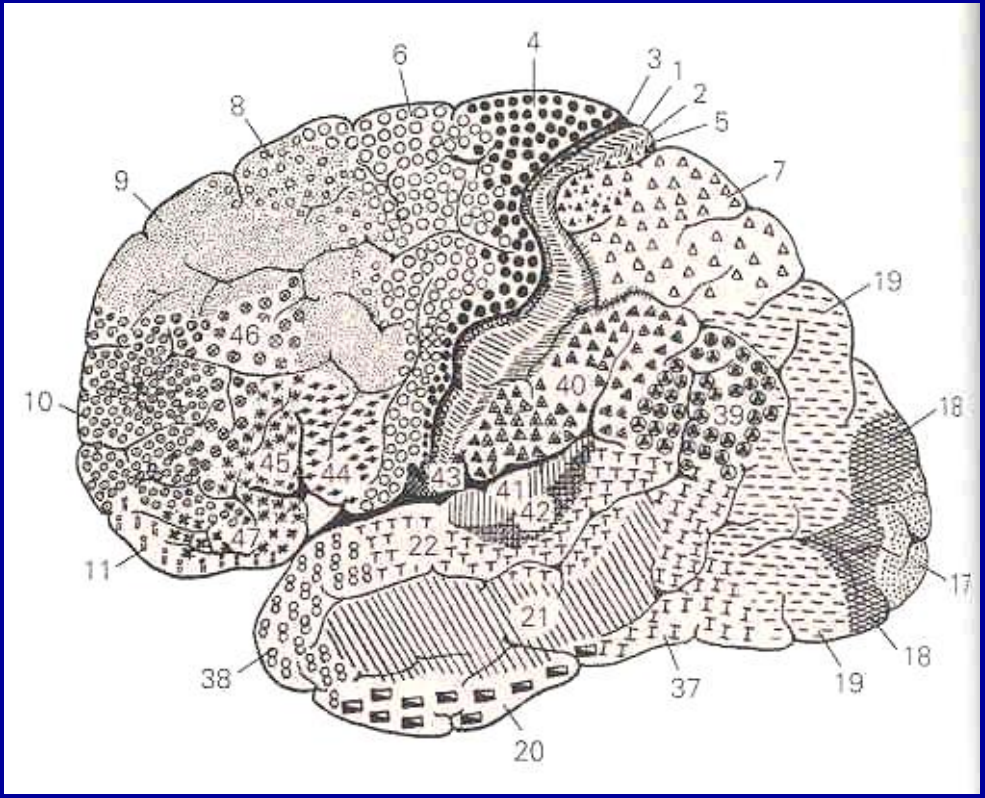


Figure 3.7. Paul Broca (1824–1880), whose association between aphasia and damage to the frontal cortex in M. Leborgne ("Tan"), in 1861, became the first cortical localization that was widely accepted. (Courtesy of the Académie de Médecine, Paris.)

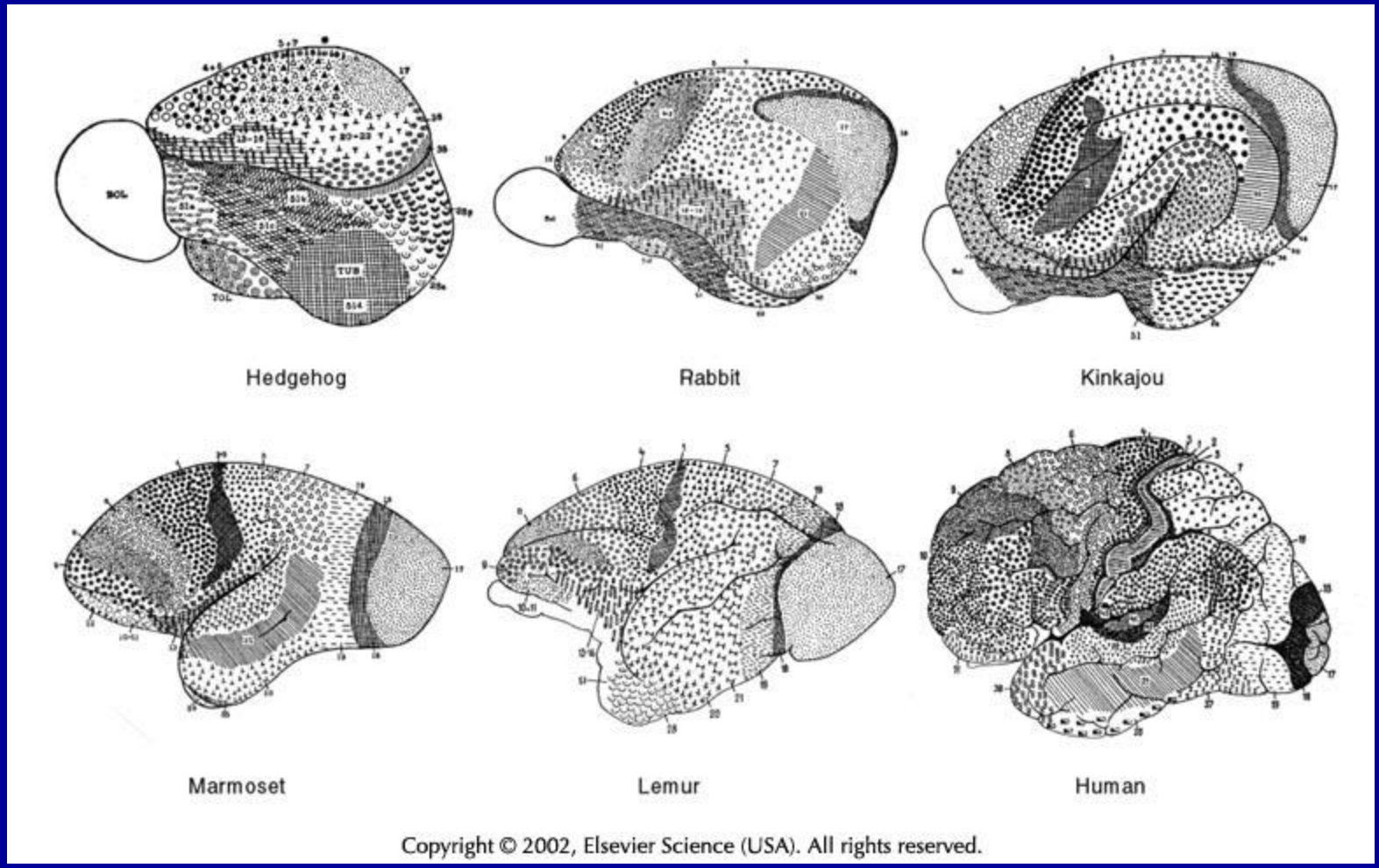
Location, Location, Location



Von Brodmann's Cytotechtonic Brain Map



Von Brodmann's Maps in Squire, et al 2003



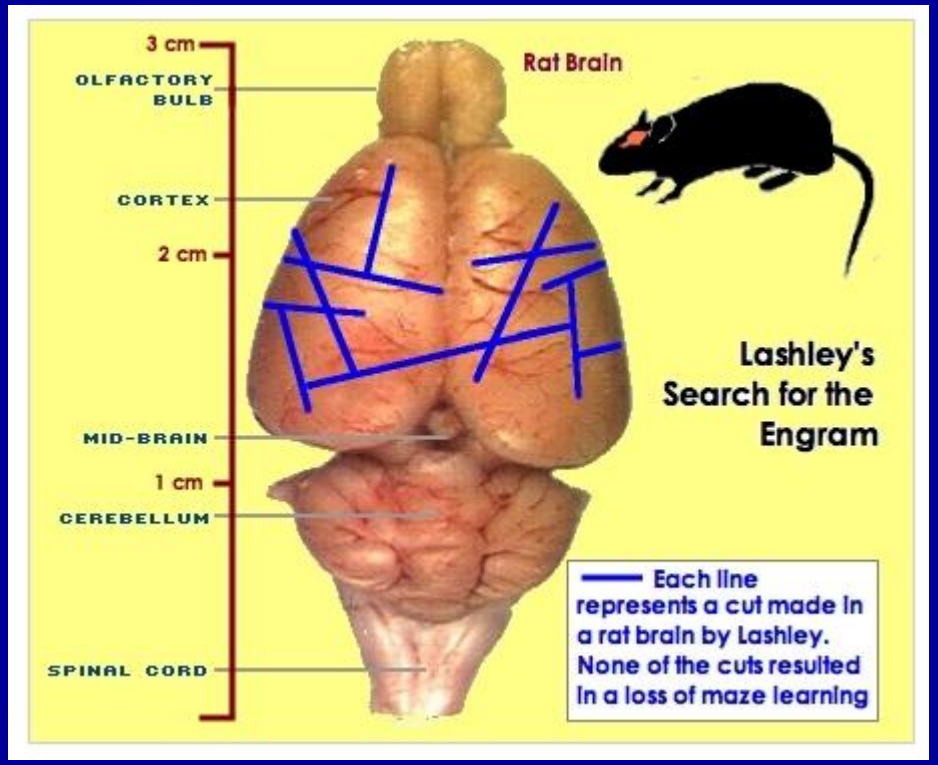
Copyright © 2002, Elsevier Science (USA). All rights reserved.

A Major Issue For Neuropsychology

- With respect to the brain, briefly define the term "function".
- Specify the brain areas required to execute the function.
- How would you conclusively show which part of the brain "controls" that function?

Karl Lashey Confronted Localization Doctrine In the Early 20th Century





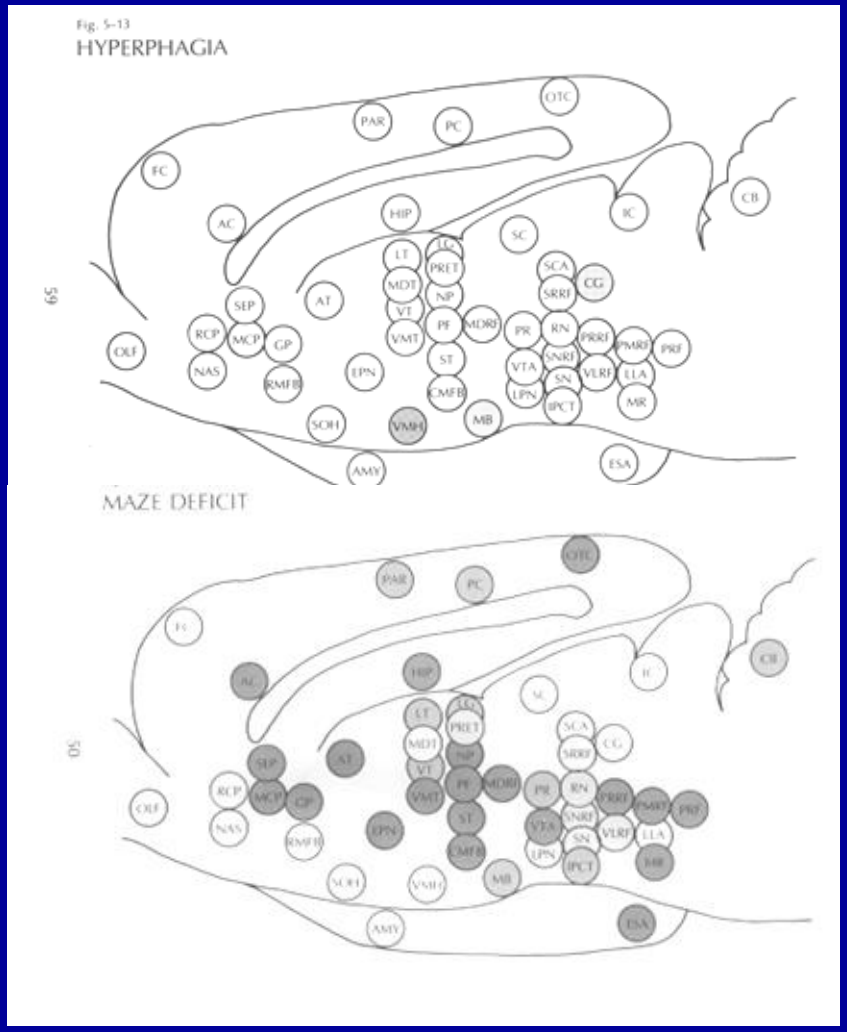
Restoring Cerebral Blood Flow Reveals Neural Regions Critical For Naming,

Hillis, AE, et al, J. Neurosci, 2006, 26, 8069

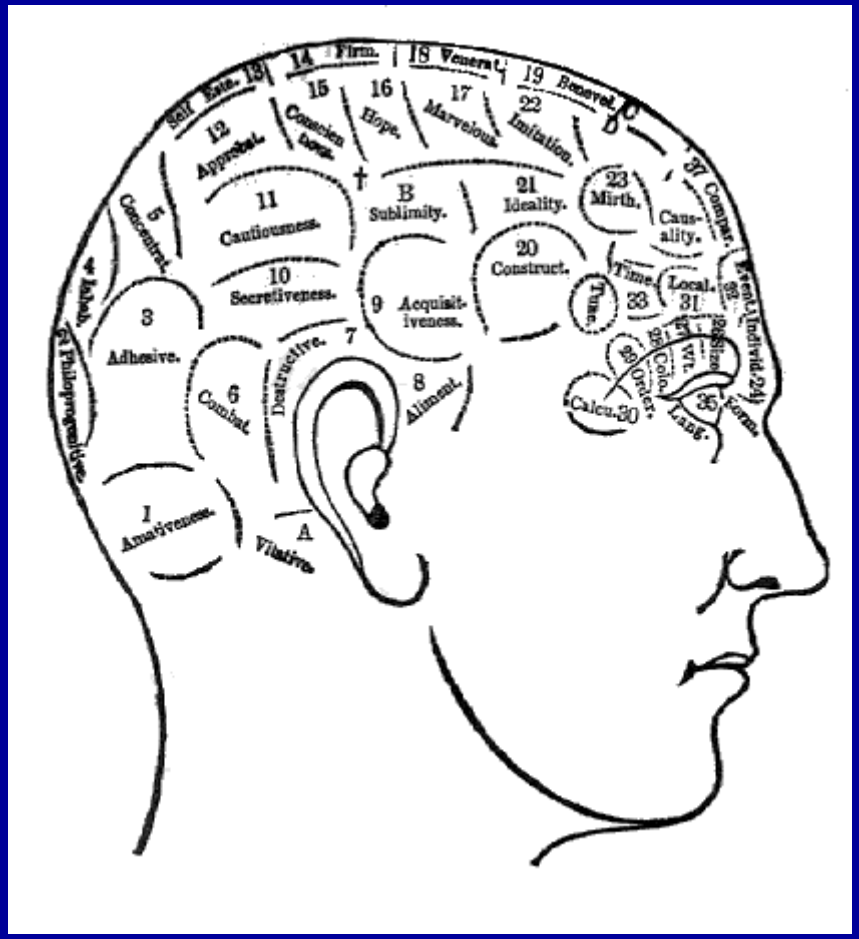
- "We identified areas of the brain that are critical for naming pictures of objects showing which areas are *essential for that task.*"

- *{middle temporal fusiform gyrus, Broca's area, and or Wernicke's area}*

LOCALIZATION OF MAZE AND EATING DISORDERS AFTER BRAIN LESIONS



Phrenology 2004



An Empirical, 21st Century Evaluation Of Phrenology

O. Parker Jones* , F. Alfaro-Almagro and S. Jbabdi

Cortex, 106, 2018

- The present study sought to test in the most exhaustive way currently possible the fundamental claim of phrenology: that measuring the contour of the head provides a reliable method for inferring mental capacities. We found no evidence for this claim.

- According to our results, a more accurate phrenological bust should be left blank since no regions on the head correlate with any of the faculties that we tested.

- However, phrenology's “faculty psychology” is not as different from current ontologies as it might first seem. One can readily find examples of 19th century faculties in the neuroimaging literature, albeit under different names.

