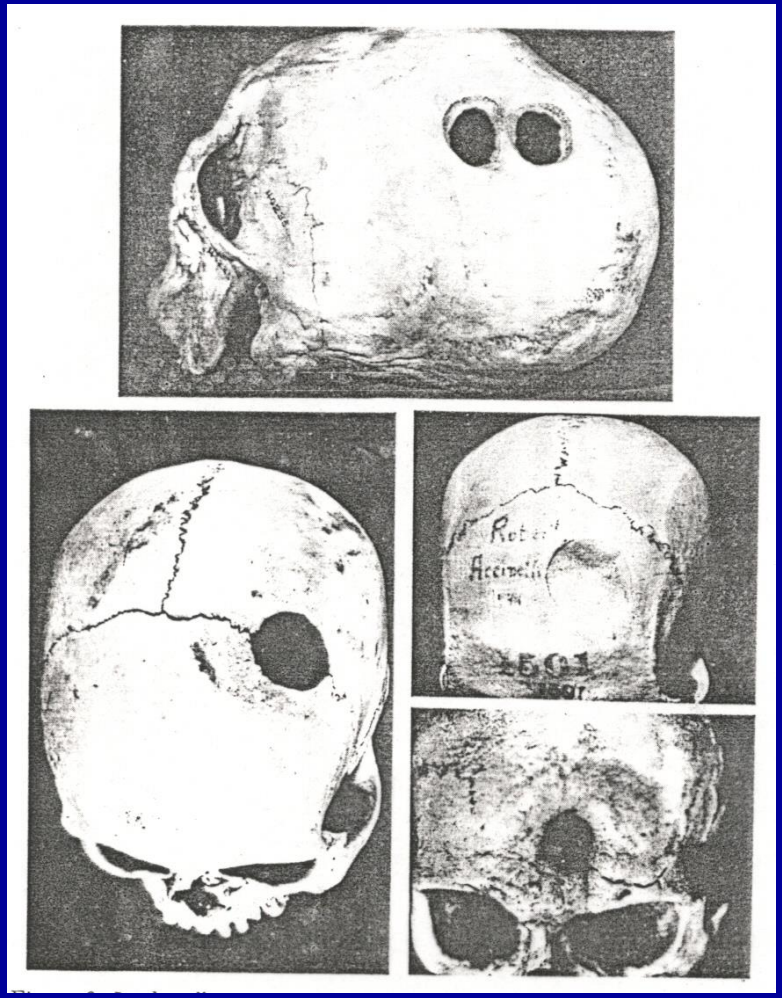
# Thinking About the Brain: Historical and Personal Perspectives

