A ”Few” Problems With Stem Cell Therapies

- Clinically, the most frequently used adult stem cell source is primary mesenchymal stem cells due to their accessibility and ease of isolation. Mesenchymal stem cells may exert trophic support but do not differentiate into the neural lineage; therefore, they cannot be used as cell replacement therapy in the brain.

- Embryonic stem cells have a greater ability to differentiate into a variety of cell types and can be propagated indefinitely as compared with adult stem cells. However, they are subject to severe ethical concerns due to the requirement of an embryo, *and they have an increased risk of tumor formation.*

- Although current preclinical cell therapy studies favor local transplantation in the brain more than half of clinical trials prefer to administer the cells through a systemic blood injection. The field is faced with a dilemma: Local intraparenchymal cell transplantation promises the maximum efficacy, but the associates risks of the injection hinder its broad application. Yet, systemic injections are minimally invasive; however, most cells end up in nondesired organs, and therefore only limited therapeutic effects can be expected.

- In the transition from acute to chronic stroke, 6 mo to 1 y after injury, usually most of the affected neural tissue and corticospinal tracts are lost; a glial scar is formed with abnormal blood supply; and many patients with impairment experience a plateau in the recovery phase.

- Immune rejection is another critical issue in cell therapy. Autologous iPSC therapy (i.e., the application of iPSCs generated from the patient’s own somatic cells) may represent the most suitable option to circumvent this problem. However, the high effort and huge costs of good manufacturing practice (GMP)–compliant production of an individual iPSC line and its quality and safety control, which are estimated at US $800,000 per cell line (Rehakova and others 2020), currently do not allow autologous therapy for a range of patients. Furthermore, the autologous approach is not applicable for acute diseases due to the time needed for clinical production of the individual’s own iPSCs.

- Cell-based regenerative therapy is not without risk. Therefore, safety measures pre- and posttransplantation are of highest importance. The scope of risks ranges from acute cerebral bleeding (at the time of stereotactic local injection), cell clotting or cell-induced embolism (for systemic injection), and functional side effects (such as seizure and involuntary movement). The biggest concern is a malignant tumor formation from the grafted cells and the deposition of transplanted cells in undesired tissues.

How Long Does "Localization" Persist?

- "One has to be foolhardy to offer a confident localization several years after an injury.
- I once saw the brain of a patient who had become aphasic 18 years before, but who shortly before death showed no signficant aphasia.
- At post-mortem there was total destruction of the left peri-Sylvian regions…of the entire classical speech area." *Norman Geshwind, 1974, p480.*


dstein

Perspectives on Plasticity and Repair after Brain Injury

Donald G. Stein, Ph.D.

Professor Emeritus, Emory University

Atlanta, Georgia USA

A Major Issue For Restorative Neuroscience: How Is "Plasticity" Defined?

- Are there precise definitions of "function" and "plasticity"?
- We need better specification of the modalities required to promote plasticity and execute function.
- How do you show which part of the brain specifically controls a particular function?
- Can functions become maladaptive as a result of experience or injury (e.g. learned disuse)? Is this still plasticity if it's harmful?

A Few Examples Of How Functions/Results Are Often Described

- Results ’may’ be interpreted to suggest….
- Our findings can be taken to indicate that…
- The hippocampus is implicated in….
- The frontal cortex is ‘associated with’…
- The caudate nucleus ‘mediates’….
- The visual cortex ‘is the center’ of visual processing.
- The reticular formation ‘regulates’ consciousness/.

Some Definitions of Neuroplasticity
Britannica, 2024

- **Neuroplasticity**, the capacity of neurons and neural networks in the brain to change their connections and behaviour in response to new information, sensory stimulation, development, damage, or dysfunction.

- Although some neural functions appear to be hard-wired in specific, localized regions of the brain, certain neural networks exhibit modularity and carry out specific functions while also retaining the capacity to deviate from their usual functions and to reorganize themselves.

- Other 'types' of neuroplasticity, such as compensatory masquerade, *can simply be described (?)* as the brain figuring out an alternative strategy for carrying out a task when the initial strategy cannot be followed due to impairment.

- When one function is carried out frequently enough through repeated behaviour or stimulus, the region of the cortical map dedicated to this function grows and shrinks as an individual "exercises" this function.