Rapid Evolution of Brain Circuitry

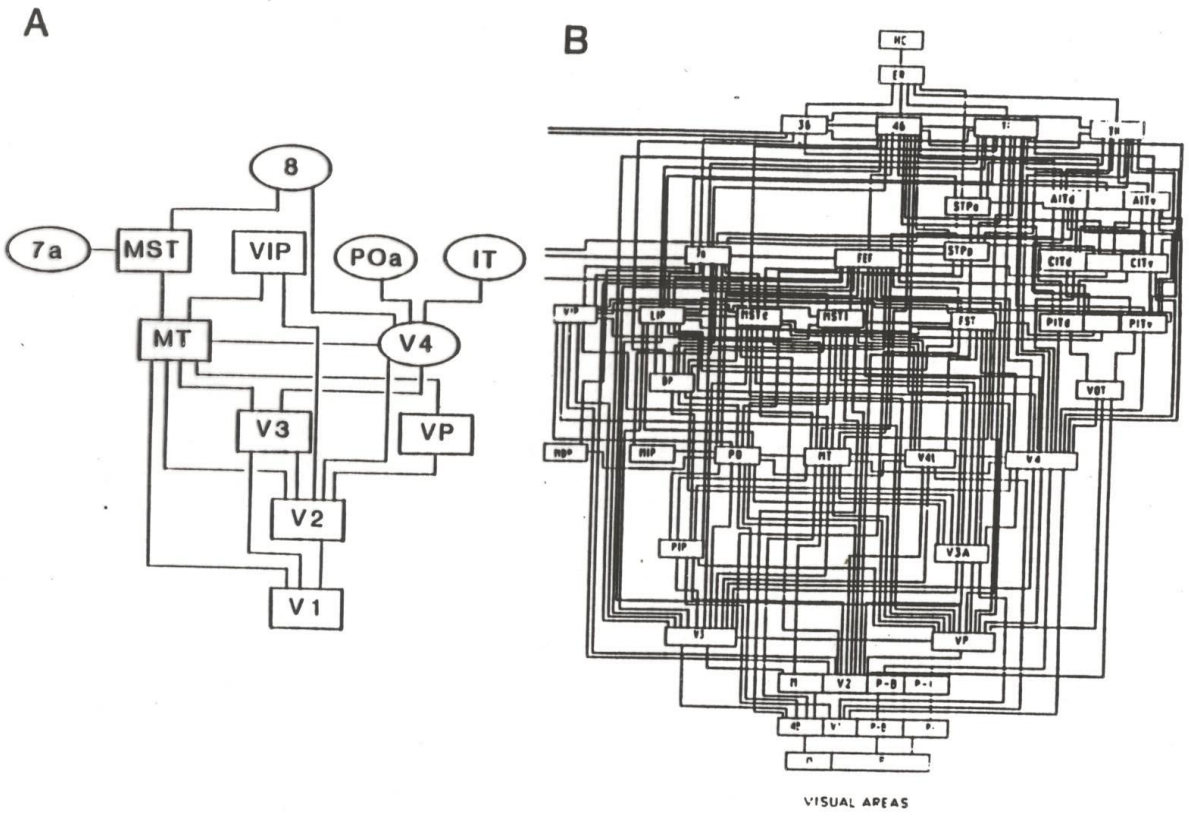


Fig. 2. *The wiring diagram of the cortical visual areas in the macaque monkey:* **(A)** *the 1983 version and* **(B)** *the 1990 version.*

FROM: DOUGLAS & MARTIN, TINS, 14, 1991, 286-293

- ***"We know that people can maintain an unshakable faith in any proposition, however absurd, when they are sustained by a community of like-minded believers."***

- ***"You will often find that knowing little makes it easier to fit everything you know into a coherent pattern."***

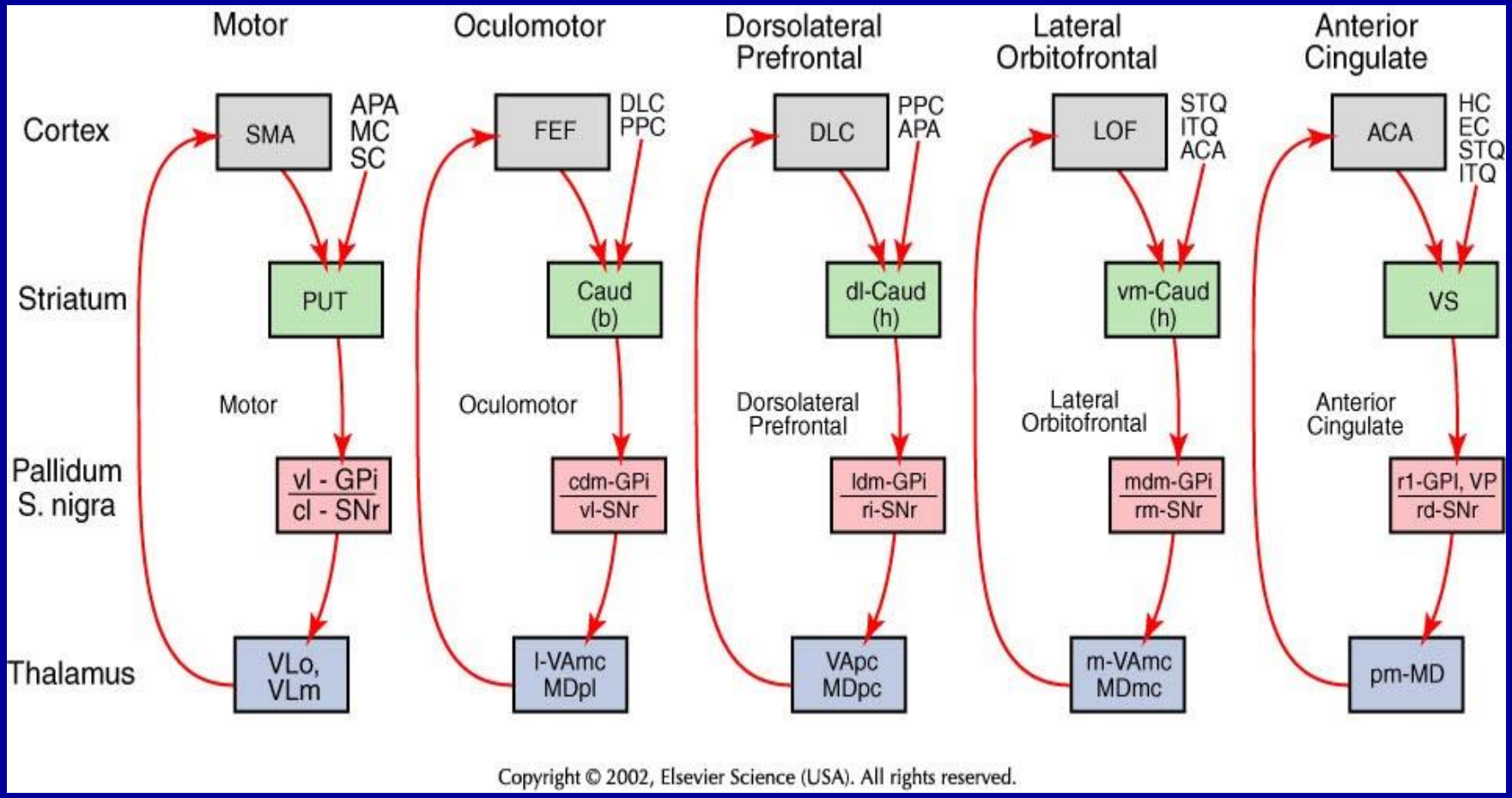
- ***I have yet to meet a successful scientist who lacks the ability to exaggerate the importance of what he or she is doing, and I believe that someone who lacks a delusional sense of significance will wilt in the face of repeated instances of multiple small failures and rare successes, the fate of most researchers.***

- ***D. Kahneman (Nobel Prize in Economic Sciences), Thinking, Fast and Slow,*** Farrar, Straus & Giroux, (2011)

Conflicts and Contrasts in Modern Phrenology

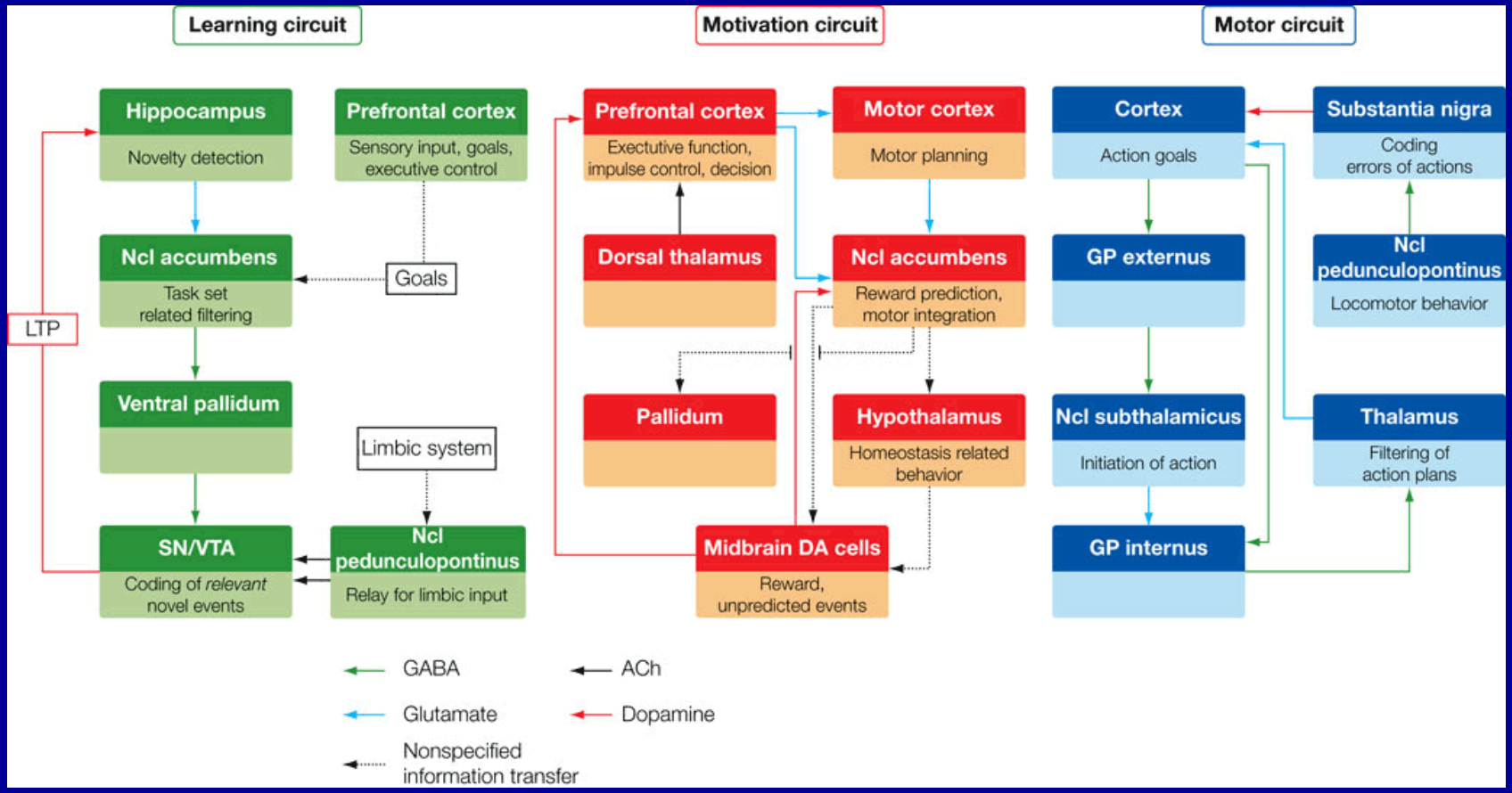
"What is so special about the brain that makes it different from any other organ? I would say that is is a structure in which the *position* of the cells within the brain and their *connections* with other brain cells play an absolutely critical role in determining their function. The cells of our brain are organized as functional units---as maps of our bodies" (Rakic, NY Acad Sci, 1999, 90)

Complex Functional Circuits



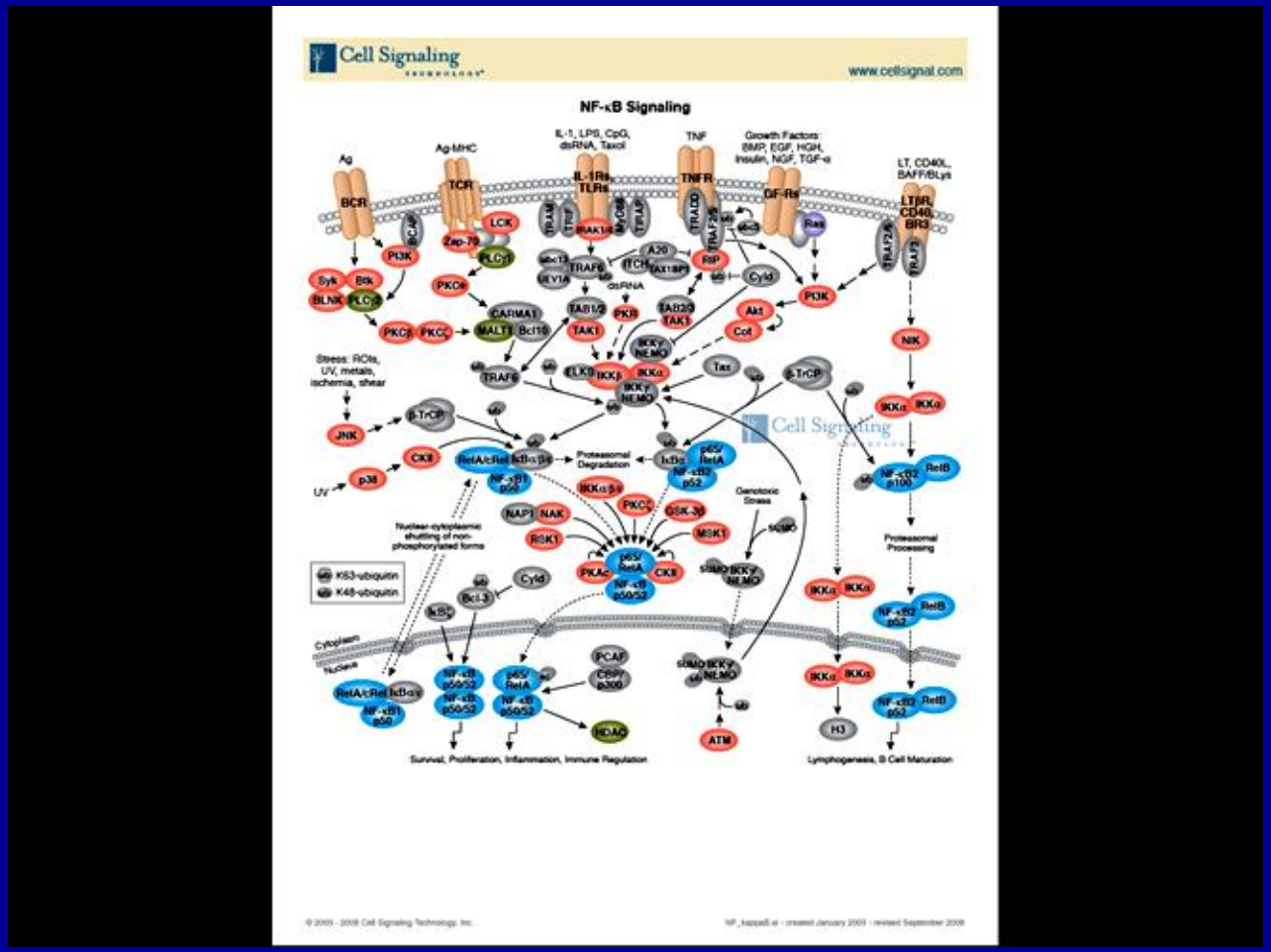
Copyright © 2002, Elsevier Science (USA). All rights reserved.