Donald G. Stein, Ph.D.
Emory University

# Trephination

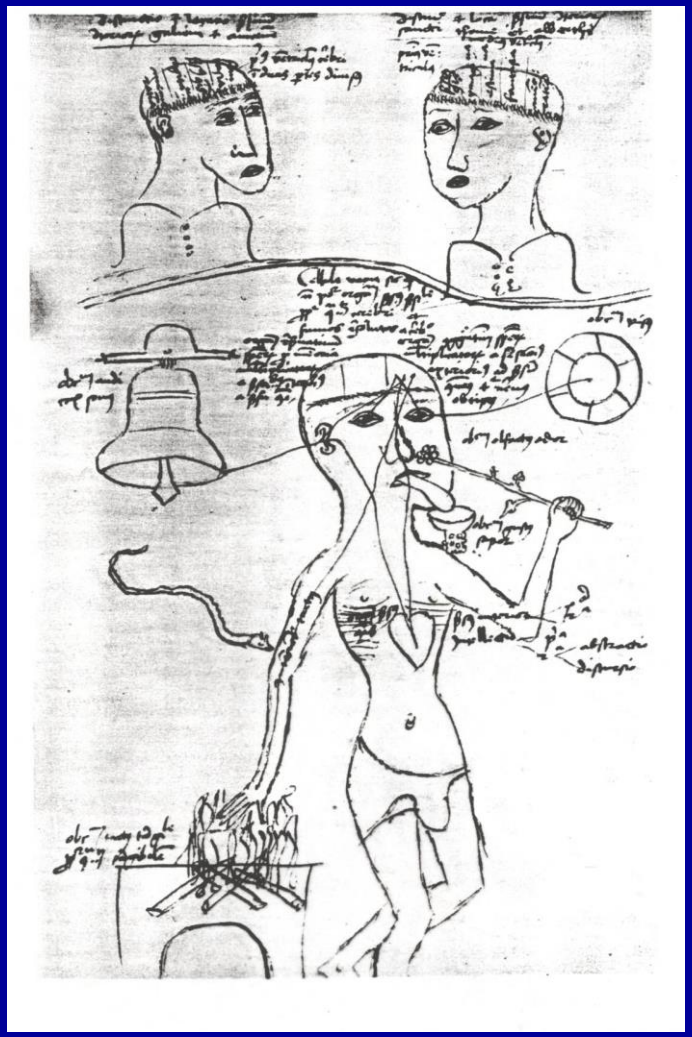


# ‘Psychosurgery’ In The Middle Ages
# Giving The Demons A Chance to Escape

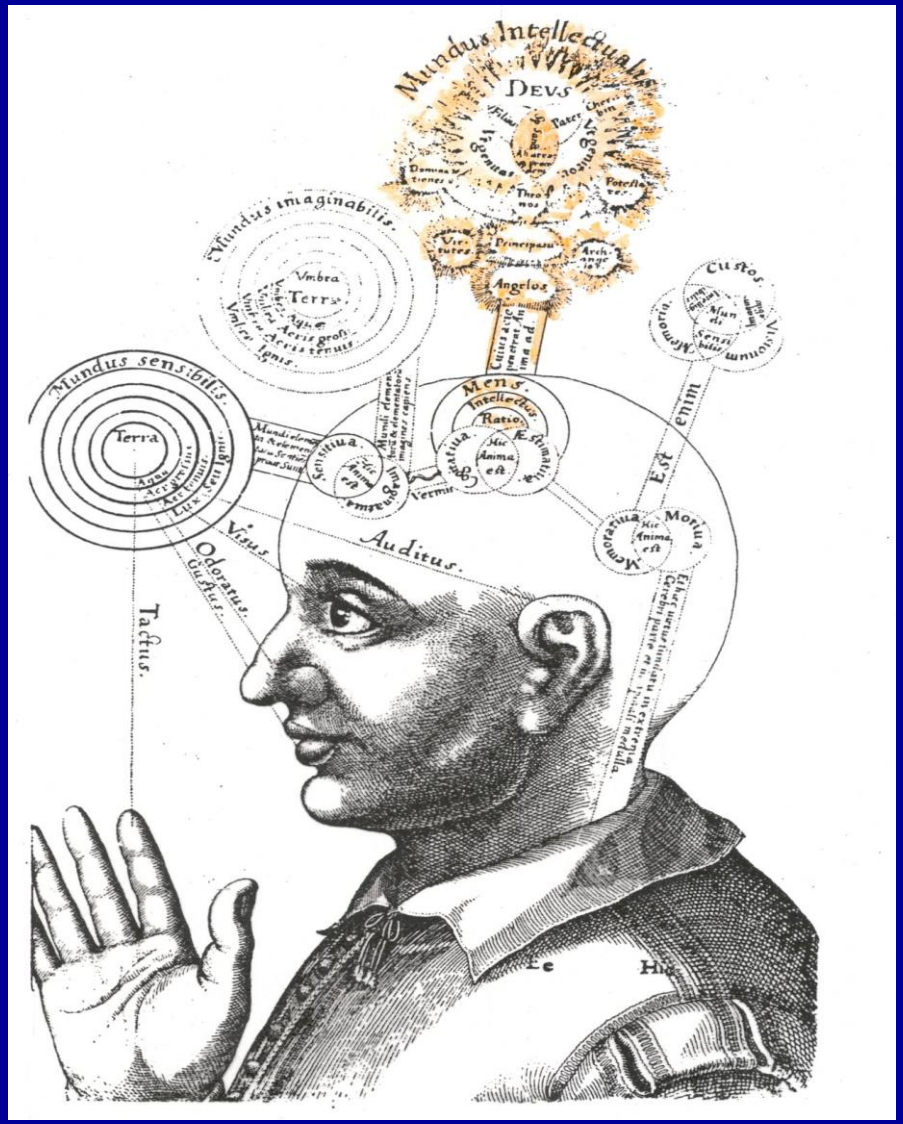
# Was “Brain Tissue” All That Important?