How Dogma Can Block Discovery

not seeing—even when it's right in front of your eyes

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

A Short True-false Test On Plasticity And Repair After Damage To The Brain

- Neurons in the adult nervous system do not regenerate!
- Only replacement of specific nerve connections will lead to recovery of function!
- Only neurons play a role in repairing brain functions!
- 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.

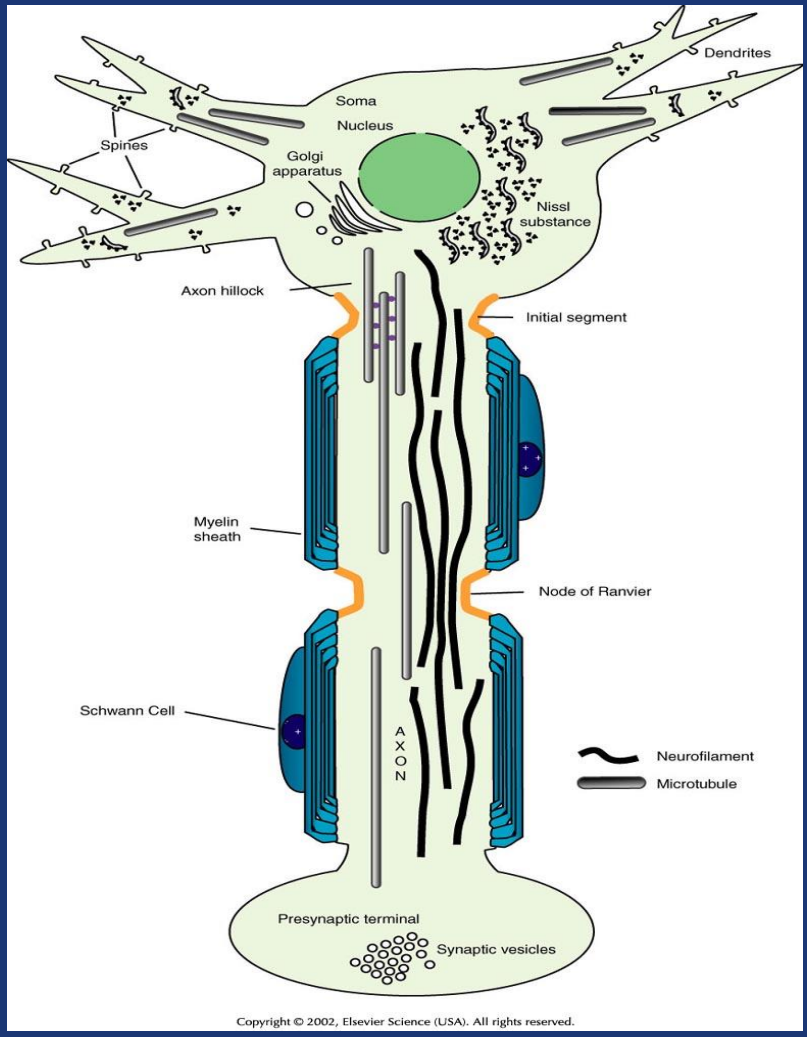
What Opportunities Are There To Enhance Plasticity In The Damaged Brain?