Complex Functional Circuits



TBI IS A COMPLEX, SYSTEMIC DISEASE

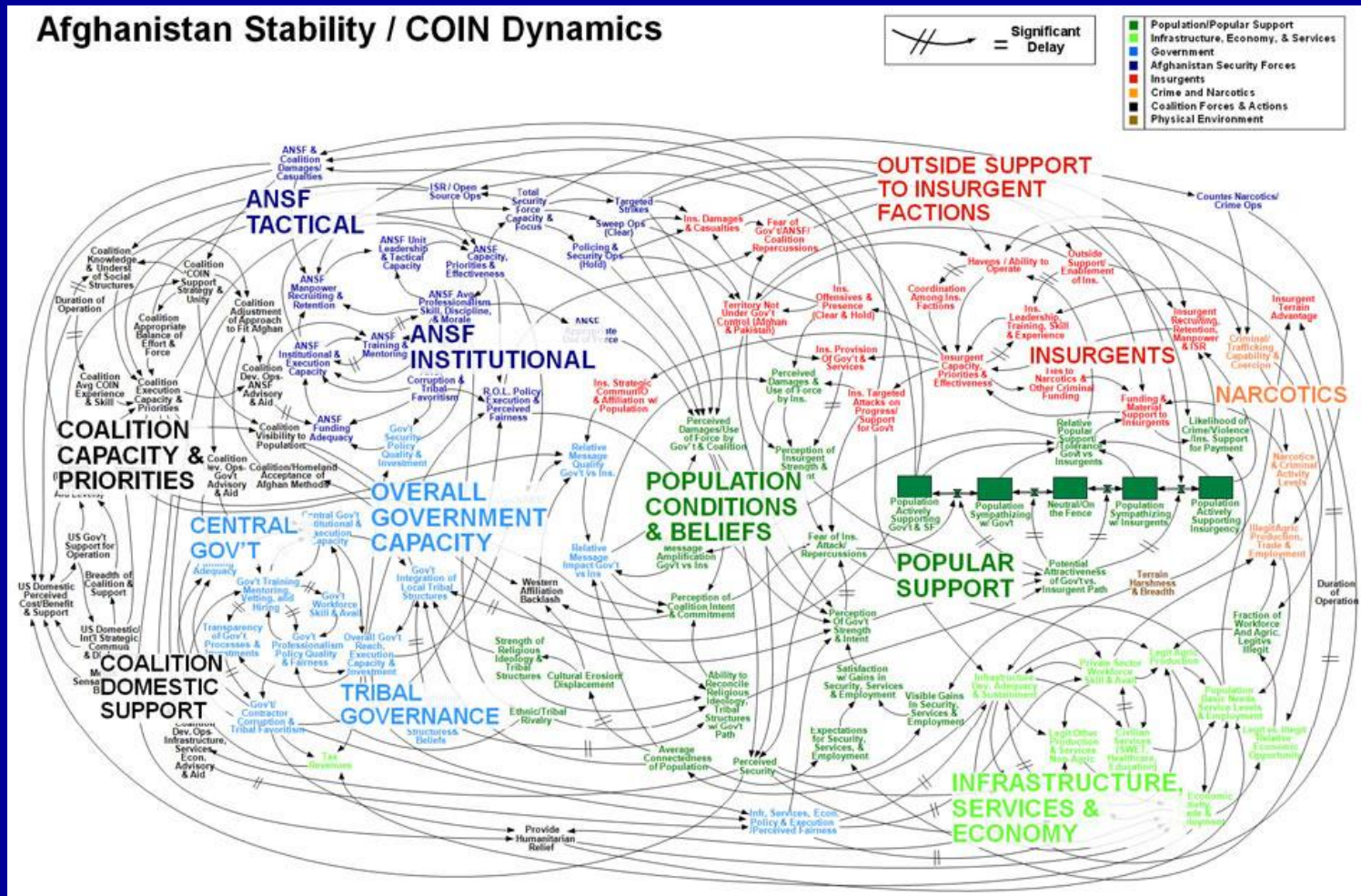
"information is not knowledge"—Albert Einstein



New York City Subway System



Afghanistan Stability / COIN Dynamics



PA Consulting Group
© PA Knowledge Limited 2009

Modern Phrenology

http://www.phrenology.org/professions.html

site visits: 449,602

•Medicine: What you need to be a doctor. Physicians require:

• Large Perceptive faculties, so that they may study and apply a knowledge of Anatomy and Physiology with skill and success;

•Full Destructiveness, lest they shrink from inflicting the pain necessary to cure;

• Large Constructiveness, to give them skill in surgery;

• Large Combativeness, to render them resolute and prompt;

• Large Cautiousness, to render them judicious and safe; and a large head, to give them general power of mind.

•Phrenology will predict, in advance, whether or not a student will succeed in this profession.

•"Scientists" at the University at Buffalo have reinvented phrenology in the form of a set of biometrics that produce a numerical score indicating the probability that you are about to commit a terrorist act.

• Computer and behavioral scientists at the University at Buffalo are developing automated systems that track faces, voices, bodies and other biometrics against scientifically tested behavioral indicators to provide a numerical score of the likelihood that an individual may be about to commit a terrorist act.

•"The goal is to identify the perpetrator in a security setting before he or she has the chance to carry out the attack," said Venu Govindaraju, Ph.D., professor of computer science and engineering in the UB School of Engineering and Applied Sciences.

• Govindaraju is co-principal investigator on the project with Mark G. Frank, Ph.D., associate professor of communication in the UB College of Arts and Sciences.

•October 2007

The Modern 'Phrenology' of Genes

- The new science of molecular genetics has made it possible to identify major genes influencing personality and forms of psychopathology.
- A group of scientists in Israel were the first to find an association between novelty-seeking (a trait very highly correlated with impulsive sensation-seeking) and a gene that codes for a class of dopamine receptor, the dopamine receptor-4 (DRD4) gene.

One of The Key Inventors of Brain Imaging Had this to say about Localizing Functions

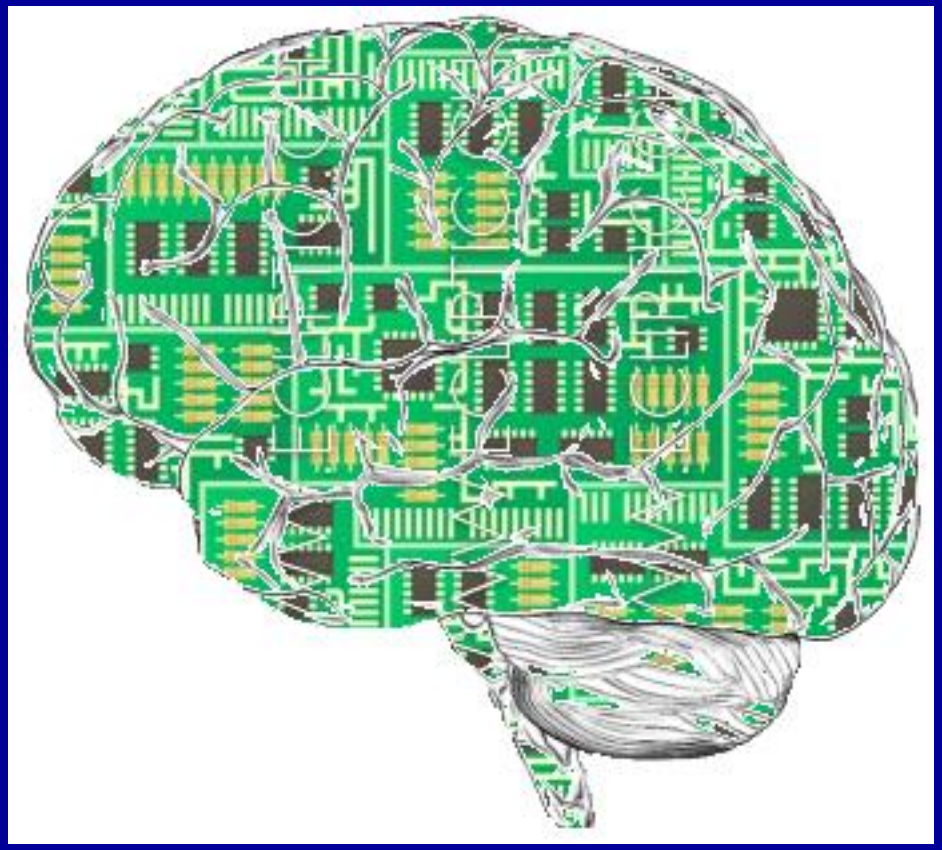
- "We no longer think of discrete areas of the brain that are responsible for an entire behavior.

- Rather, we think of these areas as elements underlying the behavior.

- I like the analogy of the brain as a symphony orchestra in which a finite number of elements can be combined in an almost infinite number of ways to create a very large number of unique products."

- (Marcus Raichle, 1999 Ann. NY Acad. Sci, 110)

Is The Brain Just Another Computer Motherboard?



•Leading scientists are claiming that they should be able to build a functional but artificial replica of a human brain within the next ten years or so.

THE HUMAN CONNECTOME PROJECT

http://www.humanconnectomeproject.org/overview/

•"The HCP is truly a grand and critical challenge: to map the wiring diagram of the entire, living human brain. Mapping the circuits and linking these circuits to the full spectrum of brain function in health and disease is an old challenge but one that can finally be addressed rigorously by combining powerful, emerging technologies," says Thomas Insel, M.D., Director of the National Institute of Mental Health (NIMH).

•Mapping of the human connectome offers a unique opportunity to understand the complete details of neural connectivity (Sporns et al., 2005, Wedeen et al., 2008, Hagmann et al., 2007).

•The Human Connectome Project (HCP) is a project to construct a map of the complete structural and functional neural connections in vivo within and across individuals. [*Even if the researchers succeed, they will only produce a static picture of a brain frozen in time, rather than something that shows how a brain responds to different types of internal or external stimuli.]*

•The HCP represents the first large-scale attempt to collect and share data of a scope and detail sufficient to begin the process of addressing deeply fundamental questions about human connectional anatomy and variation.

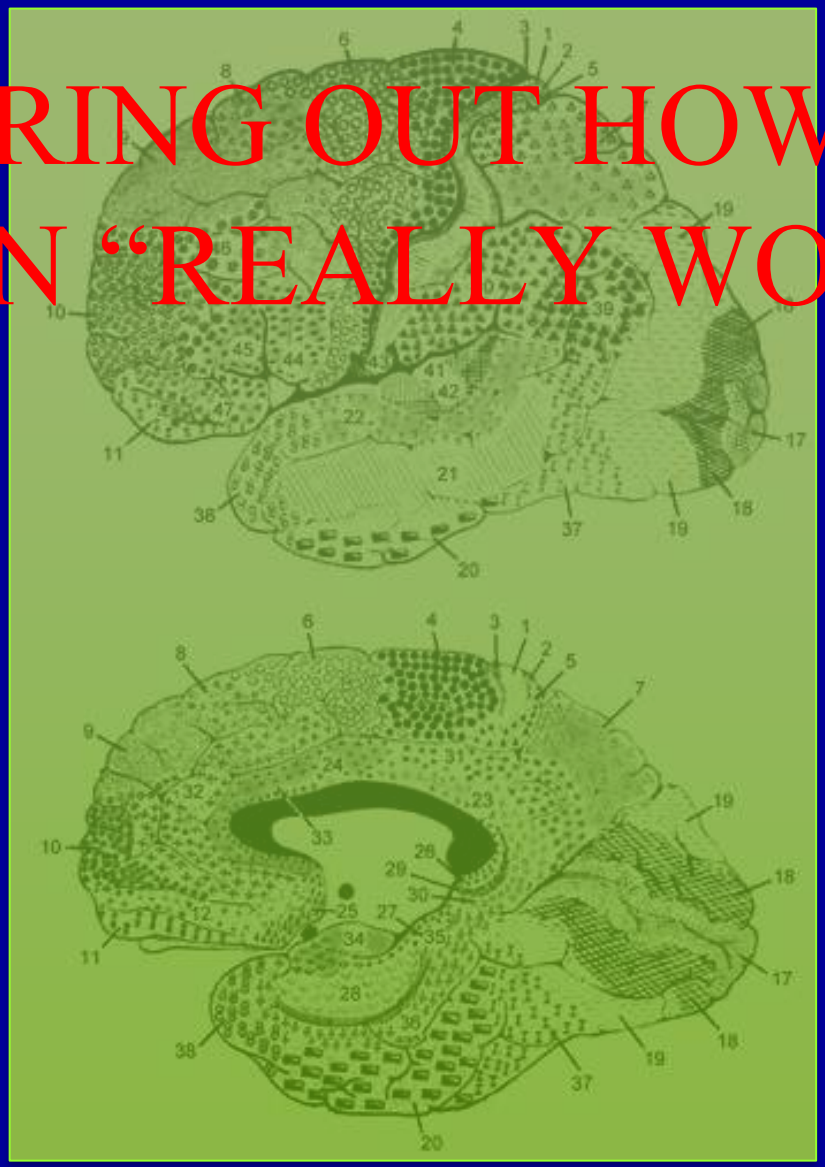
•The complexity of the brain and a lack of adequate imaging technology have hampered past research on human brain connectivity. The brain is estimated to contain more than 100 billion neurons that form trillions of connections with each other. Neurons can connect across distant regions of the brain by extending long, slender projections called axons – but the trajectories that axons take within the human brain are almost entirely uncharted. Note: This doesn't include glia! [NIH PRESS RELEASE July 16, 2009]

What is the Goal of the Project?

- The consortium will focus on optimizing MRI technology for imaging the brain's structural connections using diffusion MRI.

- Using a combination of non-invasive imaging technologies, including resting-state fMRI and task-based functional MRI, MEG and EEG, and diffusion MRI, the they will be mapping connectomes at the macro scale — mapping large brain systems that can be divided into anatomically and functionally distinct areas, rather than mapping individual. Using this imaging method, the long extensions of neurons, called white matter, can be seen in sharp relief.

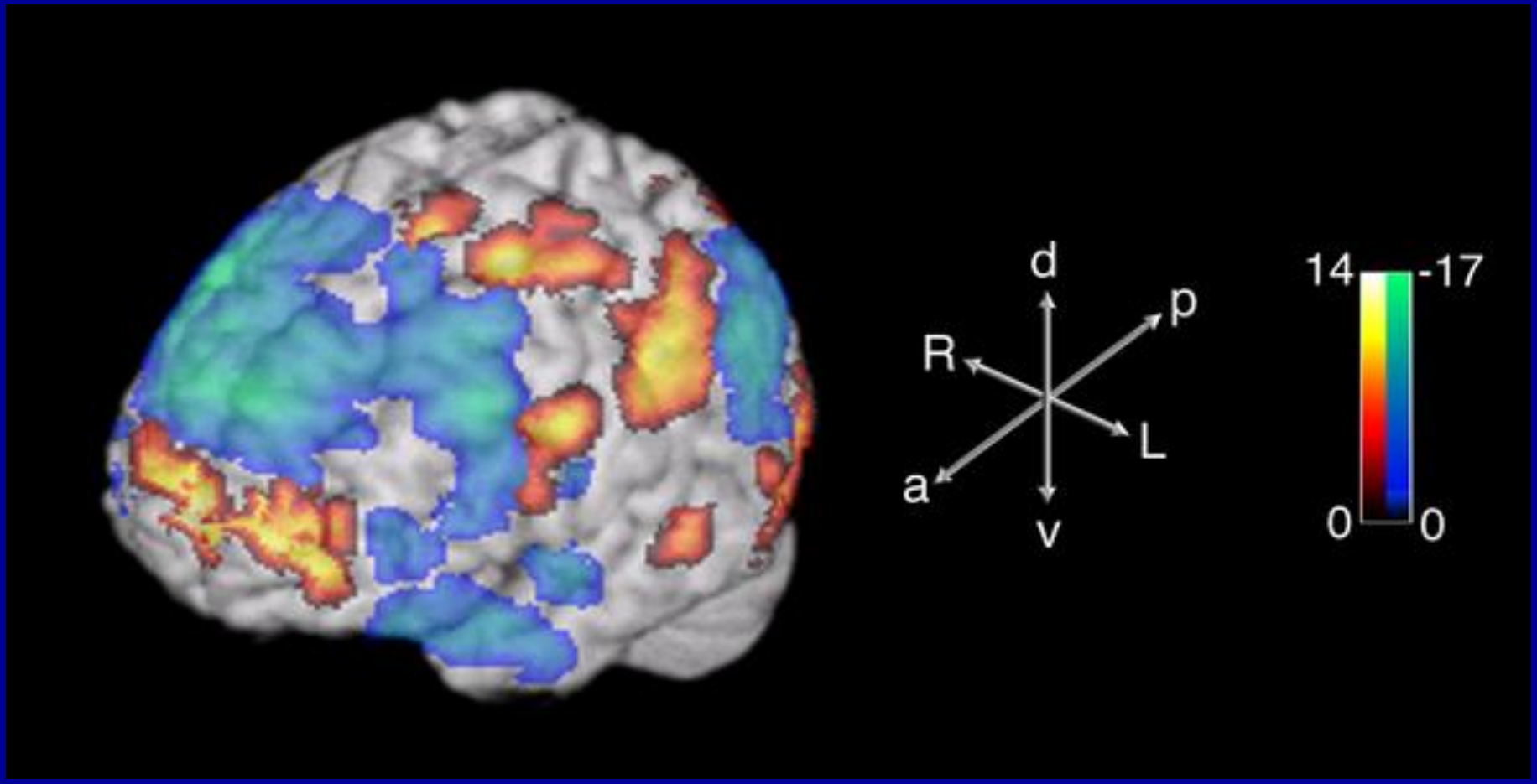
FIGURING OUT HOW THE BRAIN "REALLY WORKS"



Agreed: WE Can Map The Brain! But…

- What is the best representation of the thing mapped?
- What is the difference between a ‘reliable’ and a ‘valid’ map?
- Who gets to decide the ‘metric’?

Figure 3. Three-dimensional surface projection of activations and deactivations associated with improvisation during the Jazz paradigm.