The Doctrine Of Ventricular Localization

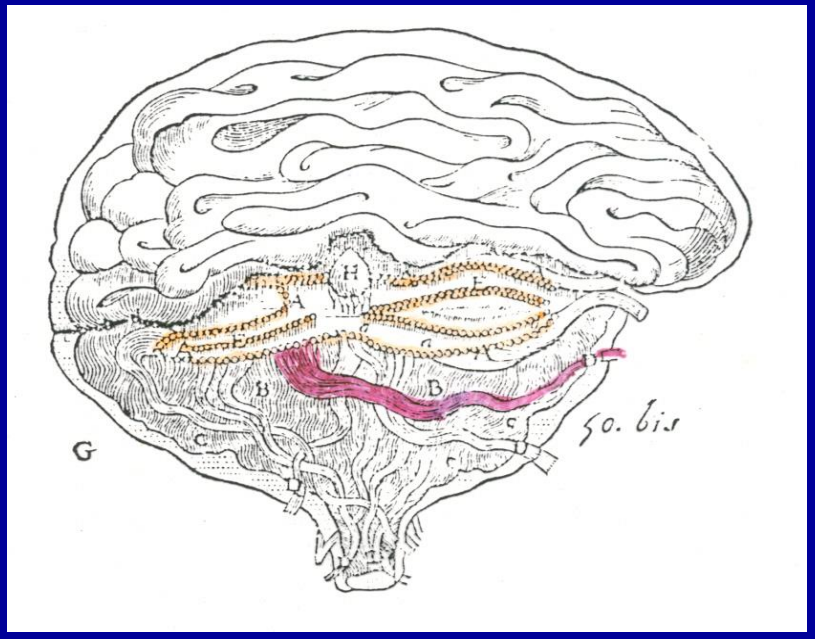
# Medieval Ventricular Theory

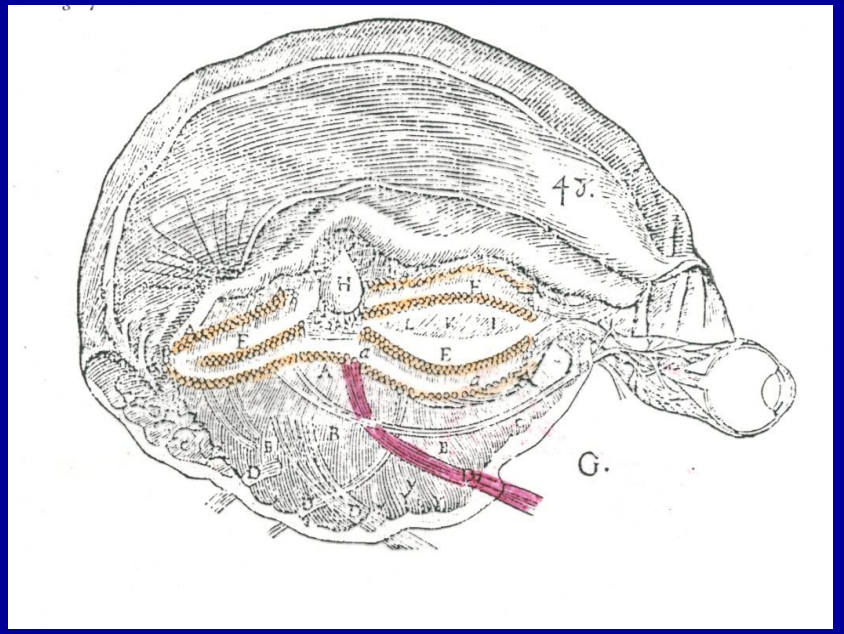


# Renaissance Ventricular Theory

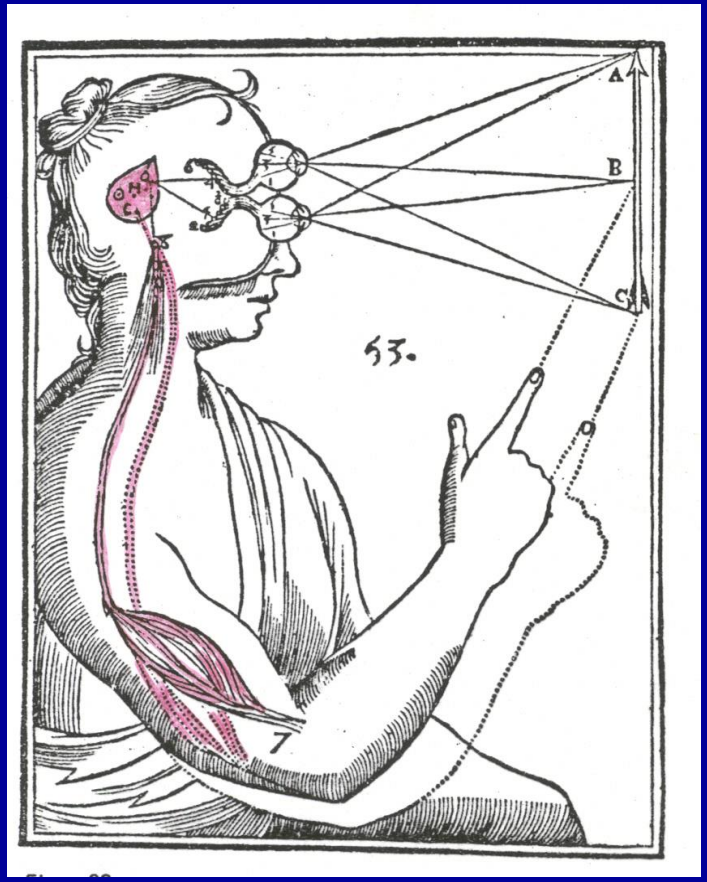


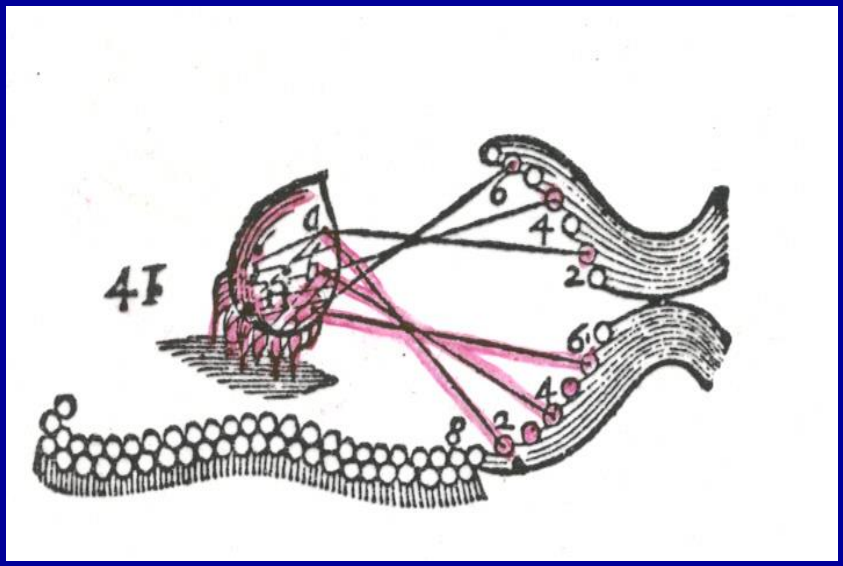
# Descartes' Convolutions



# Descartes, The Pineal Gland & The Seat Of The Soul



# Soul Made Flesh

- Where does sensation,thinking, and memory take place?
- Where is the “center” for rational thought?
- What structure in the brain controls our personality?
- What causes aberrations in behavior?
- The beginnings of modern neurology.

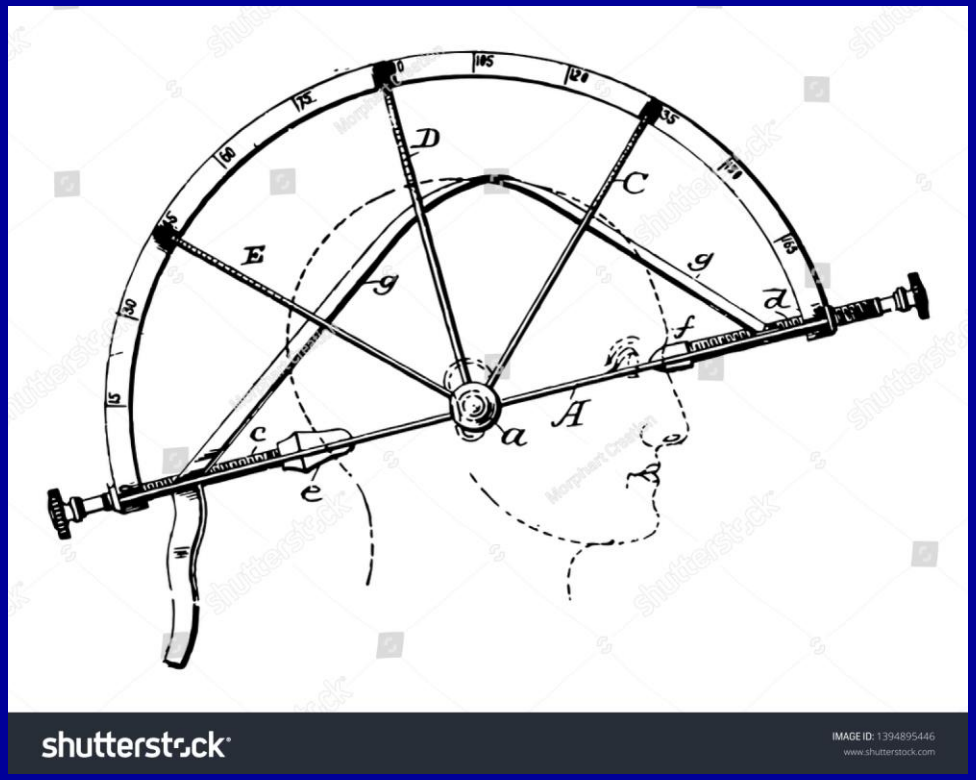
# Franz Gall (1758 – 1828) And Cortical Localization