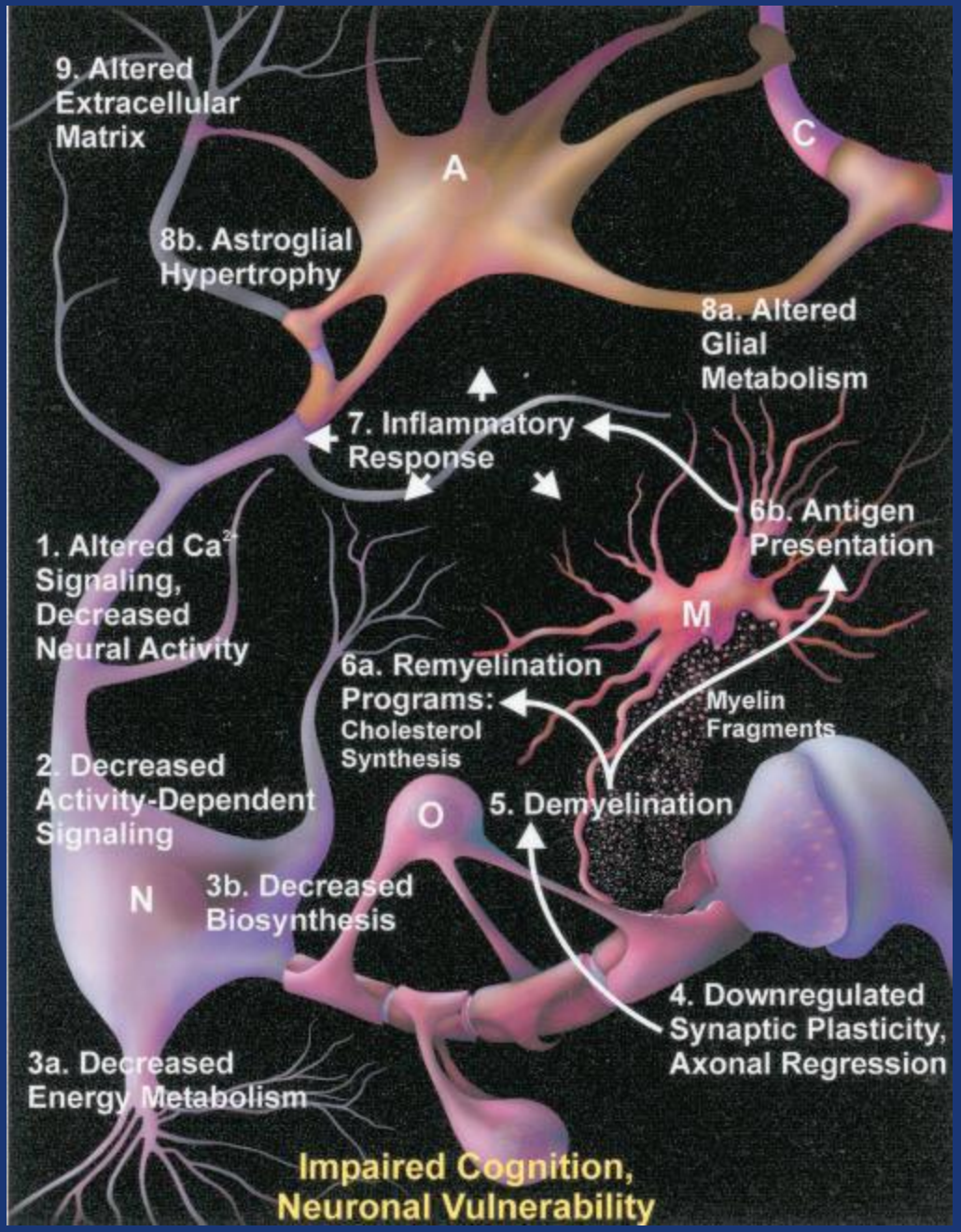
Early Work On Neural Regeneration & Repair