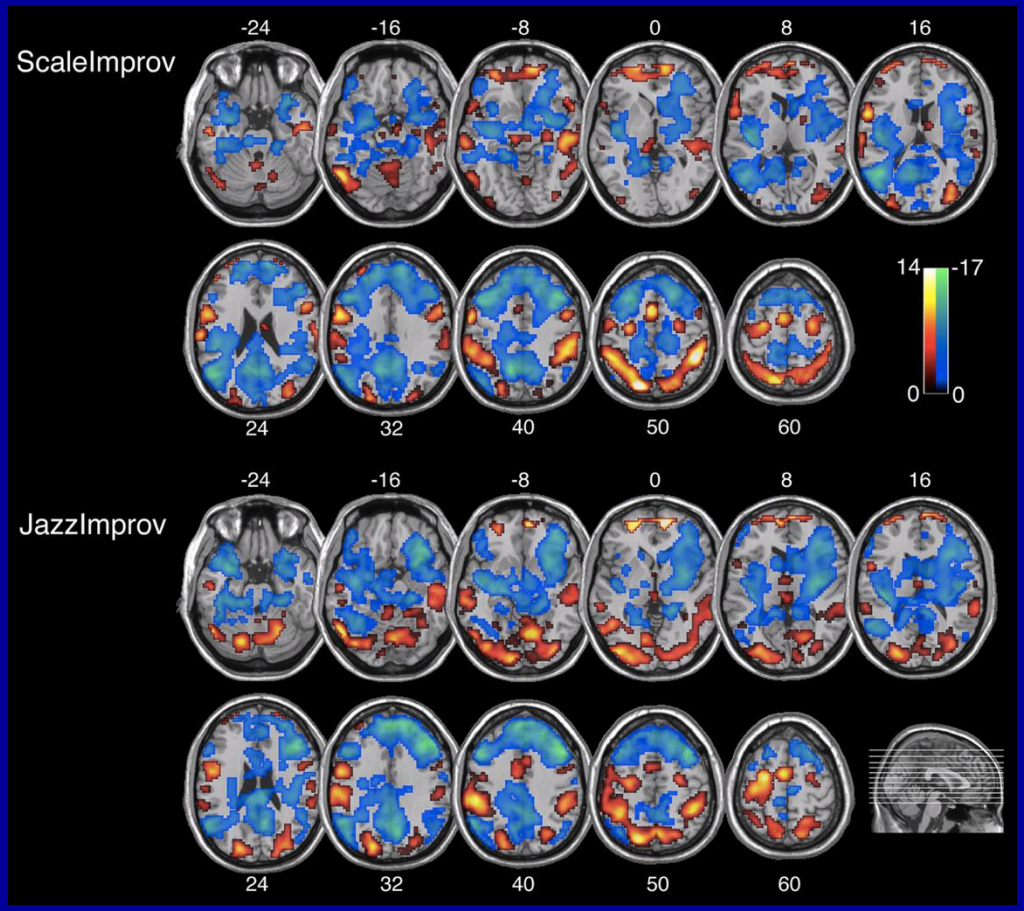
•Limb CJ, Braun AR (2008) Neural Substrates of Spontaneous Musical Performance: An fMRI Study of Jazz Improvisation. PLoS ONE 3(2): e1679. doi:10.1371/journal.pone.0001679

•http://www.plosone.org/article/info:doi/10.1371/journal.pone.0001679

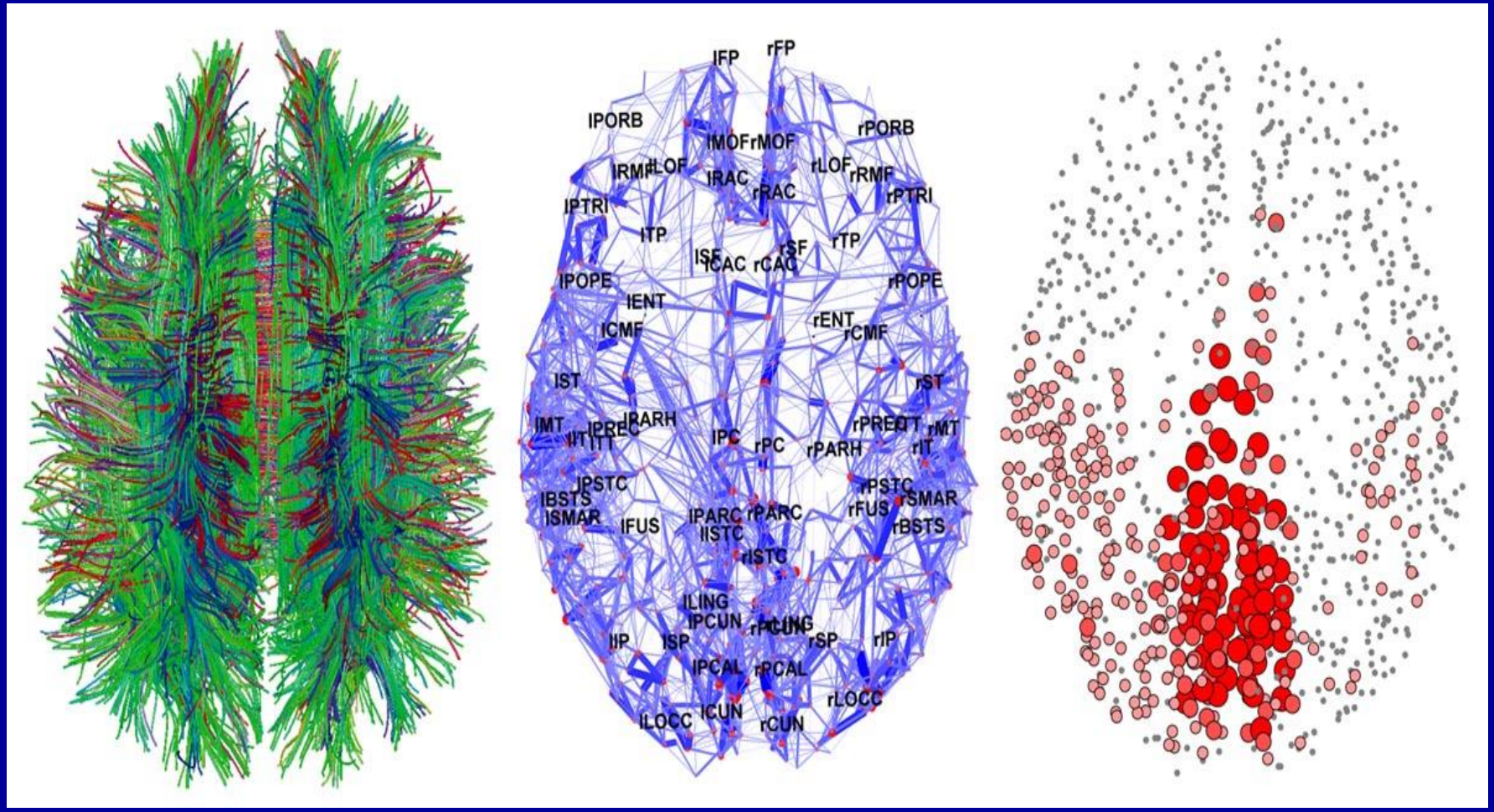
PLOS | ONE

Neural Substrates of Spontaneous Musical Performance: An fMRI Study of Jazz Improvisation

Charles J. LimbAllen R. Braun [PLOS1]



The Connectome: Mapping All The Connections Of The Brain



•The human connectome. Images show the fiber architecture of the human brain as revealed by diffusion imaging (left), a reconstructed structural brain network (middle) and the location of the brain's core, its most highly and densely interconnected hub (right). THIS IS MEASURED DURING “REST”.

What Do the Frontal Lobes "Do"? 2025 Version

- *mediate*, *involved in , implicated in, control, the seat of, responsible for:*

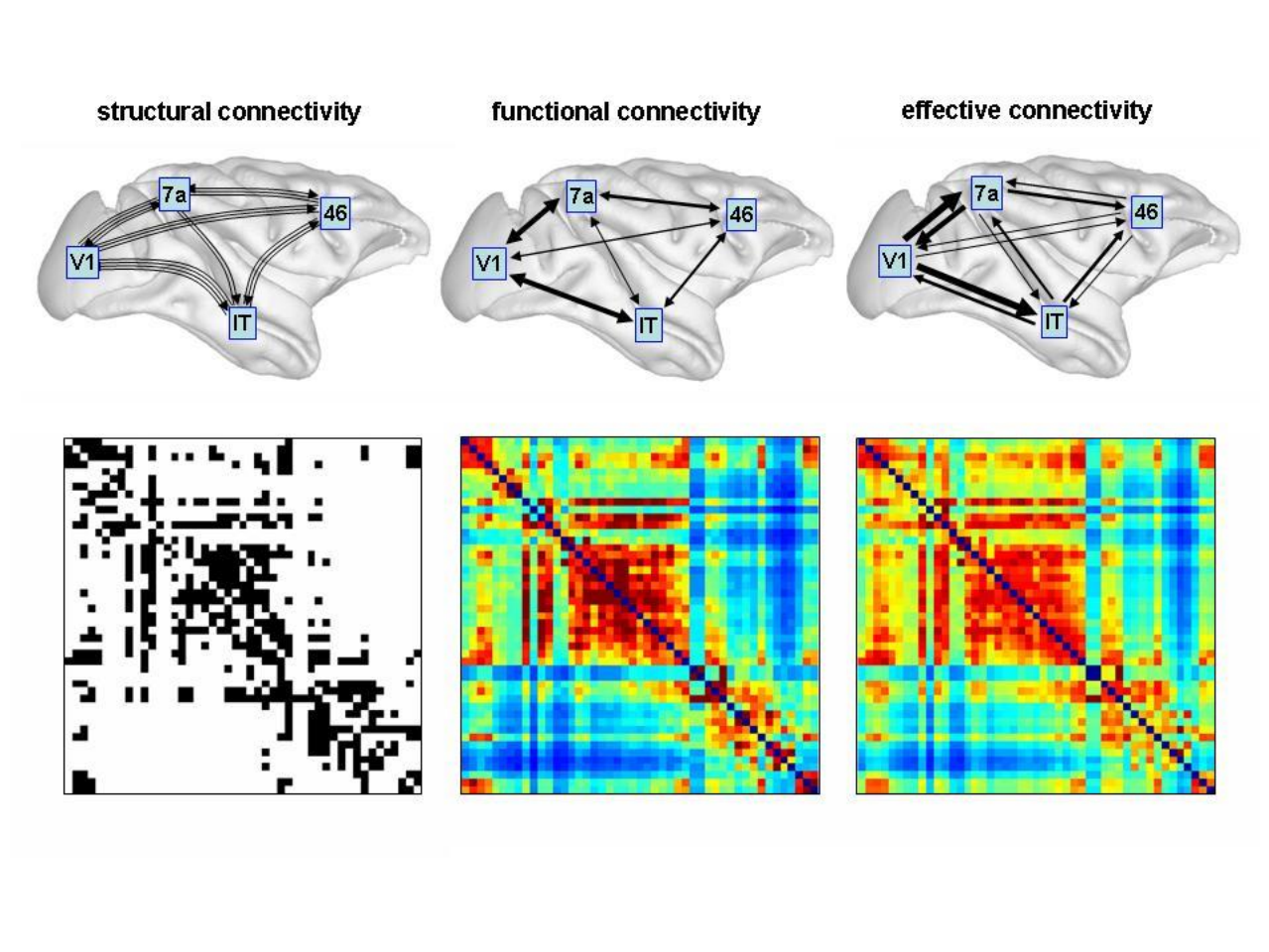
- Executive Planning, problem solving, memory, impulse control, decision-making, selective attention, controlling behavior and emotions.

- "The frontal lobe *is a critical center and it controls* the "essence" of our humanity", according to Dr. Donald Stuss director of The Rotman Research Institute, Toronto, Canada.

- The lobes are *the seat of emotions* and judgments related to sympathy, the ability to feel sorrow for someone else's suffering, and empathy, ability to understand another's feelings and problems.

- They are *the seat* of understanding humor, including subtle witticisms and word plays. They recognize sarcasm and irony.

The Connectome: Mapping All The Connections Of The Brain



Stanford Psychologists Uncover Brain-imaging Inaccuracies

- Traditional methods of fMRI analysis systematically skew which regions of the brain appear to be activating, potentially invalidating hundreds of papers that use the technique.

- Many of the most common analyses in use today are holdovers from older, lower-resolution types of imaging and seem to have some undesired effects on the finer-grained signals fMRI can provide.

- Activity in smaller brain structures is often overlooked, or even shifted to areas that receive more blood flow and where the blood oxygenation level-dependent signal is stronger.

An Empirical, 21st Century Evaluation Of Phrenology

O. Parker Jones* , F. Alfaro-Almagro and S. Jbabdi

Cortex, 106, 2018

- The present study sought to test in the most exhaustive way currently possible the fundamental claim of phrenology: that measuring the contour of the head provides a reliable method for inferring mental capacities. We found no evidence for this claim.

- According to our results, a more accurate phrenological bust should be left blank since no regions on the head correlate with any of the faculties that we tested.

- However, phrenology's “faculty psychology” is not as different from current ontologies as it might first seem. One can readily find examples of 19th century faculties in the neuroimaging literature, albeit under different names.

"Normal science, the activity in which most scientists inevitably spend almost all their time, is predicated on the assumption that the scientific community knows what the world is like. Much of the success of the (scientific) enterprise derives from the community's willingness to defend that assumption even at considerable cost. Normal science often suppresses fundamental novelties because they are necessarily subversive of its basic commitments."

-Kuhn, T.S. "The Structure of Scientific Revolution"
2nd Edition, 1970 Univ. Chicago Press

HOW AI CAN READ MINDS



1 Patient is exposed to hours of podcasts

Patient is exposed to hours of podcasts while in MRI machine. Trains AI algorithm to associate brain activity with certain words.

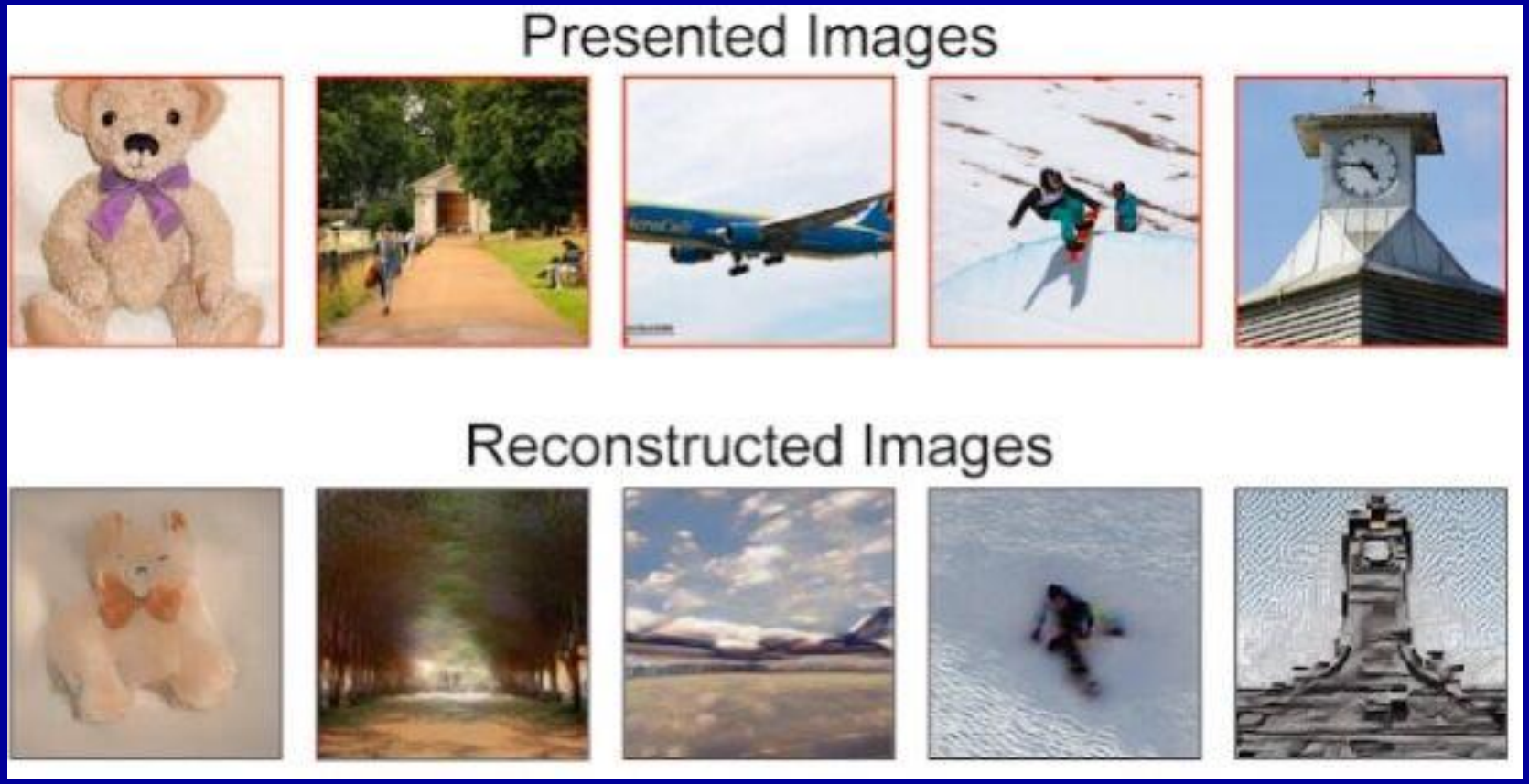


2 Person is exposed to news stories or told to tell own story

Patient reacts to news story or tells their own story by thinking. MRI reads brain scans, converting them into words with about 50% accuracy.