Figure 13
Franz Josef Gall (1758-1828)

# Mapping the Skull & Localizing Functions

# Phrenological Skull

# ‘Objective’ Measurement Of Brain Structure And Functio-- Late 1800s.



# 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.*

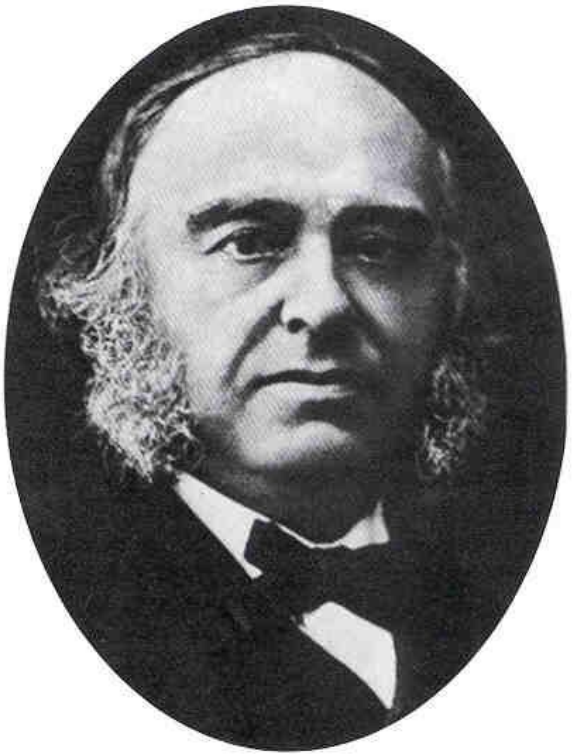


**Figure 3.7.** Paul Broca (1824–1880), whose association between aphasia and damage to the frontal cortex in M. Leborgne ("Tan"), in 1861, became the first cortical localization that was widely accepted. (Courtesy of the Académie de Médecine, Paris.)

# Early Localization of Brain Function

Broca's Patient

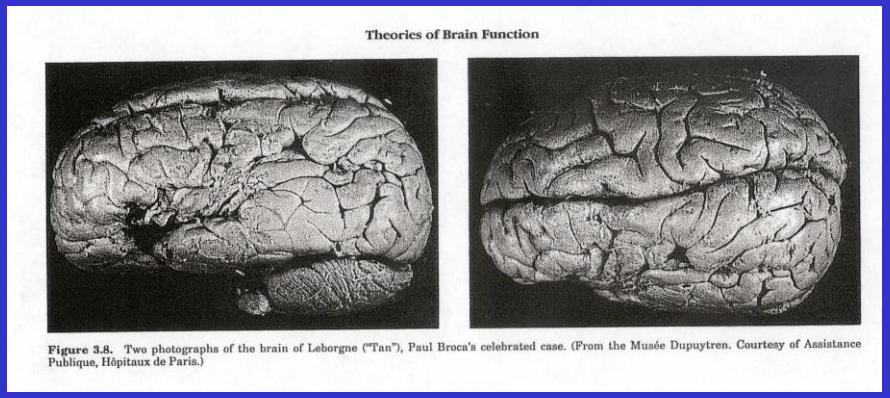
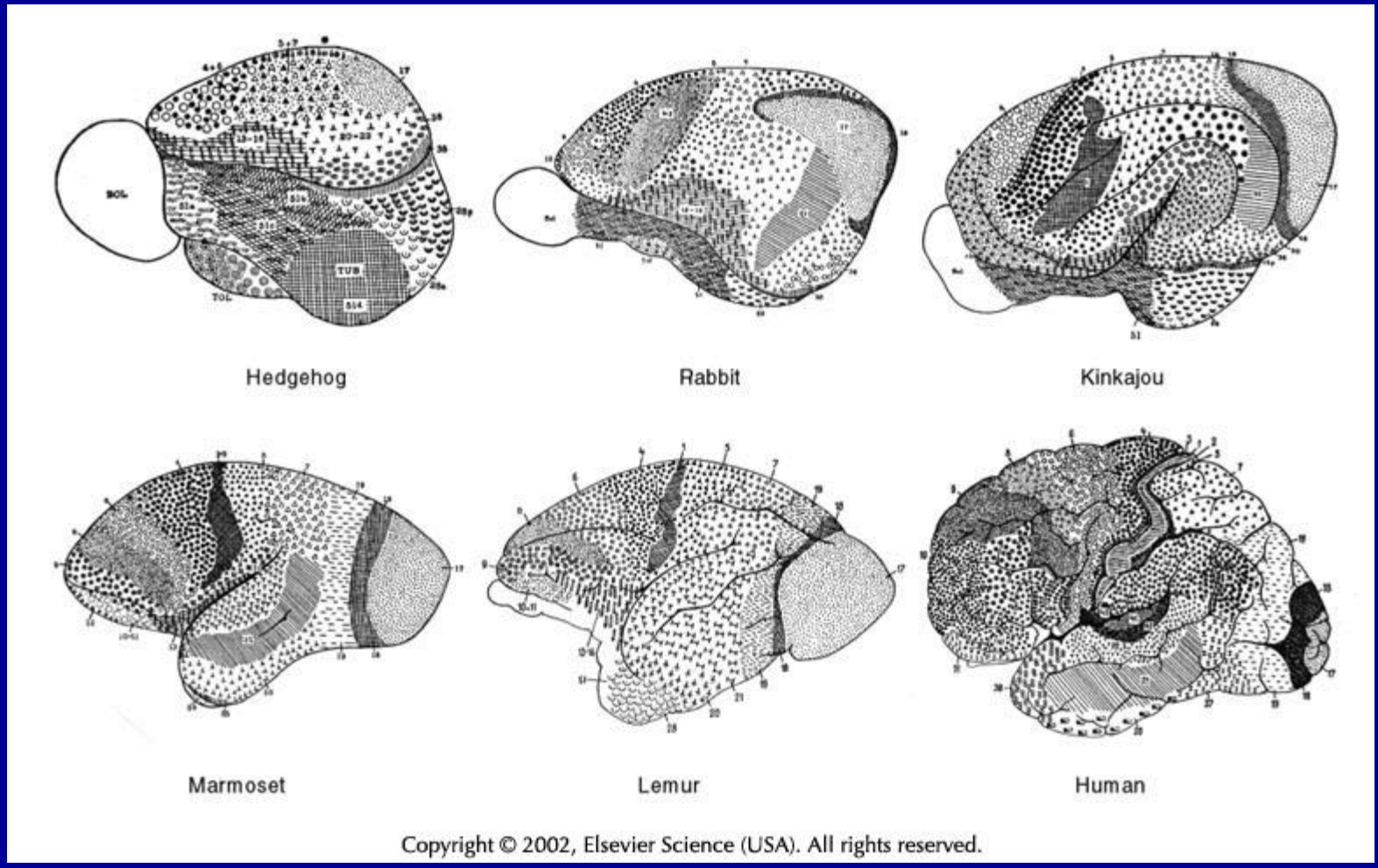
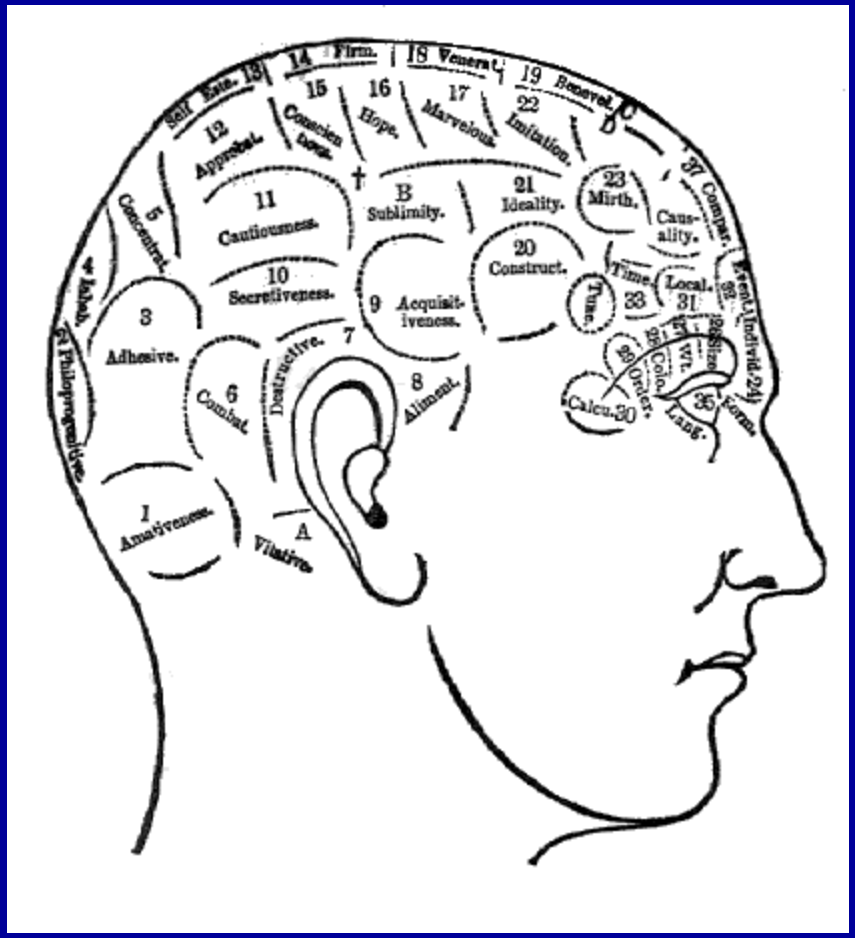