Collateral Sprouting & Regeneration

Opportunities For Plasticity Events At Many Levels Of Organization

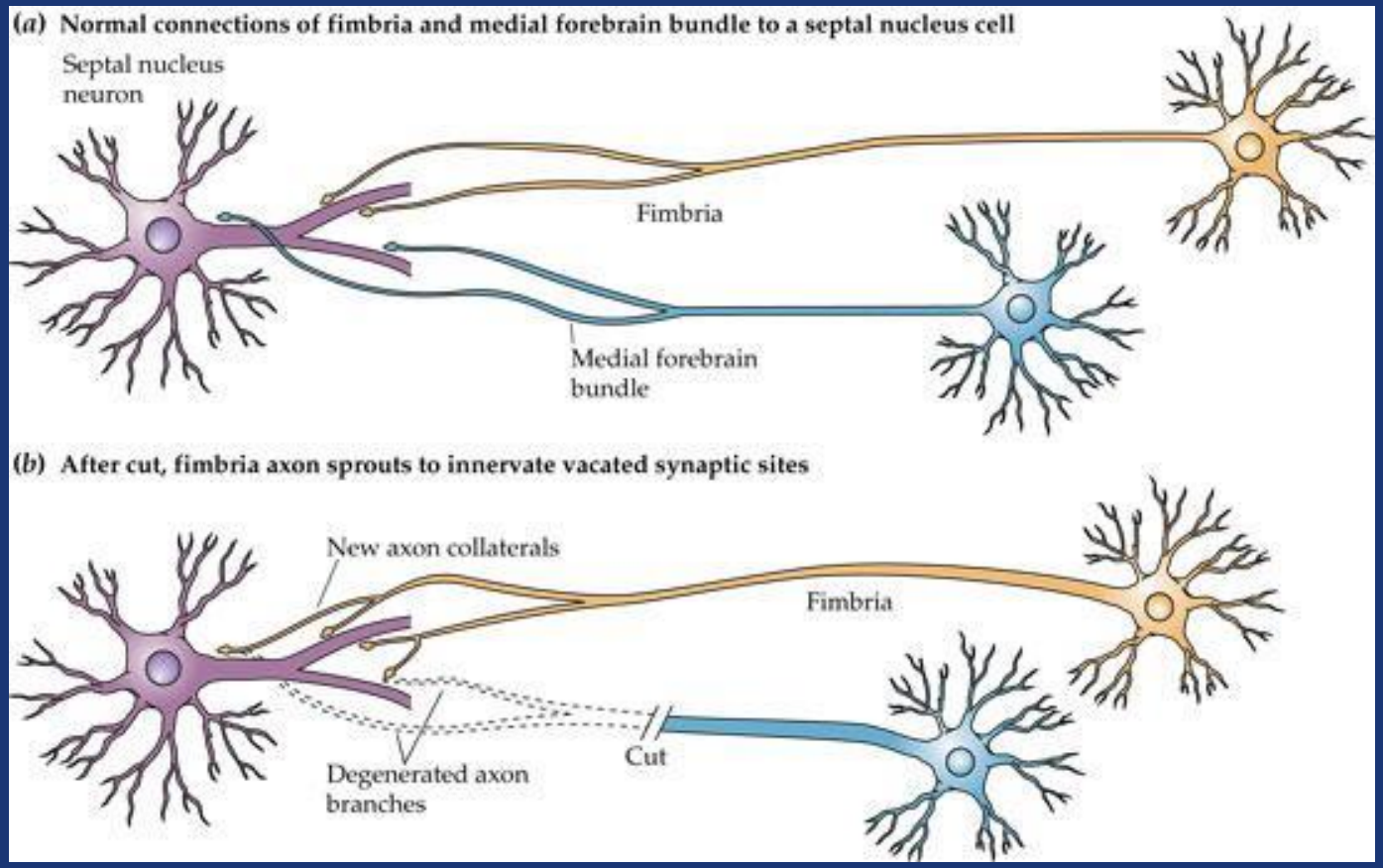
- Nucleus
- Dendrites
- Membrane receptors
- Presynaptic terminals
- Post-synaptic membranes




9. Altered Extracellular Matrix
A
C
8b. Astroglial Hypertrophy
8a. Altered Glial Metabolism
7. Inflammatory Response
6b. Antigen Presentation
1. Altered Ca^{2+} Signaling, Decreased Neural Activity
M
6a. Remyelination Programs: Cholesterol Synthesis
Myelin Fragments
2. Decreased Activity-Dependent Signaling
O
5. Demyelination
N
3b. Decreased Biosynthesis
4. Downregulated Synaptic Plasticity, Axonal Regression
3a. Decreased Energy Metabolism
Impaired Cognition, Neuronal Vulnerability