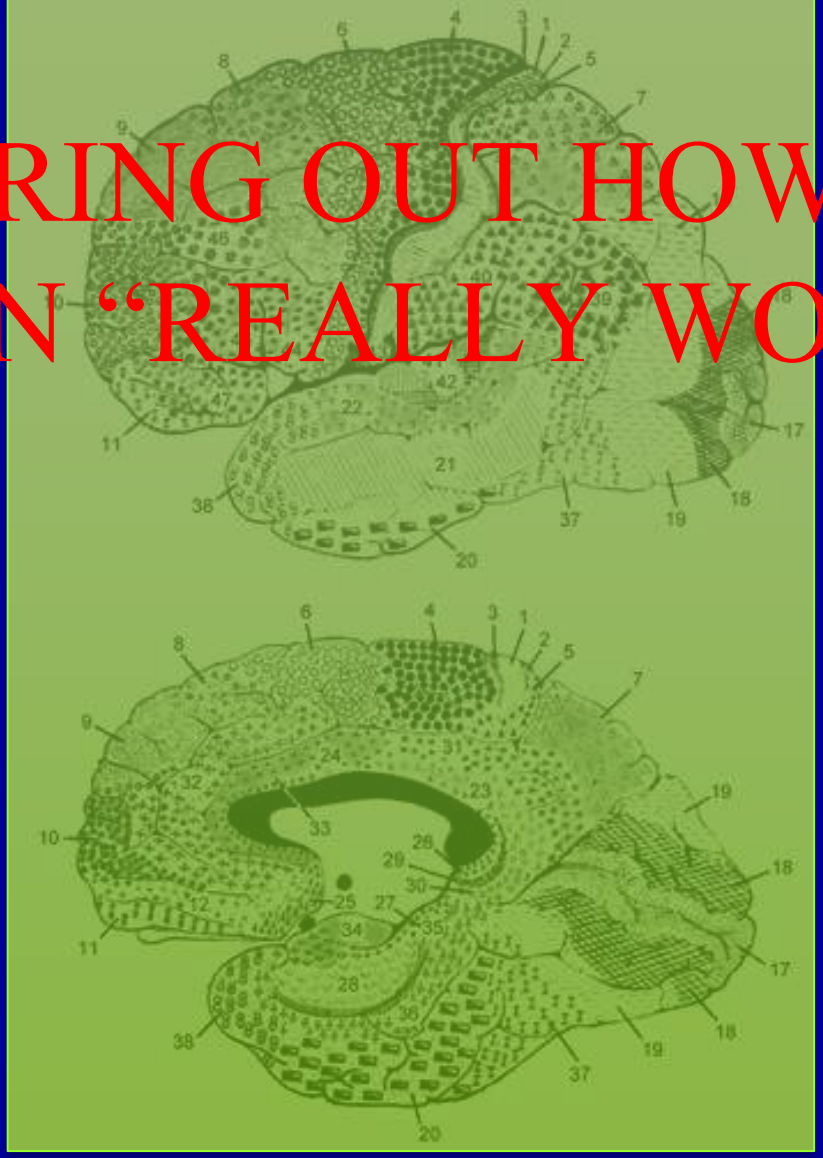


What AI Was Able To Produce From An MRI Of A Patient Looking At Images



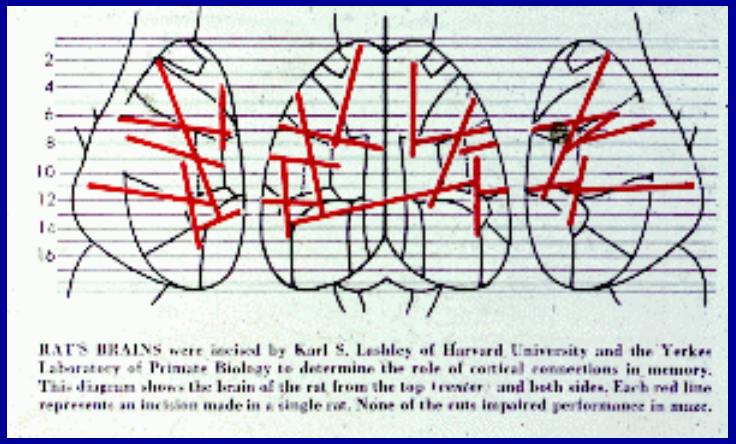
End, Part I

FIGURING OUT HOW THE BRAIN "REALLY WORKS"



Some Contemporary Issues in Recovery Research and Theory

Mass Action & Equipotentiality: The Contribution of Karl Lashley



RAT'S BRAINS were incised by Karl S. Lashley of Harvard University and the Yerkes Laboratory of Primate Biology to determine the role of cortical connections in memory. This diagram shows the brain of the rat from the top (center) and both sides. Each red line represents an incision made in a single rat. None of the cuts impaired performance in maze.

Is There Anything Like "Equipotentiality" in the Real World? Can We Expect to See This in Higher Mammals?

Auditory Compensation for Early Blindness in Cat Cerebral Cortex.

Rauschecker, JP & Corte, M.; J. Neurosci., 1993

- Recorded single cells in visual cortex of cats deprived of vision for several years after birth & compared to normal cats.
- Normals responded to visual stimulation.
- Deprived responded only to auditory or somatosensory stimulation.
- *Conc.* **Cortical representation (function) changed as a result of experience from visual to auditory.**

Another Interesting Question: "Contextual Plasticity"

- The Serial Lesion Effect.
- Implications for Localization.
- Mechanisms of Intrinsic Plasticity.

Plasticity of the Human Motor Cortex

Seitz, RJ & Freund, H-J., Adv. Neurol. 1997

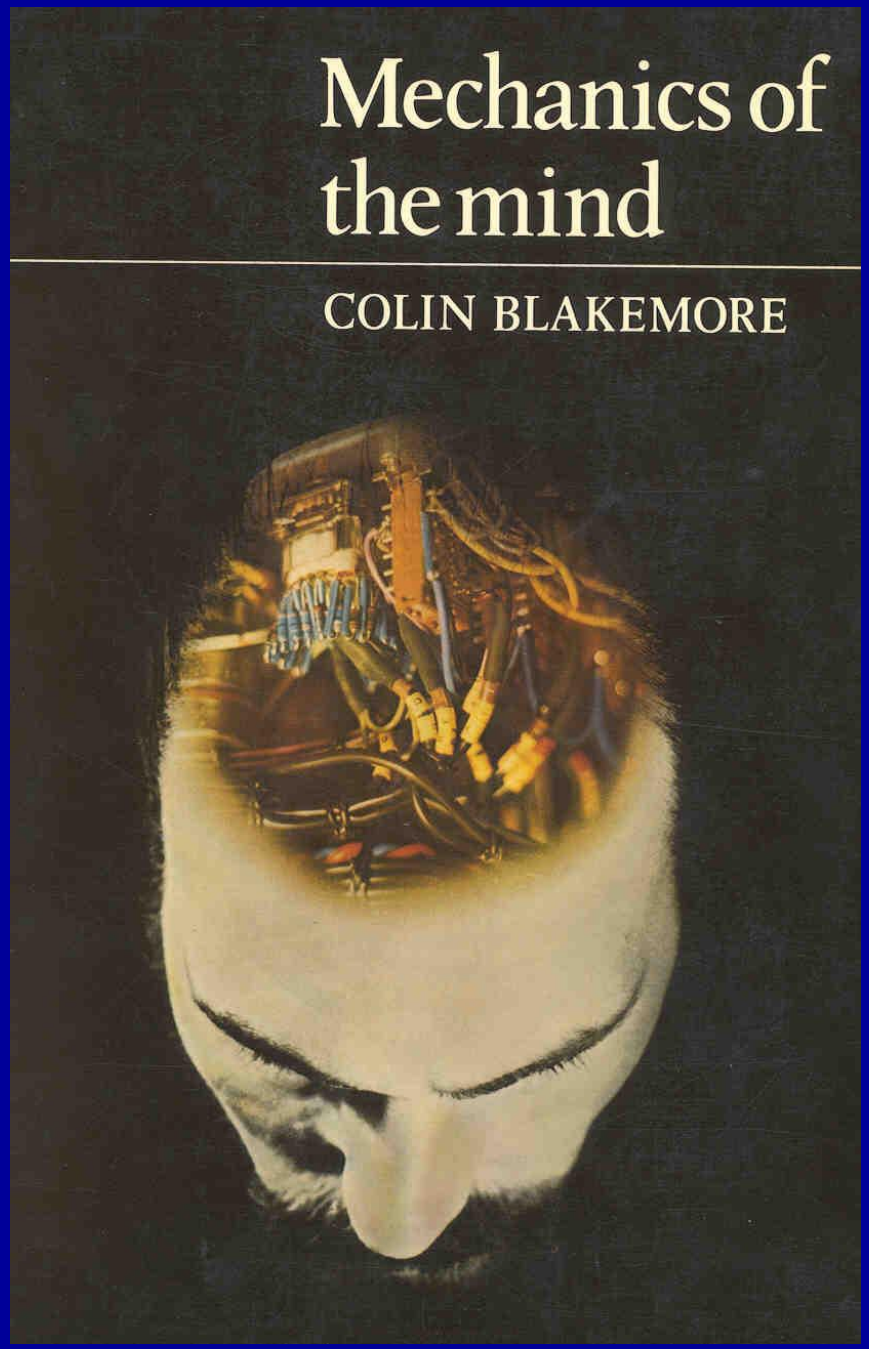
- Examined adult Ss with lesions of pyramidal system (acute infarct and slow-growing lesions) using evoked motor potentials and rCBF.
- In acute Ss ROF of MEPs is variable and correlates with rCBF changes in a number of related motor areas.
- Progressive (but same extent) lesions do not result in similar deficits & removal of the affected areas does not produce motor deficit, indicating marked reorganization of function.

Components of a Theory of Recovery of Function

- A workable definition of ‘function’.
- Meaningful and reliable measures of recovery outcome.
- Specified and predictive physiological mechanisms.

Mechanics of the mind

COLIN BLAKEMORE



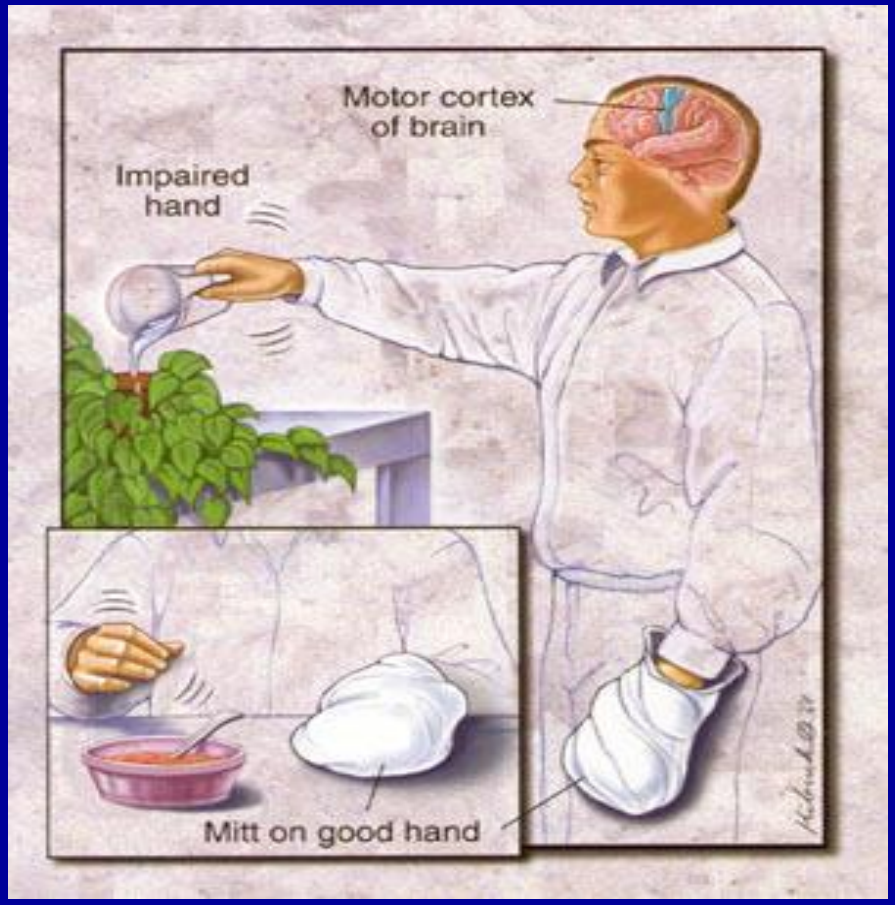
Compensation and Substitution

- Is ‘recovery’ just a trick? Does actual recovery *ever* occur?
- Is all compensation always beneficial (e.g. exuberant axonal sprouting)?
- Is compensation sometimes bad (e.g. learned helplessness, spasticity)?

Brain Organization (and Reorganization) Is Dependent Upon Experience (II).

- PET used to measure rCBF in sighted and congentially blind adult Ss performing auditory localization tasks.
- Blind Ss activated areas in the right occipital cortex during auditory localization.
- ***"The right occipital cortex participates in a functional network for auditory localization arising from input from the posterior parietal".***
- **Weeks, et al, J. Neurosci., 20, 2000.**

Forced Use Paradigm and Recovery



Spontaneous Recovery and Diaschisis

- Distal effects of a brain injury: inhibition.
- There are focal and widespread alterations in response to TBI.
- Such ‘alterations’ can take place months and years after the initial injury.

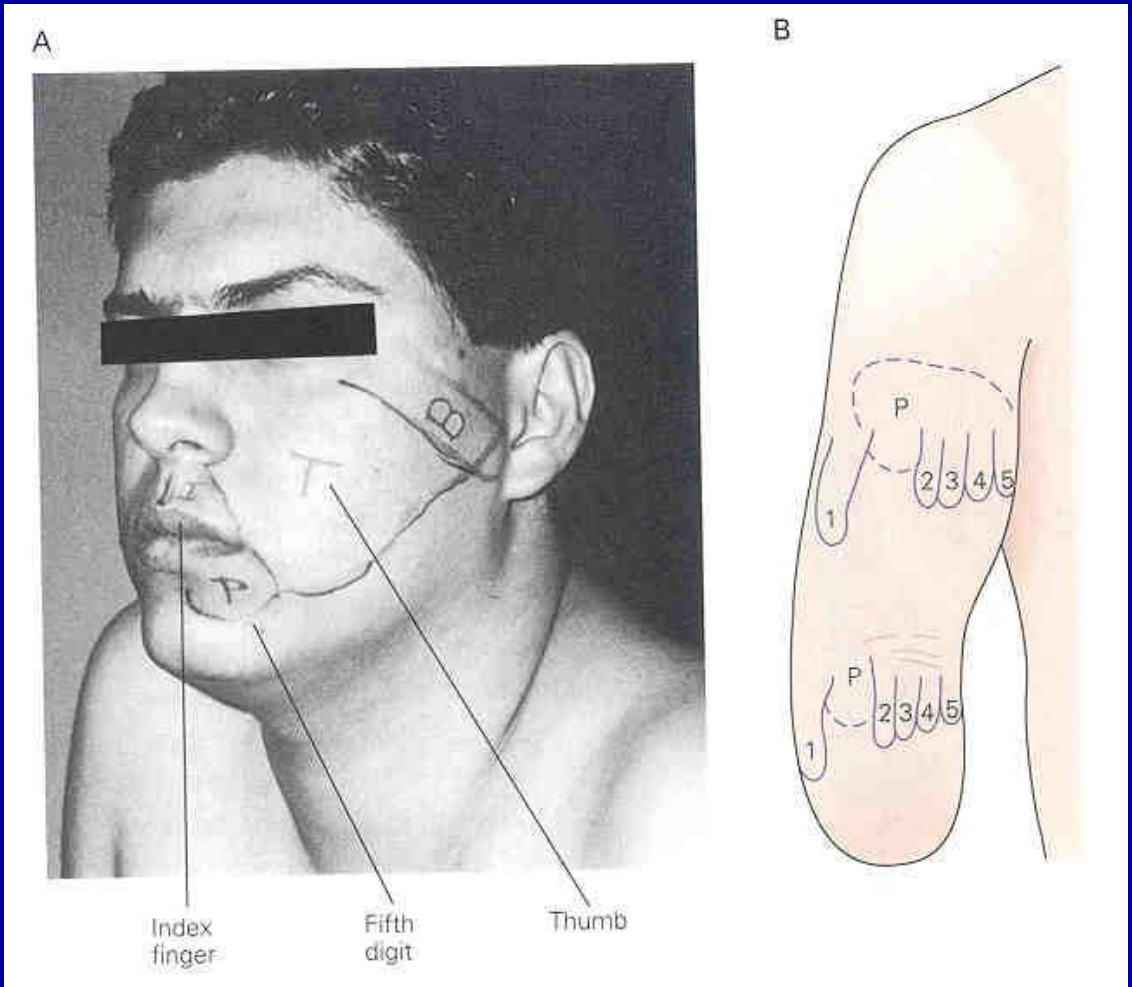
Spontaneous Recovery and Diaschisis

- Other areas can ‘take over’ for damaged tissue (are they “de-blocked’?).
- Do previously ‘uninvolved’ areas play a role in the compensation?
- *How* does area ‘A’ take over for ‘B’ and still do ‘A’ effectively-- especially if the injury is bilateral?