**Figure 3.8.** Two photographs of the brain of Leborgne ("Tan"), Paul Broca's celebrated case. (From the Musée Dupuytren. Courtesy of Assistance Publique, Hôpitaux de Paris.)

# Von Brodmann's Maps (2002)



# Phrenology 2004



# The Concept of the Brain As A Hard-wired, Immutable Structure

The Story Of How One Man Can Make Such A Lasting Difference In How We Think!

# Dogma Is Often The Handmaiden of Contemporary Science

**"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***

**Figure 3.26.** Santiago Ramón y Cajal (1852–1934), winner of the 1906 Nobel Prize for his extensive contributions to neuroanatomy.

**“Once development was ended the fonts of growth and regeneration of the axon and dendrites dried up irrevocably. In adult centers, everything may die, nothing may be regenerated.”**

***-Santiago Ramon Y Cajal***

# An Interesting Story About Paradigms And How They Shape Science

## Galo Leoz: The Last Student of Cajal

Dr. Galo Leoz, Honorary President of the Conference, at the age of 28 and today at the age of 107.

# Are Beliefs About How The Brain Works Slowly Changing (Again)? Yes, But Not Without Controversy

# Dogma Surrounding Brain Repair: The Defense Of A 'Paradigm'

- Neurons in the adult nervous system do not regenerate!
- Only replacement of specific nerve connections will lead to recovery of function!
- Once a brain structure is lost its specific 'functions' are lost forever!
- If functional recovery does not occur in the first few months after injury—it will never occur!
- Any recovery observed is just a 'trick' used to compensate for the loss of function.