First Steps: Geoff Raisman Helped Change The Story

Collateral Sprouting After Injury 1968

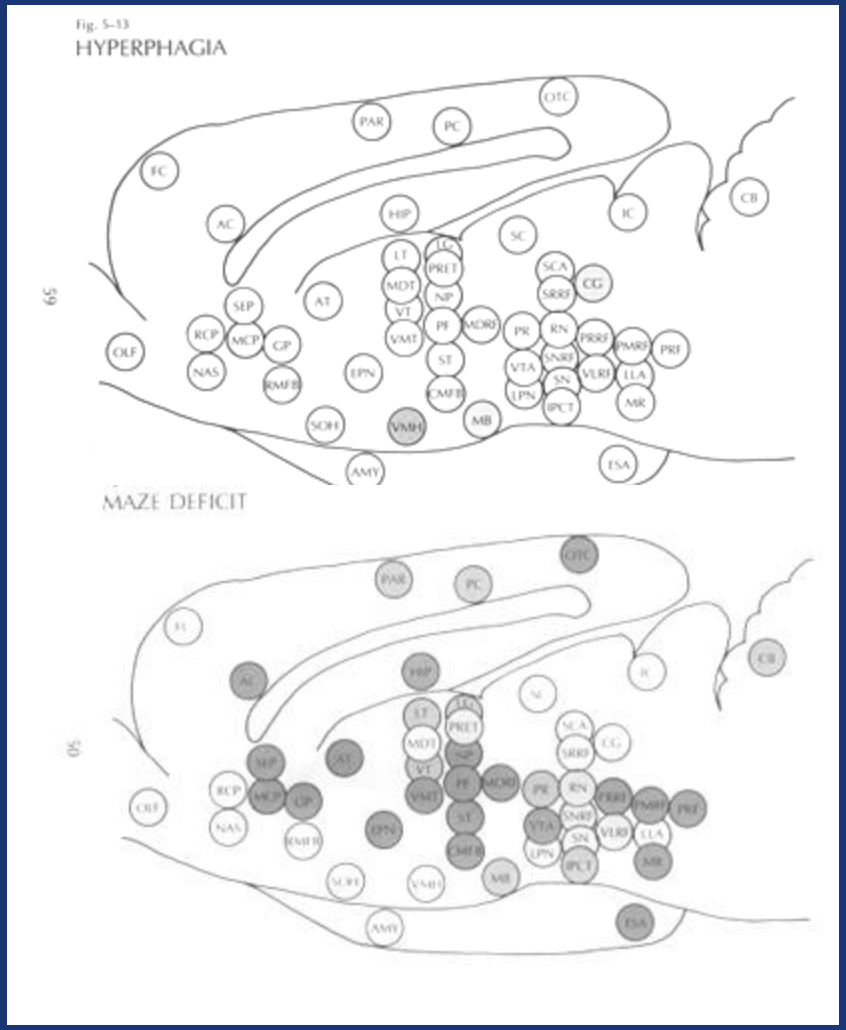


An Important Question

If Plasticity And Recovery Occur, How Does This Fit With The Idea That Functions Are Hardwired And Localized

?