Rapid Reorganization and Re-mapping the Brain

- **Reorganization in response to injury can occur within minutes after the damage.**
- **Can loss of input into one cortical area lead to capture of that area by another modality?**
- **Is this kind of synesthesia adaptive or an example of ‘negative’ plasticity?**

Phantom Limb Reorganization



Rapid Reorganization and Re-mapping the Brain

- **Rapid reorganization occurs in motor *and* sensory systems.**
- **Training and rehabilitation (therapy) may be needed to produce sustained reorganization.**
- **Inappropriate or ill-timed training can increase extent of injury and prevent recovery.**
- **Individual differences in cerebral organization are important and history plays a role.**

The Role of Glia in CNS

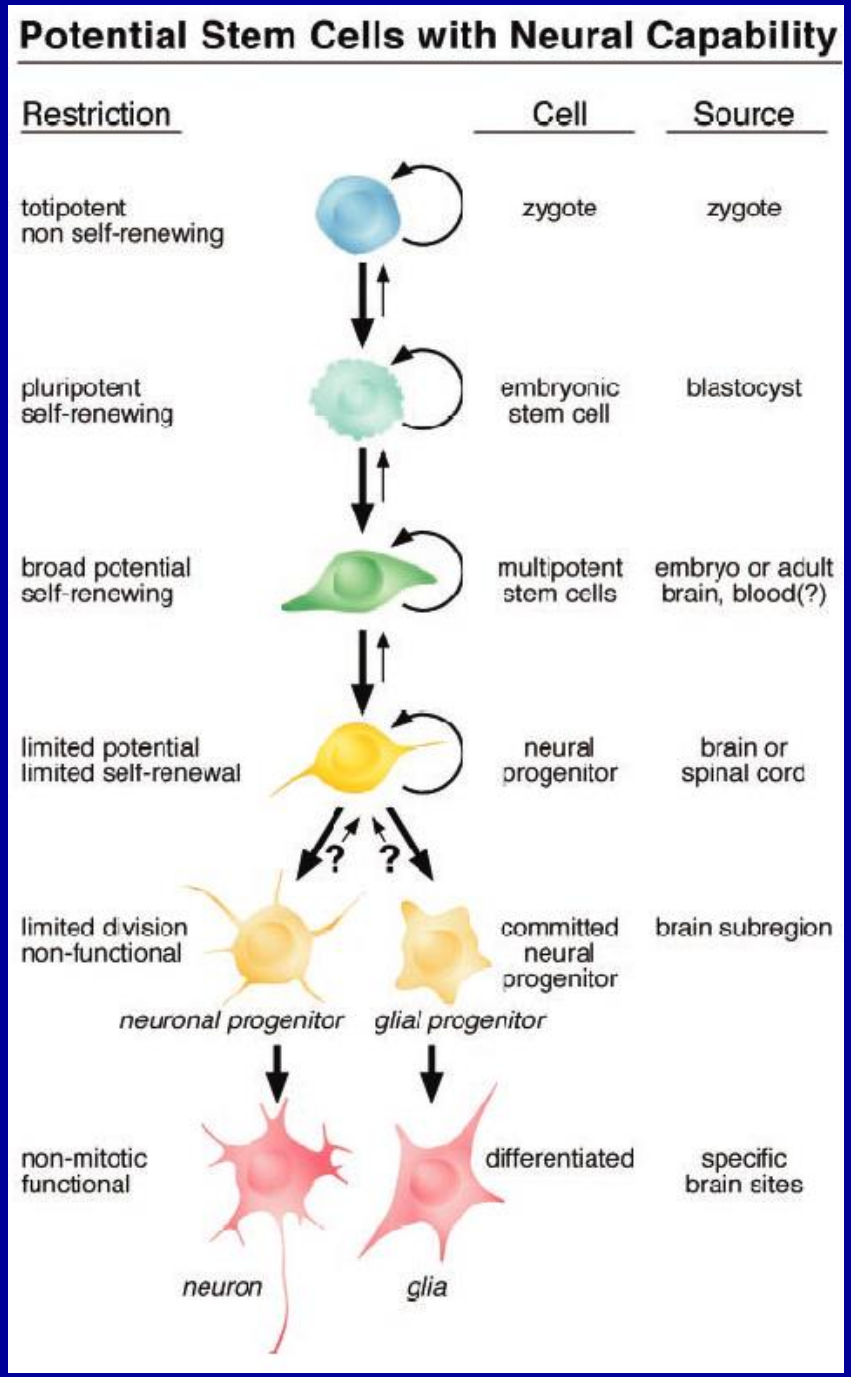
- Glia are the principle regulators of cell number in the CNS
- Glia influence neuronal migration, axon specification and growth
- Glia influence neuronal migration, axon specification and growth
- Glia can coordinate circuit wide neuronal differentiation
- Glia regulate synapse formation and pruning
- Neuro-glial-vascular coupling provides metabolic support
- Astrocytes dynamically alter brain states

Working Hypotheses on Recovery

- Neuronal sprouting and regeneration may directly mediate recovery.
- Neurogenesis in adult patients can re-establish functional connections and enhance recovery.
- Transplantation of fetal, genetically modified, neural or progenitor cells can mediate functional recovery.

Stem Cells Can Be Transplanted Into the Damaged Brain Where They May Survive and Promote Functional Recovery

Stem Cells Are Reproted to Take on Different Structures and Functions in the Brain



Stem Cells Originate in Different Brain Structures

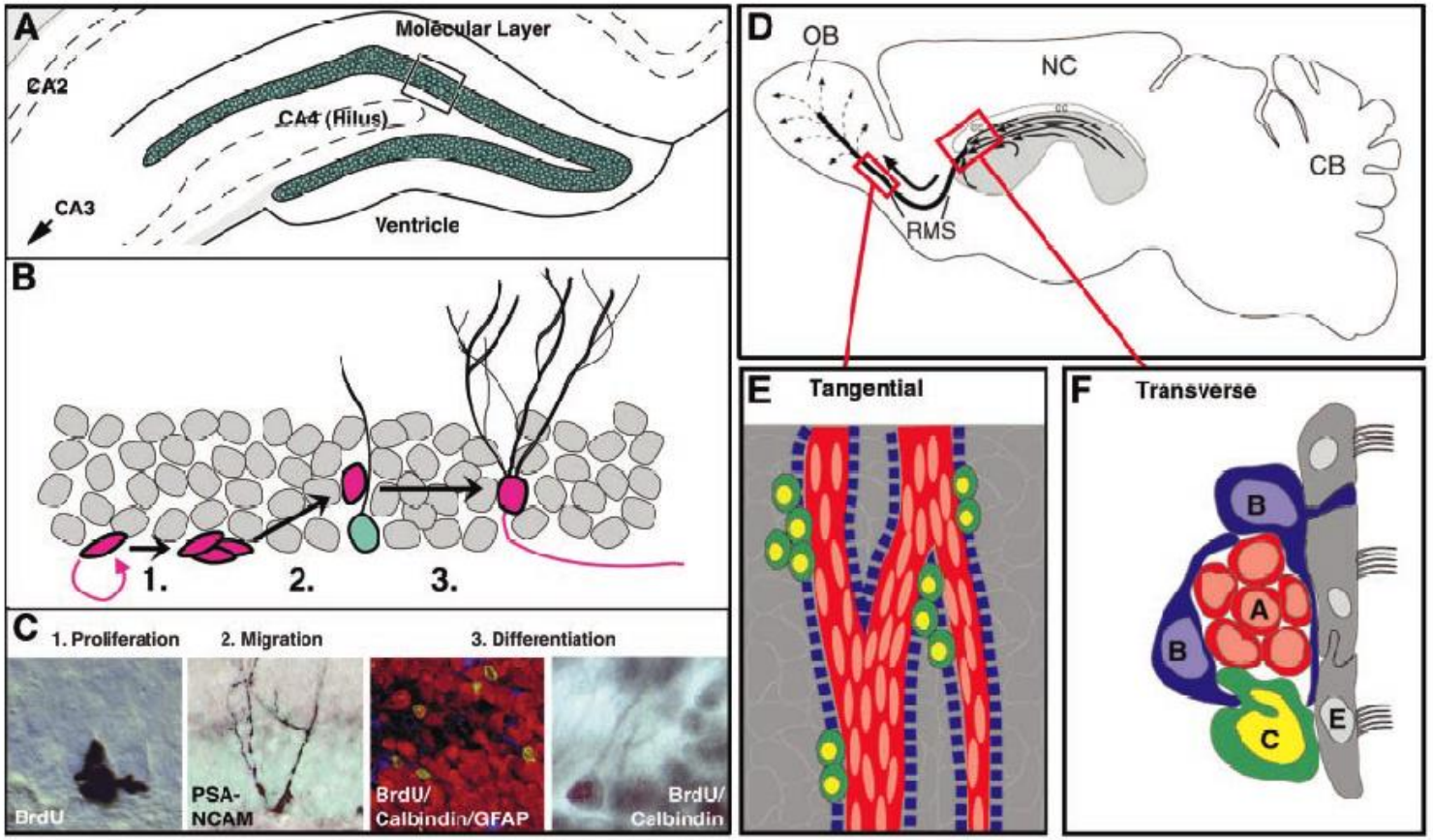


Fig. 3. Examples of the origin and migratory pattern of the stem cells observed in situ in (**A** through **C**) the adult dentate gyrus and (**D**) the subependymal RMS. The box in (A) indicates the granule cell layer illustrated in (B). The numbers in (B) refer to the three steps shown in (C). OB, olfactory bulb; NC, neocortex; CB, cerebellum. (**E**) A schematic of the chain migration of the cells in the RMS, which originate in the subependymal zone. (**F**) The red cells (A label) are the neural progenitor cells, the purple (B label) cells are astrocytes, and the green (C label) cells are precursor cells that are found scattered along the RMS (E label). (A) through (D) are a composite by H. G. Kuhn, and (D) through (F) are from (*55*), reprinted by permission of Wiley-Liss Inc., a subsidiary of John Wiley & Sons, Inc.

Gage, (2000) VOL 287 SCIENCE; 1433-38.

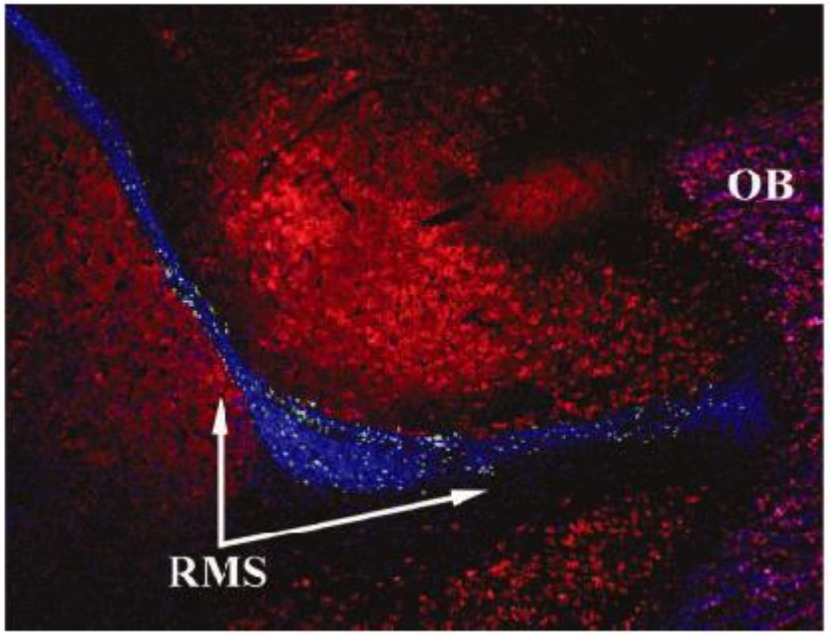
But, Are They *Really* Neurons? And What If They Aren't--who Cares?

{Transplanted Glial Cells Can Also Enhance and Promote Recovery of Function}

Can Neurons Be Born in the Adult Brain?

New Neurons in the Adult Brain

Fig. 2. Adult forebrain neurogenesis. A sagittal section of the adult mouse forebrain [with mature neurons labeled for NeuN (a neuronal antigen) in red] shows neuronal precursors labeled with bromodeoxyuridine (green) migrating along the rostral migratory stream (RMS; blue Hoechst stain) toward their final destination in the olfactory bulb (OB).



Neurogenesis in the Adult Hippocampus of the Monkey

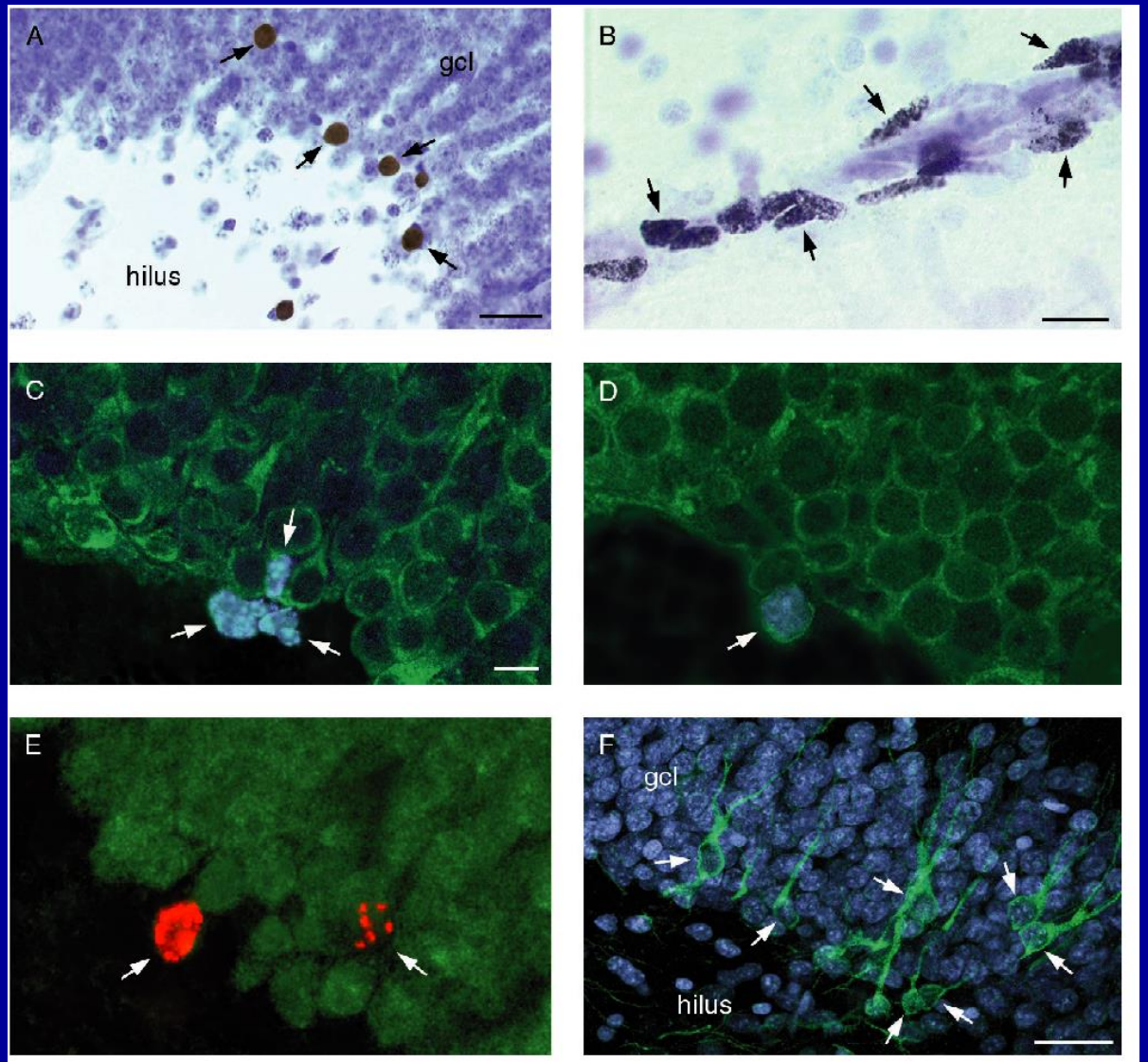
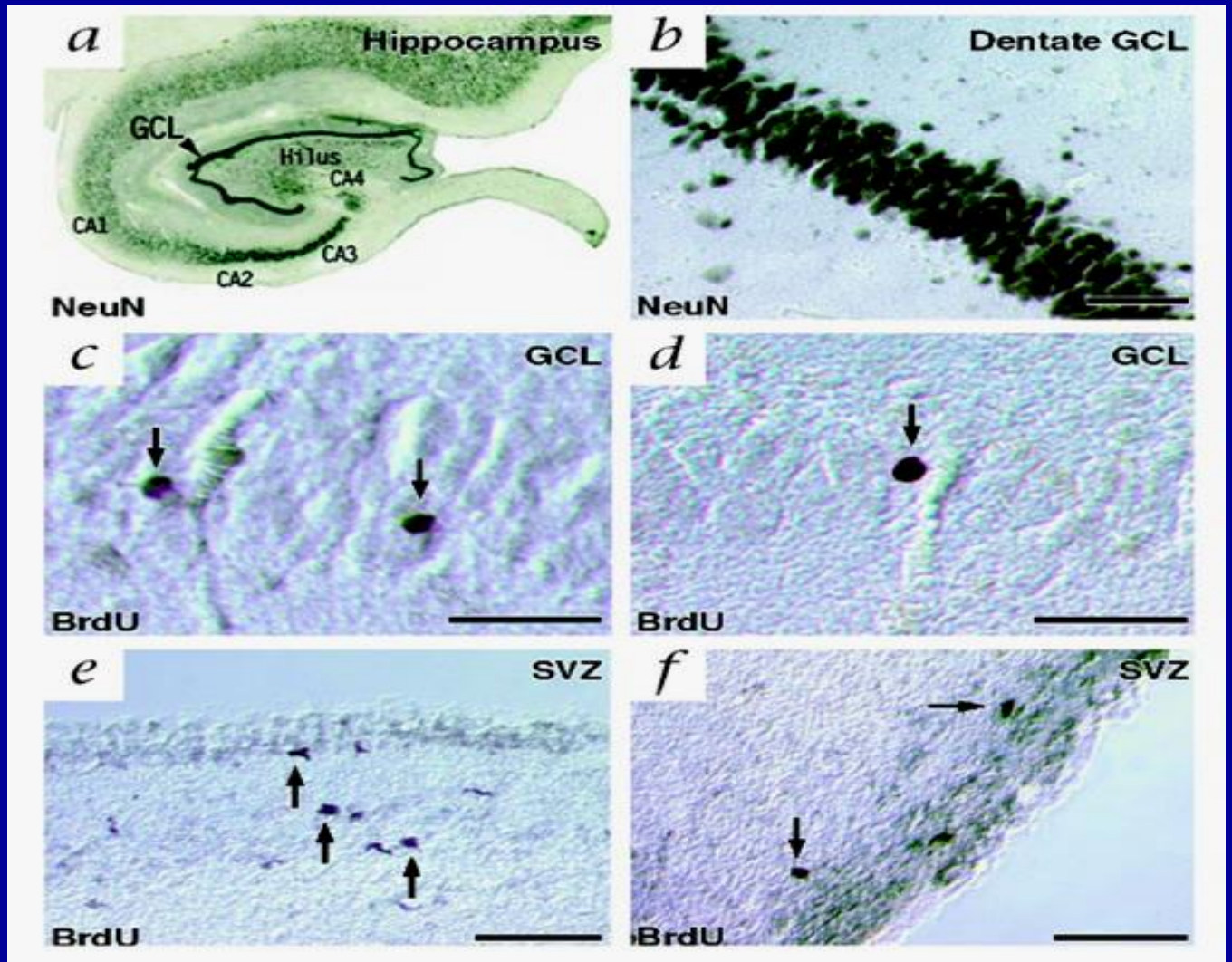