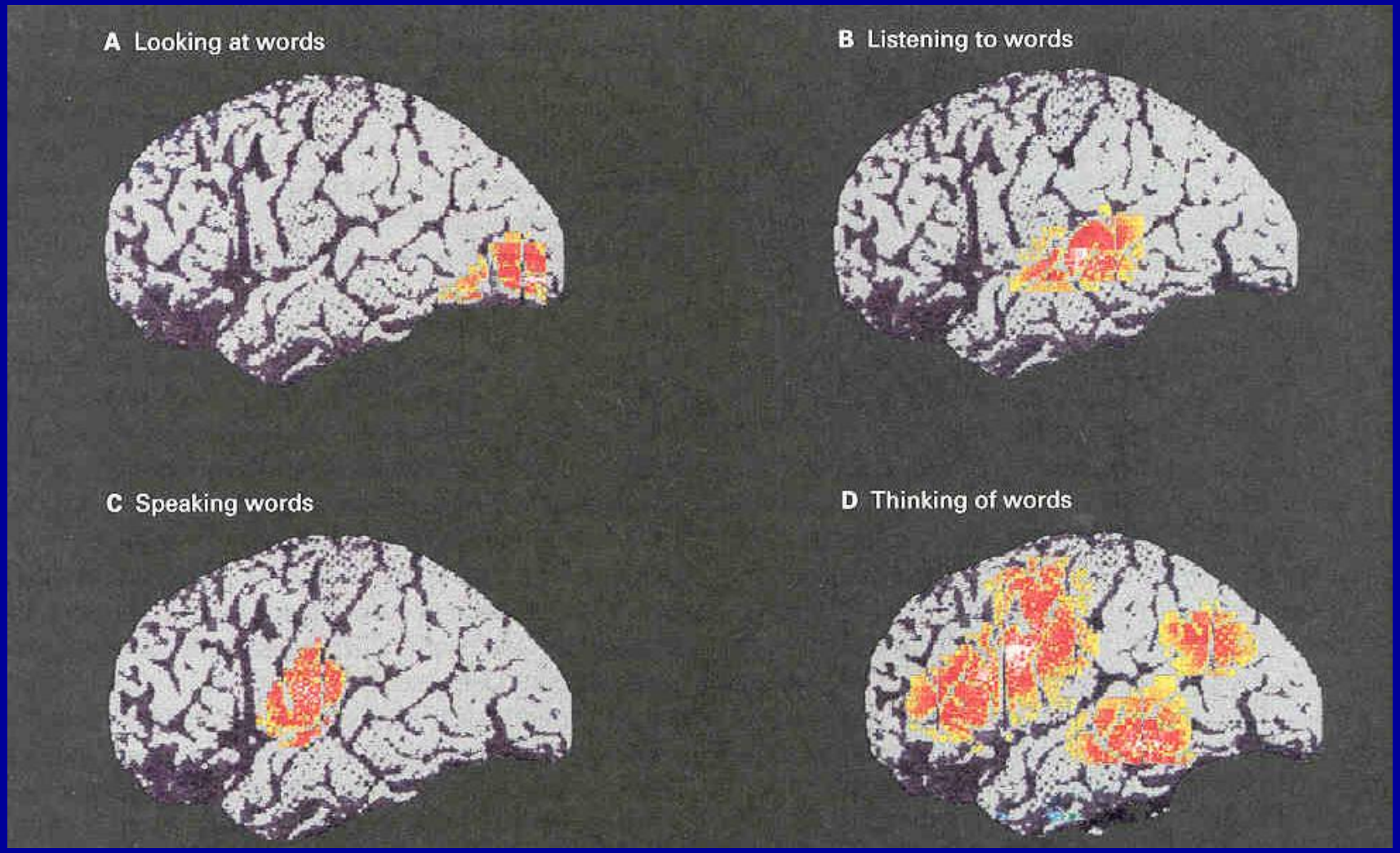
**“Clinical studies and their counterparts in experimental animals suggest that all behavior, including higher (cognitive as well as affective) mental functioning is localizable to specific regions or constellations of regions within the brain. The role of descriptive neuroanatomy is therefore to provide us with a functional guide to localization within the three dimensional neural space---a map of behavior.”**

***Kandel, E. & Schwartz, J.H.***
***Principles of Neuroscience, 1981.***

**“We now appreciate that all cognitive abilities result from the interaction of many simple processing mechanisms distributed in many different regions of the brain. Perception, movement, language, thought and memory are all made possible by the serial and parallel interlinkages of several brain regions, each with specific functions.** ***As a result, damage to a single area need not result in the loss of an entire faculty as many earlier neurologists predicted.”***