MAPPING THE BRAIN: LOCALIZATION OF MAZE AND EATING DISORDERS AFTER BRAIN LESIONS IN A RAT BRAIN ATLAS



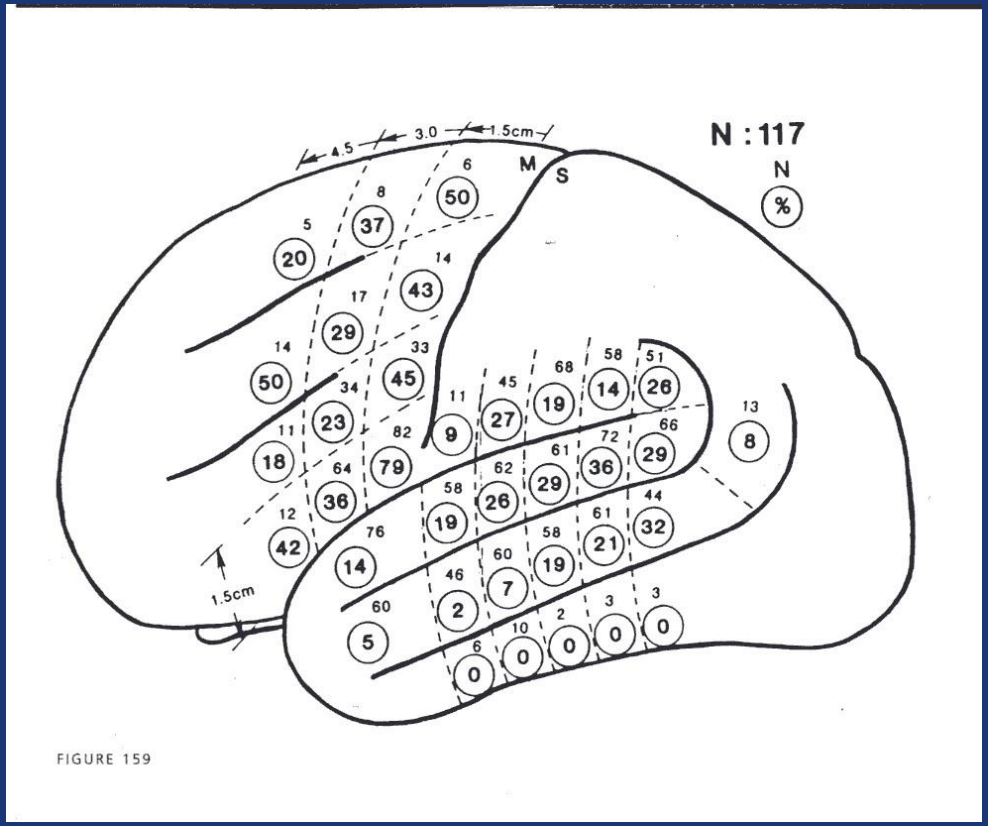


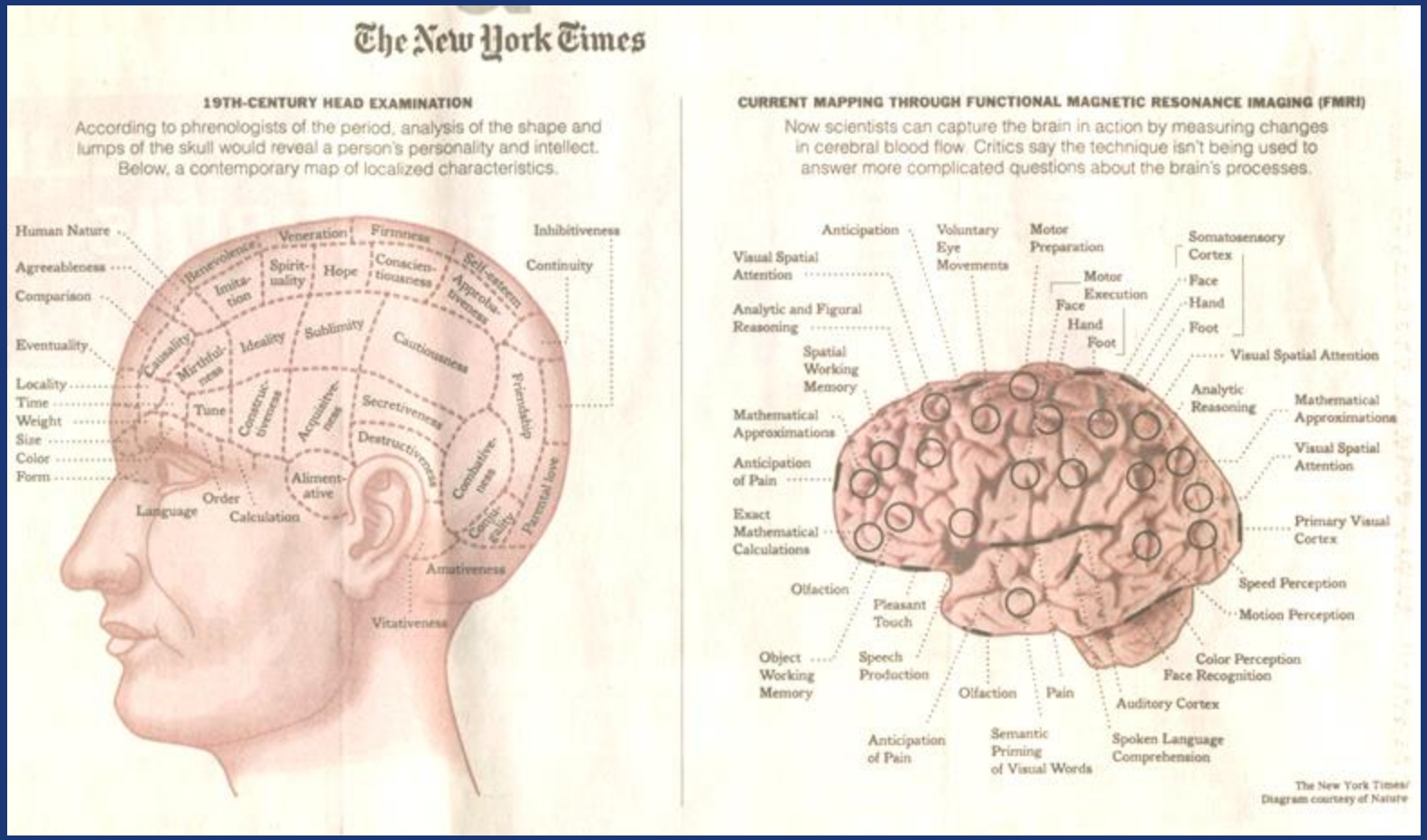
FIGURE 159

LOCALIZATION OF LANGUAGE FUNCTIONS BY ELECTRICAL STIMULATION OF THE CORTEX IN 117 PATIENTS

(reveal substantial variability)

Ojemann G, et al., 1999, J Neurosurg 71:316

Even The New York Times Discussed The Question Of Distinct Mapping And Localization Of Functions