FIG. 1. Photomicrographs (*A* and *B*) and confocal laser scanning microscopic images (*C–F*) depicting new cells produced in the adult monkey brain. BrdUrd-labeled cells were observed in the granule cell layer of the dentate gyrus (*A*) (arrows) (animal 7) and in a region corresponding to the rostral migratory stream in rodents (*B*) (arrows) (animal 4). (*C*) Clusters of BrdUrd-labeled cells (blue nuclear stain) were observed in the subgranular zone of the dentate gyrus (arrows) (animal 2). Many of these clustered cells in animals injected with BrdUrd followed by short survival times (2 hr after BrdUrd injection) were not immunoreactive for NSE (green cytoplasmic stain). (*D*) In monkeys perfused 1–2 weeks after the last BrdUrd injection, BrdUrd-labeled cells expressing the neuronal marker NSE were observed (arrow is an example from animal 3). (*E*) BrdUrd-labeled cells in the granule cell layer of animals perfused 2 weeks after the last of five BrdUrd injections were immunoreactive for NeuN (arrows indicate double-labeled cells) (animal 1). (*F*) TOAD-64 stained cells with the morphology of granule cells were observed in the granule cell layer (arrows) (animal 1) (granule cells stained here with the DNA dye Hoechst 44323) gcl, granule cell layer. [Bars = 30 μm (*A*), = 15 μm (*B*), = 10 μm (*C*, *D*, and *E*), and = 40 μm (*F*).]

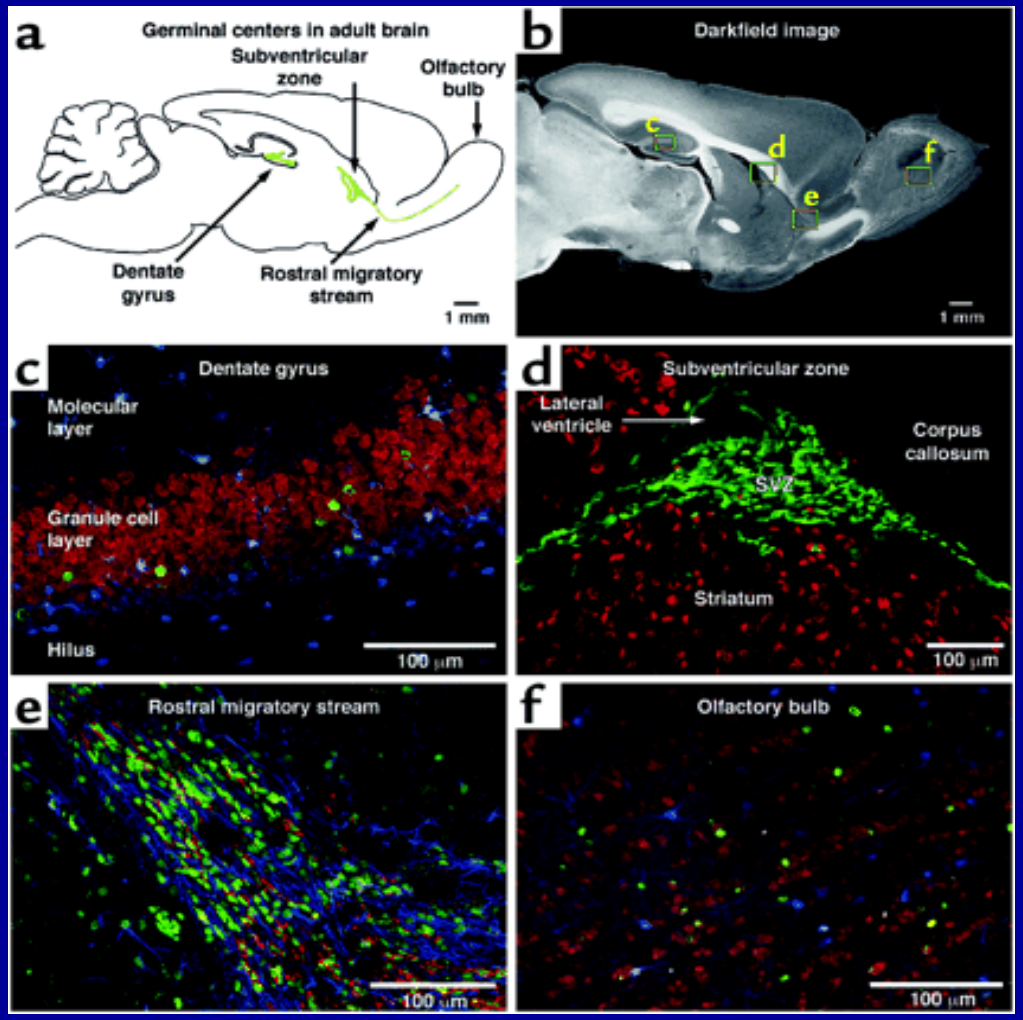
Gould, et al Vol. 96, Issue 9, 5263-5267, April 27, 1999.

Neurogenesis In the Adult Human Hippocampus
Erikson, Et Al , Nature Med. 1999

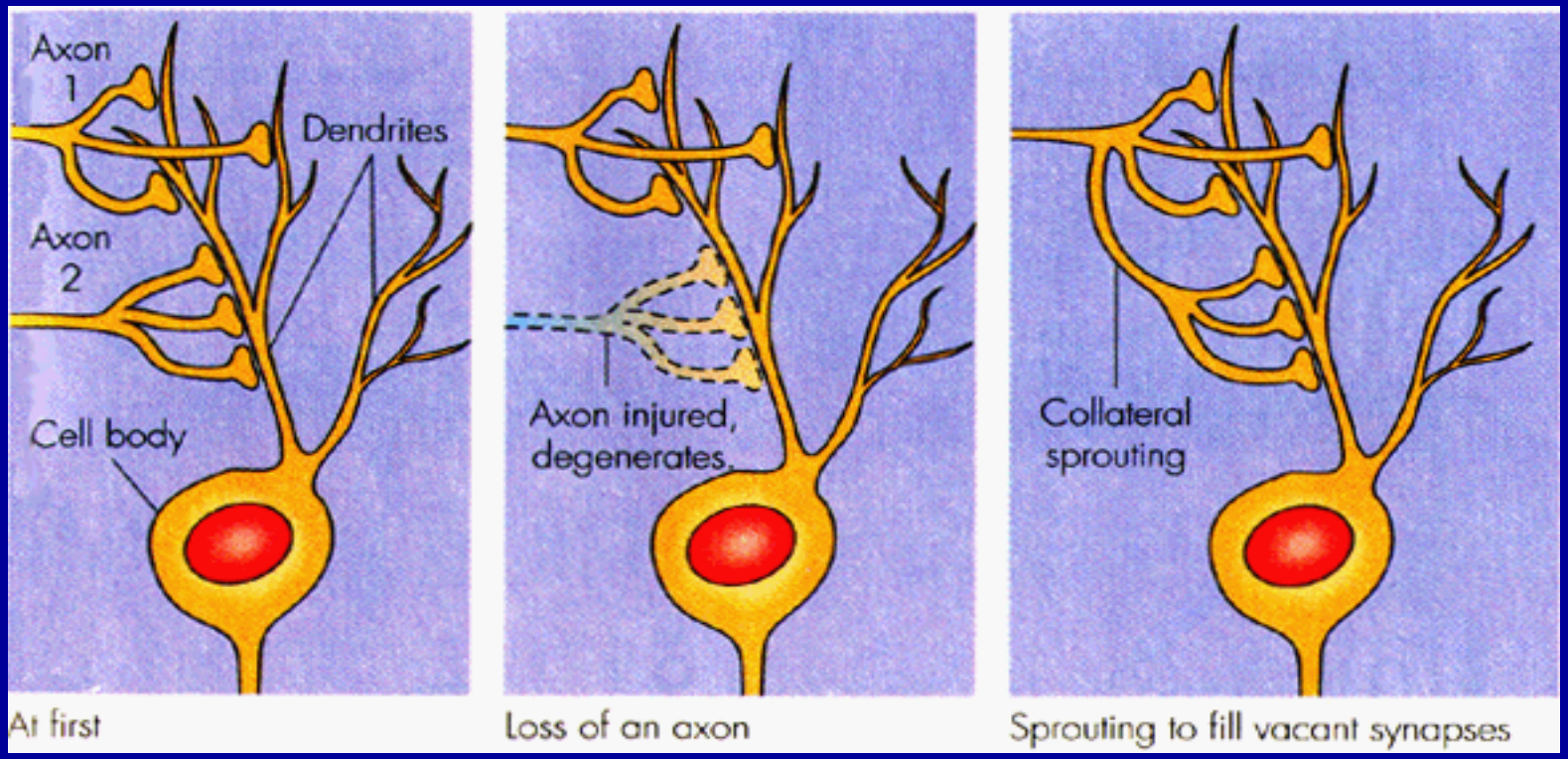


Germinal Centers in the Adult Brain

Hallbergson, Et Al, J Clin Invest, 112, 2003



Dendritic and Axonal Sprouting In Response to Injury Can Enhance Recovery



Environment and Experience Can Alter Neurogenesis in the Adult Brain

Seasonal Changes in Songbird Brain Structure

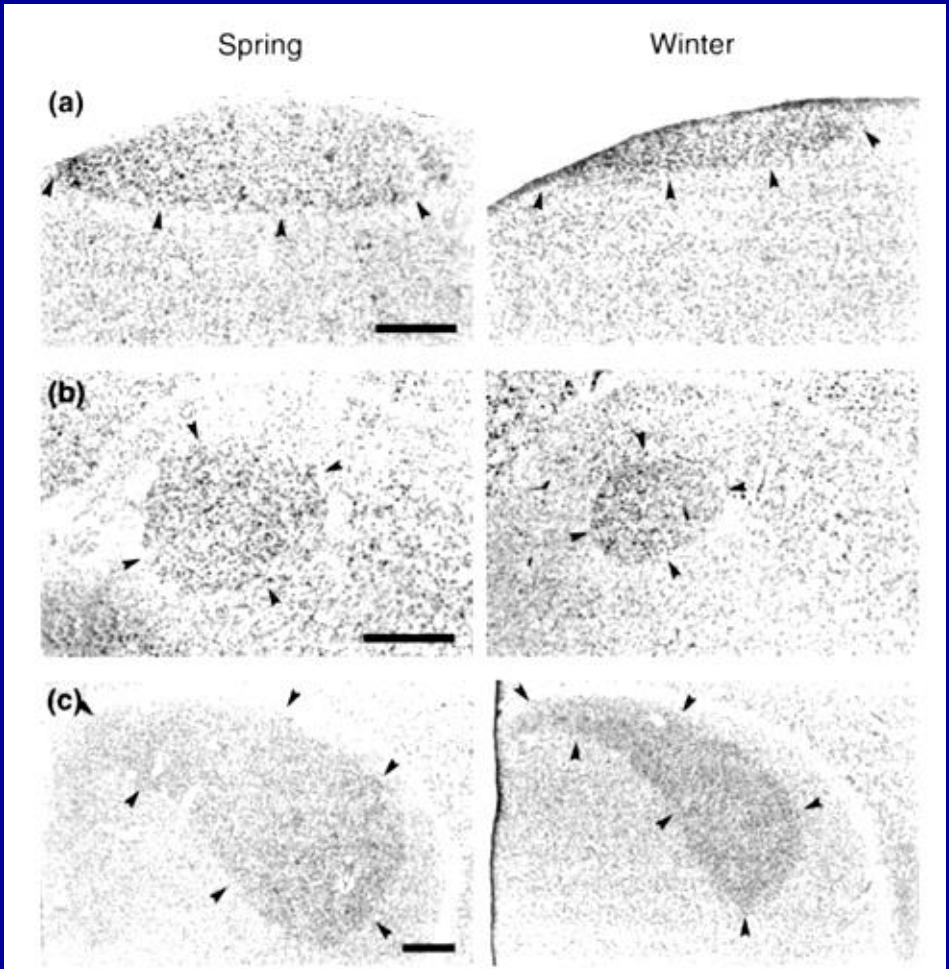


Fig. 2. ***Seasonal volumetric changes in the songbird brain.*** *Wild male spotted towhees were collected and killed during the spring breeding season (left) and during the winter non-breeding season (right). Nissl-stained coronal sections through HVc* **(a)**, *robust nucleus of the archistriatum (RA)* **(b)** *and area X* **(c)** *are shown. The overlying hippocampal formation has been removed in* (a). *Scale bars, 0.5 mm.* Modified, with permission, from Ref. 40.

The Modern 'Phrenology' of Genes

The new science of molecular genetics has made it possible to identify major genes influencing personality and forms of psychopathology. A group of scientists in Israel were the first to find an association between novelty-seeking (a trait very highly correlated with impulsive sensation-seeking) and a gene that codes for a class of dopamine receptor, the dopamine receptor-4 (DRD4) gene.

‘Genetic Phrenology”

A multivariate analysis of 59 candidate genes in personality traits: the temperament and character inventory

Cloninger proposed three basic personality dimensions for temperament: novelty seeking, harm avoidance, and reward dependence. He suggested that novelty seeking primarily utilized dopamine pathways, harm avoidance utilized serotonin pathways, and reward dependence utilized norepinephrine pathways. Subsequently, one additional temperament dimension (persistence) and three character dimensions (cooperativeness, self-directedness, and self-transcendence) were added to form the temperament and character inventory (TCI). (Cloninger CR. Neurogenetic adaptive mechanisms in alcoholism. Science 1987: 236: 410-416)

Conclusions (I)

- Context in brain injury determines outcome:
  - -Age at time of injury.
  - -Gender of the subject.
  - -Time to treatment & duration.
  - -Experience and training.