***Kandel, E., Schwartz, J.H., Jessell, T.M.***
***Principles of Neuroscience, 2000***

# Metabolic Assessments of Cognitive Functions



# Contemporary Brain Circuitry

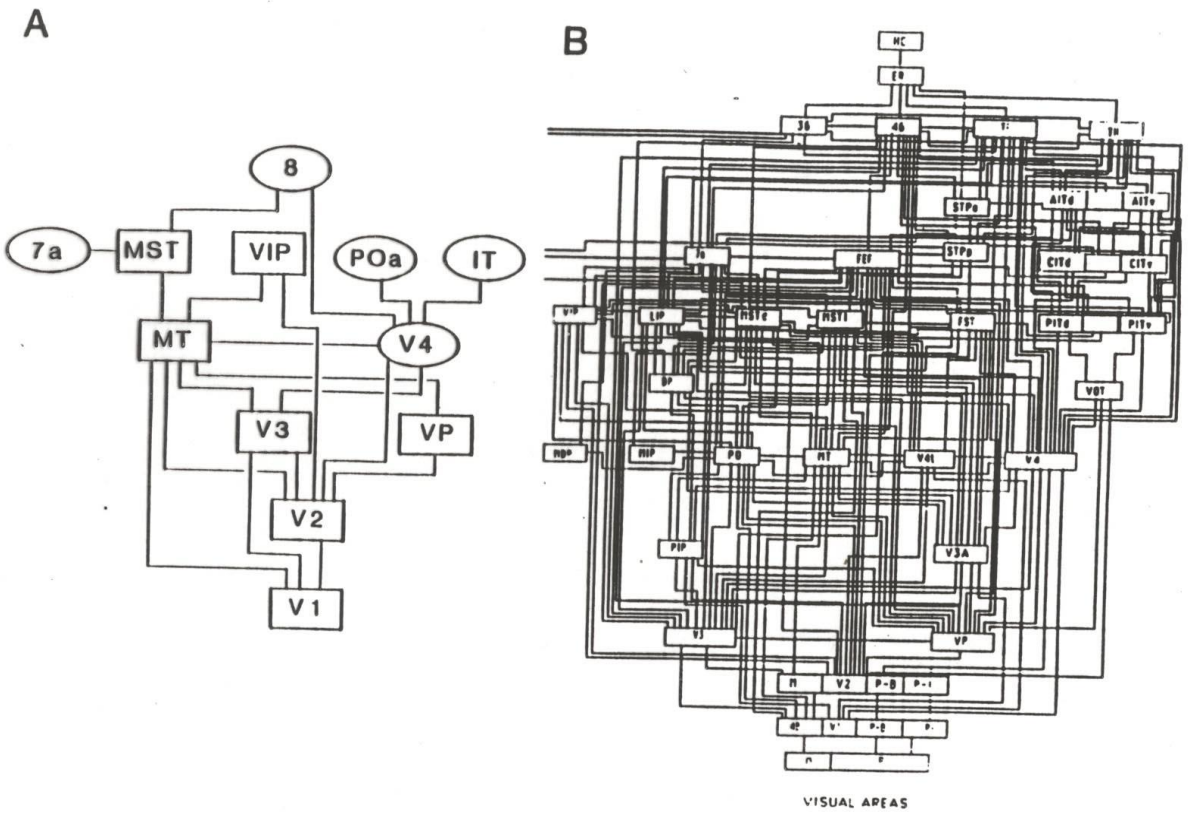
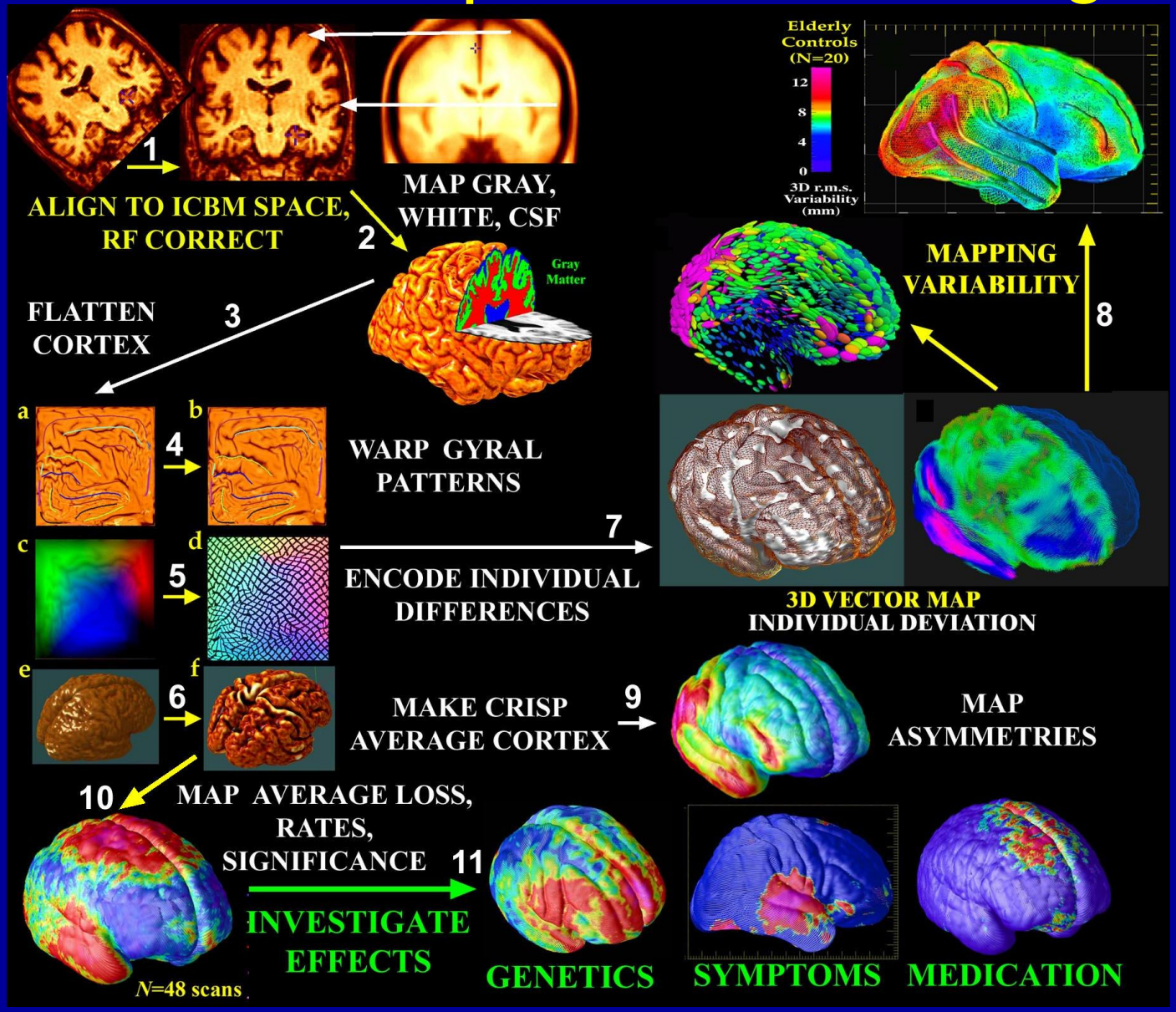



**Fig. 2.** *The wiring diagram of the cortical visual areas in the macaque monkey:* **(A)** *the 1983 version and* **(B)** *the 1990 version.*