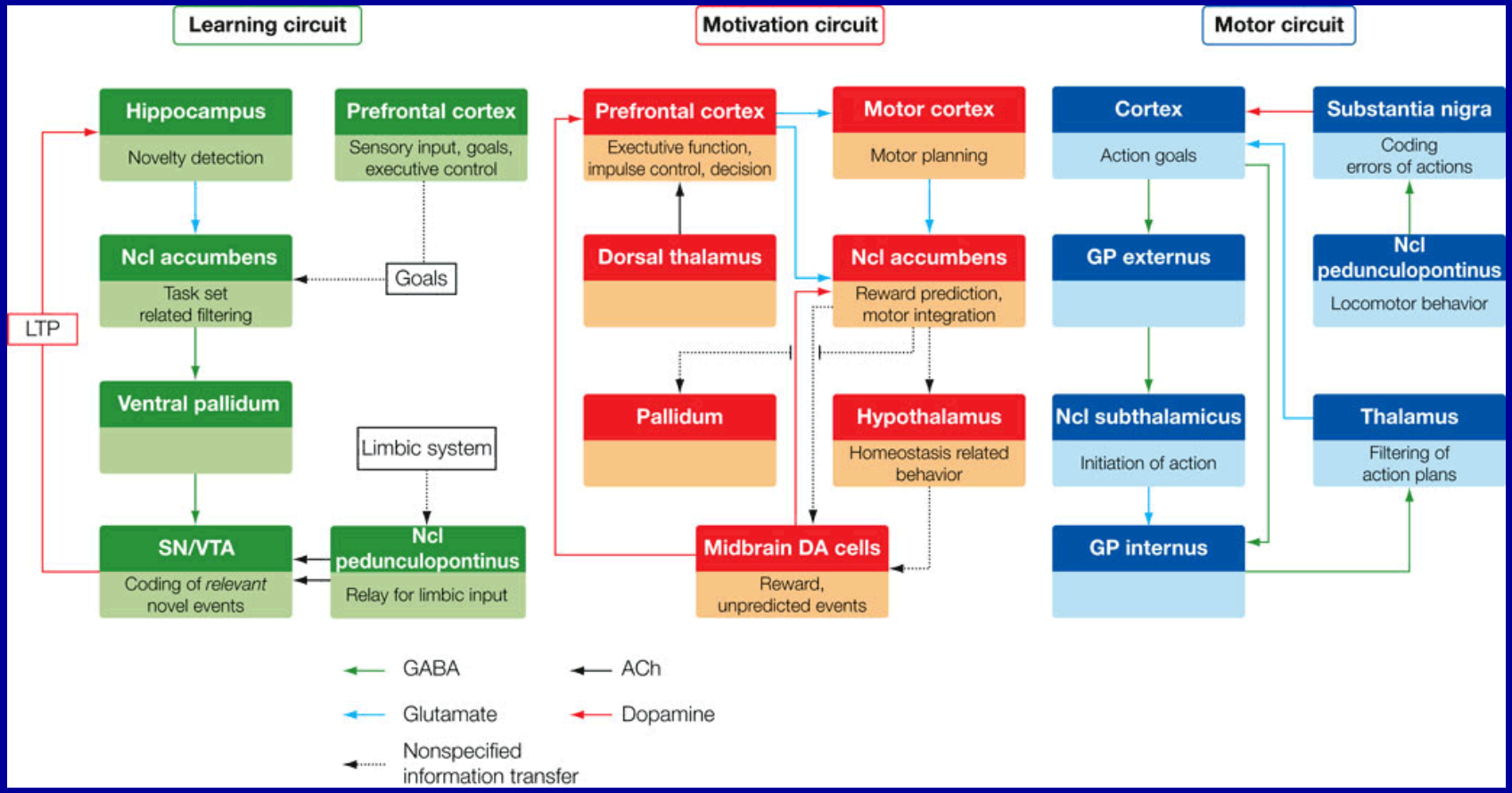
Conclusions (II)!

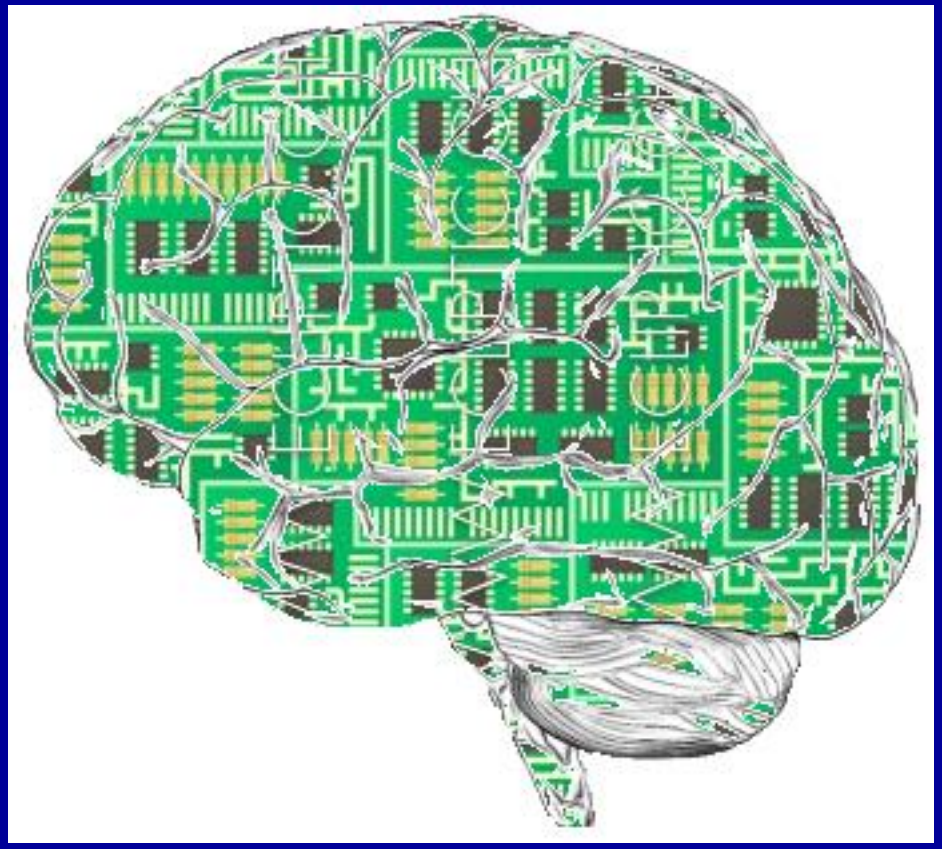
- **Plasticity is an inherent capacity of the CNS, but it has to be 'unlocked' and encouraged.**
- ***Functional* recovery is likely to be dependent upon multiple mechanisms.**
- **Past history, training and experience of the patient can influence the extent and type of cerebral reorganization.**

- ***I have yet to meet a successful scientist who lacks the ability to exaggerate the importance of what he or she is doing, and I believe that someone who lacks a delusional sense of significance will wilt in the face of repeated instances of multiple small failures and rare successes, the fate of most researchers.***
-
- ***D. Kahneman (Nobel Prize in Economic Sciences), Thinking, Fast and Slow,*** Farrar, Straus & Giroux, (2011)



End


Learning circuit
Motivation circuit
Motor circuit
Hippocampus
Novelty detection
Prefrontal cortex
Sensory input, goals, executive control
Ncl accumbens
Task set related filtering
Goals
LTP
Ventral pallidum
Limbic system
SN/VTA
Coding of relevant novel events
Ncl pedunculopontinus
Relay for limbic input
Prefrontal cortex
Exectutive function, impulse control, decision
Motor cortex
Motor planning
Dorsal thalamus
Ncl accumbens
Reward prediction, motor integration
Pallidum
Hypothalamus
Homeostasis related behavior
Midbrain DA cells
Reward, unpredicted events
Cortex
Action goals
Substantia nigra
Coding errors of actions
GP externus
Ncl pedunculopontinus
Locomotor behavior
Ncl subthalamicus
Initiation of action
Thalamus
Filtering of action plans
GP internus
GABA
ACh
Glutamate
Dopamine
Nonspecified information transfer



•Leading scientists are claiming that they should be able to build a functional but artificial replica of a human brain within the next ten years or so.

Modern Phrenology

http://www.phrenology.org/professions.html

site visits: 449,602

•Medicine: What you need to be a doctor. Physicians require:

• Large Perceptive faculties, so that they may study and apply a knowledge of Anatomy and Physiology with skill and success;

•Full Destructiveness, lest they shrink from inflicting the pain necessary to cure;

• Large Constructiveness, to give them skill in surgery;

• Large Combativeness, to render them resolute and prompt;

• Large Cautiousness, to render them judicious and safe; and a large head, to give them general power of mind.

•Phrenology will predict, in advance, whether or not a student will succeed in this profession.

•"Scientists" at the University at Buffalo have reinvented phrenology in the form of a set of biometrics that produce a numerical score indicating the probability that you are about to commit a terrorist act.

• Computer and behavioral scientists at the University at Buffalo are developing automated systems that track faces, voices, bodies and other biometrics against scientifically tested behavioral indicators to provide a numerical score of the likelihood that an individual may be about to commit a terrorist act.

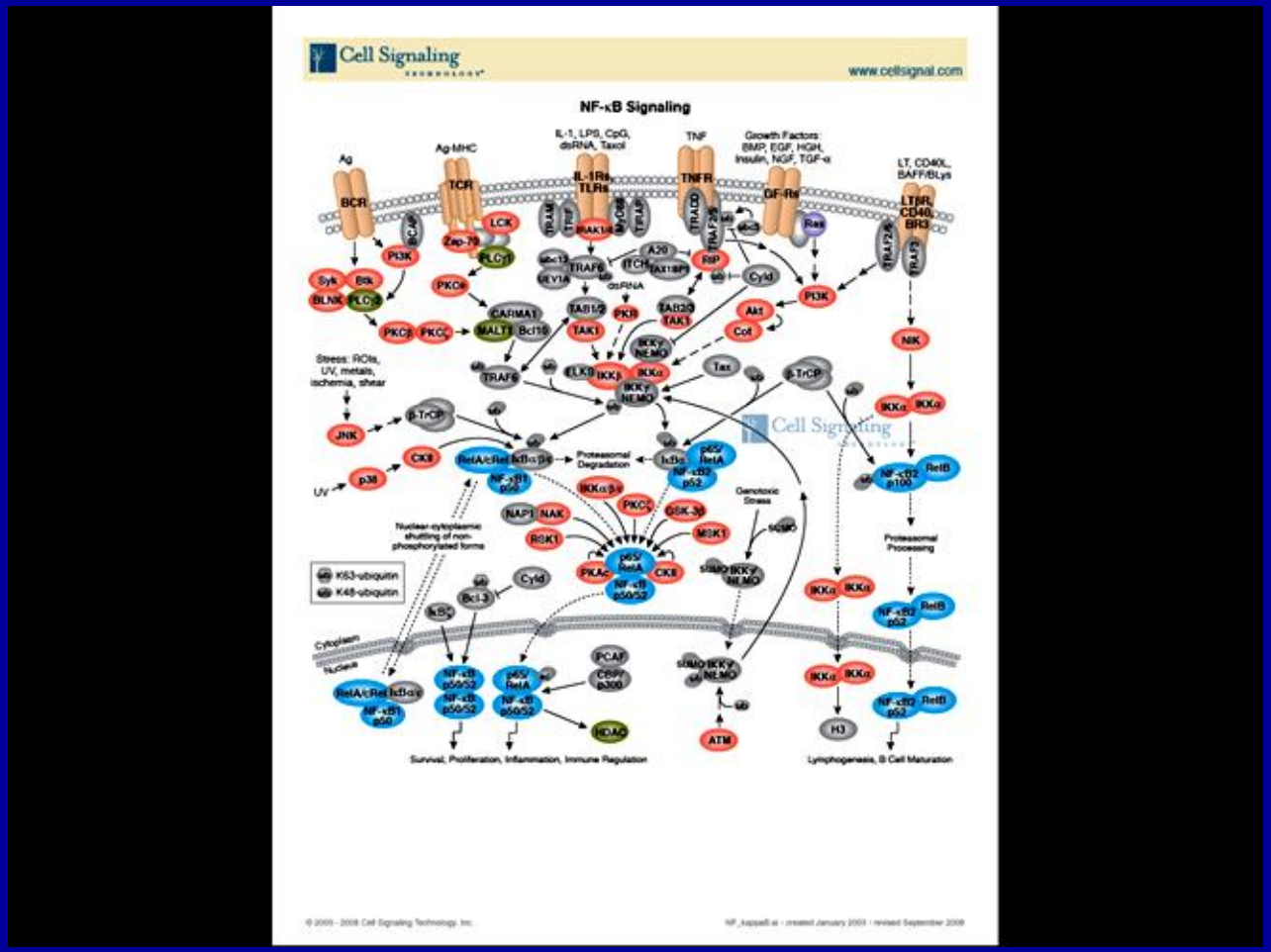
•"The goal is to identify the perpetrator in a security setting before he or she has the chance to carry out the attack," said Venu Govindaraju, Ph.D., professor of computer science and engineering in the UB School of Engineering and Applied Sciences.

• Govindaraju is co-principal investigator on the project with Mark G. Frank, Ph.D., associate professor of communication in the UB College of Arts and Sciences.

•October 2007

TBI IS A COMPLEX, SYSTEMIC DISEASE

"information is not knowledge"—Albert Einstein

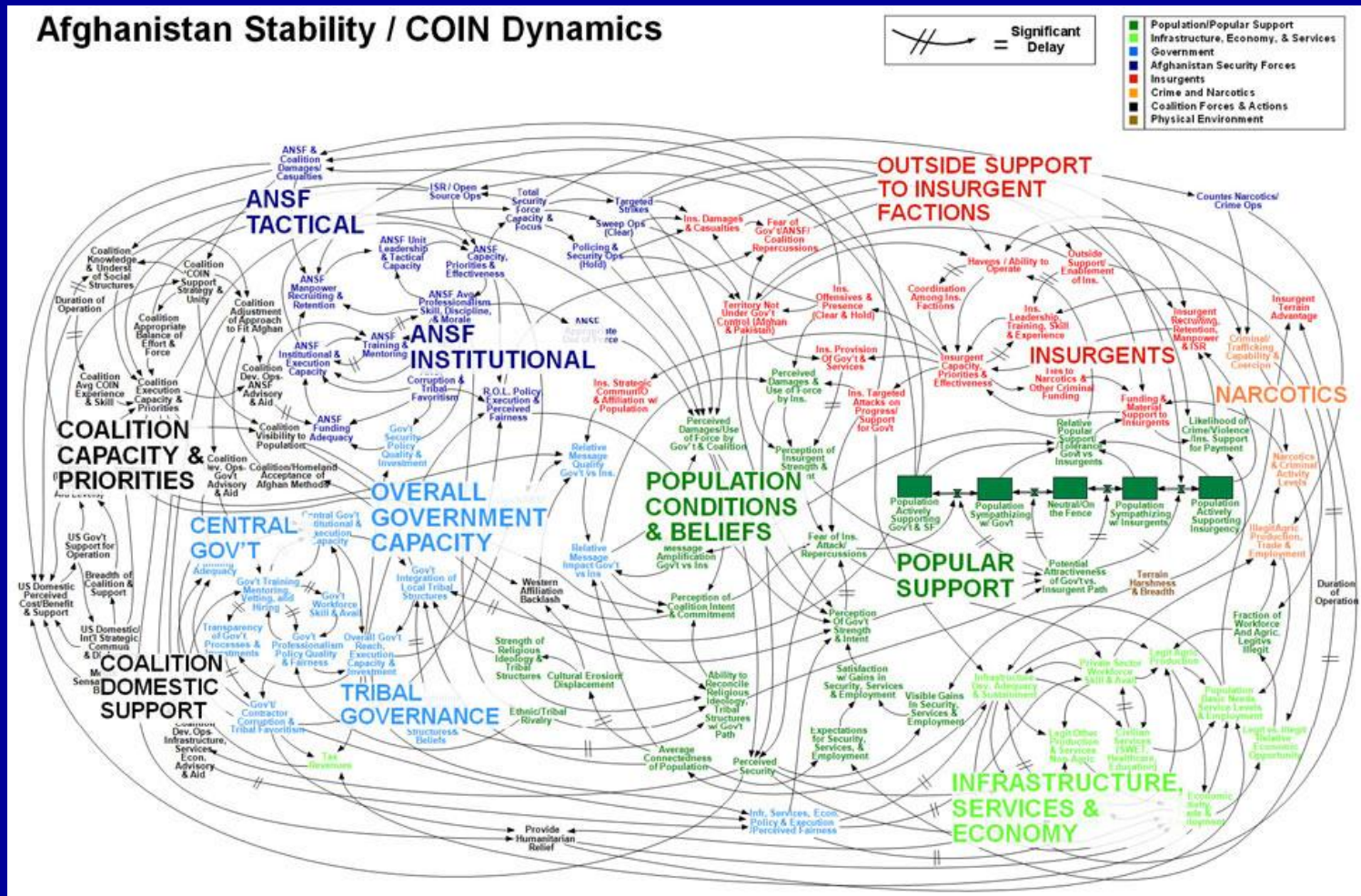


“Truthiness” In Science

- **“I know that most men, including those at ease with problems of the greatest complexity, can seldom accept even the simplest and most obvious truth if it be such as would oblige them to admit the falsity of conclusions which they have delighted in explaining to their colleagues, which they have proudly taught to others, and which they have woven, thread- by-thread, into the fabric of their lives.”**

- -- Leon Tolstoy

Afghanistan Stability / COIN Dynamics



© PA Knowledge Limited 2009