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

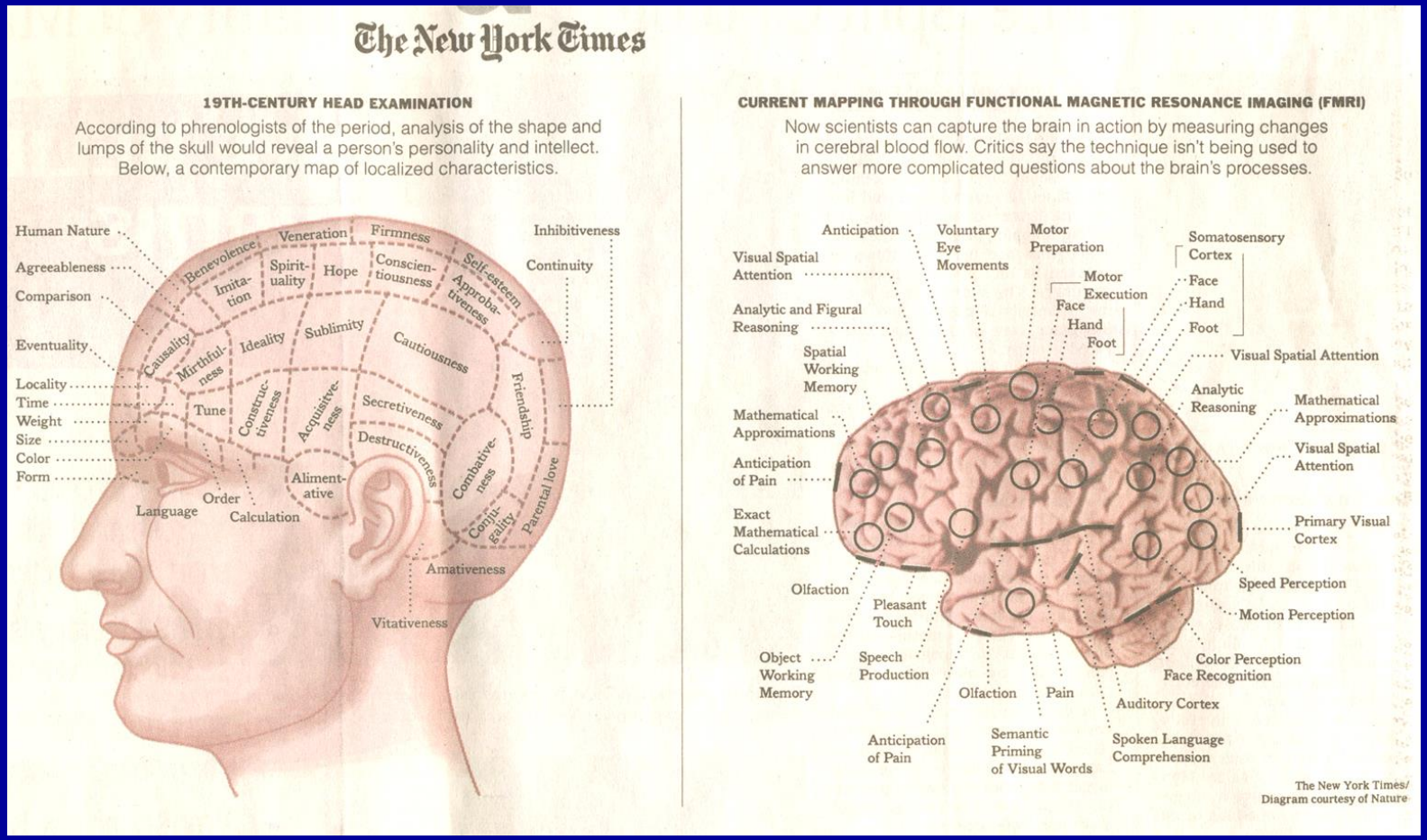
# Newer Techniques In Brain Imaging



# Individual Differences In Brain Mapping

- Three Individuals performing the same finger-tapping task—note variability in activation.
- Where is it localized?

# Just What's Going On Inside That Head Of Yours?



# 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)

# Frontal Lobotomy: Phrenology In Practice?

•A lobotomy, also called a leucotomy, is a type of psychosurgery that was used to treat mental health conditions such as mood disorders and schizophrenia. Psychosurgeries are procedures that involve the physical removal or alteration of part of the brain.

•Few medical procedures in history have garnered as much controversy as the lobotomy.

•Tens of thousands of lobotomies were performed in the United States in the mid-1900s, often leading to devastating outcomes.

•Lobotomies involved separating tissue in an area called the prefrontal cortex in one of two primary ways:

•**Frontal lobotomy.** A surgeon drilled a hole into each side of the skull and cut through brain tissue with an instrument resembling an ice pick called a leucotome.

•**Transorbital lobotomy**. A surgeon inserted a leucotome through the eye socket and drove it through a thin layer of bone with a mallet to access the brain.

•These procedures are no longer performed in the United States.

# Not That Long. Ago

- **Uses and benefits of psychosurgery:**
- With advancements in medications, psychosurgeries are now rarely performed. Surgery is usually only used when all other treatment options have failed. Surgical techniques still in use today include:
- Cingulotomy is the most commonly performed psychosurgery in North America. It's a type of surgery that involves altering tissue in the anterior cingulate region associated with feeling chronic pain.
- It's sometimes used to manage symptoms of:
  - chronic and severe anxiety disorders, such as obsessive-compulsive disorder (OCD)
  - severe mood disorders, such as treatment-resistance depression or bipolar disorder
  - heroin addiction
  - chronic pain syndromes that don't respond to other treatments
  - severe schizophrenia with aggressive behavior

# In Our Time,—Psychosurgery Was Common

- American neurologist Walter Freeman and surgeon James Watts championed the procedure in America. Influenced by an Italian colleague, Freeman eventually switched to the transorbital method, in which an icepick-like instrument was inserted through the eye socket to reach the brain. He passionately spread the surgery across North America, despite haphazardly performing surgeries without proper sterilization.

- Tens of thousands of lobotomies were performed in the United States between the 1930s and 1960s, often without informed consent. Eventually, lack of evidence supporting the procedure finally caught up with it, and it was largely abandoned once the medication chlorpromazine (a potent tranquilizer)was developed.

- Septal Region bilateral, electrocoagulation surgeries were performed to treat “stubborn child syndrome up to the late 1950’s

- Now, a substantial number of ‘psychotropic’ drugs are used to treat ‘abnormal’ behaviors.

# ‘Contemporary 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)*

# A More Contemporary Approach

"We no longer think of discrete areas of the brain that instantiate (control) 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)

End

# Some Exciting Prospects In Brain Repair

- Gene splicing and Gene Therapies.
- Stem Cell and Glial Cell Transplantation.
- Neurosteroid Hormones.
- Direct Brain Stimulation.
- Constraint Induced Behavioral Therapies.
- Dietary and Nutritional Factors And The ‘Biome’.
- More Focus On Sex Differences In CNS Repair.

# CONCLUSIONS

- **Transplanted NSCs migrate towards the site of injury and survive in the host brain up to 12 months post-transplantation.**
- **NSCs enhance and accelerate cognitive and motor recovery following TBI in the mouse.**
- **At 12 months post-transplant, the majority of transplanted NSCs co-label for NG2 suggesting they are expressing an oligodendrocyte progenitor cell phenotype.**

# The Pitfalls of Commercialization

- Industry dominates the research agenda.
- Objectivity and careful evaluation of research data suffers.
- Secrecy and patent right replace collegiality and collaborations.
- Emphasis on product development and less on the development of new knowledge.