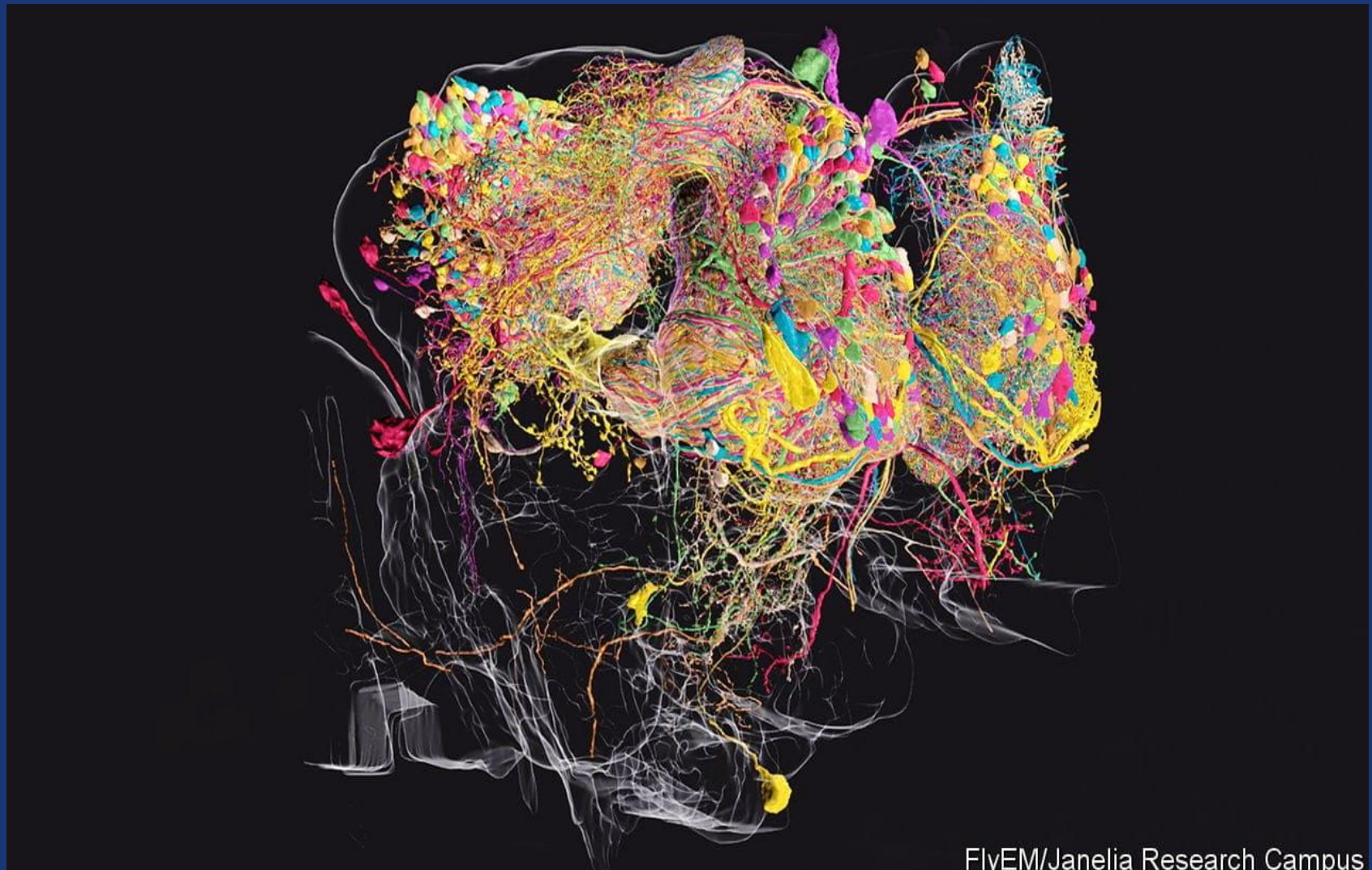
The Serial LESION Effect. Why Is It Important In Understanding Brain Function And Repair

70 Years Ago, A Cautionary Note

- "A disturbance of a particular complex function does not in fact arise in association with a narrowly circumscribed lesion of one part of the cortex."
- "The performance of a given function necessitates the integrity of far more extensive and far more structurally varied zones of the cortex than is assumed by classical neurology."
- "We must conclude that there is no evidence for isolated cerebral 'centers' for any of the complex forms of mental activity."

Alexander Luria, Human Brain & Psychological Processes, 1966

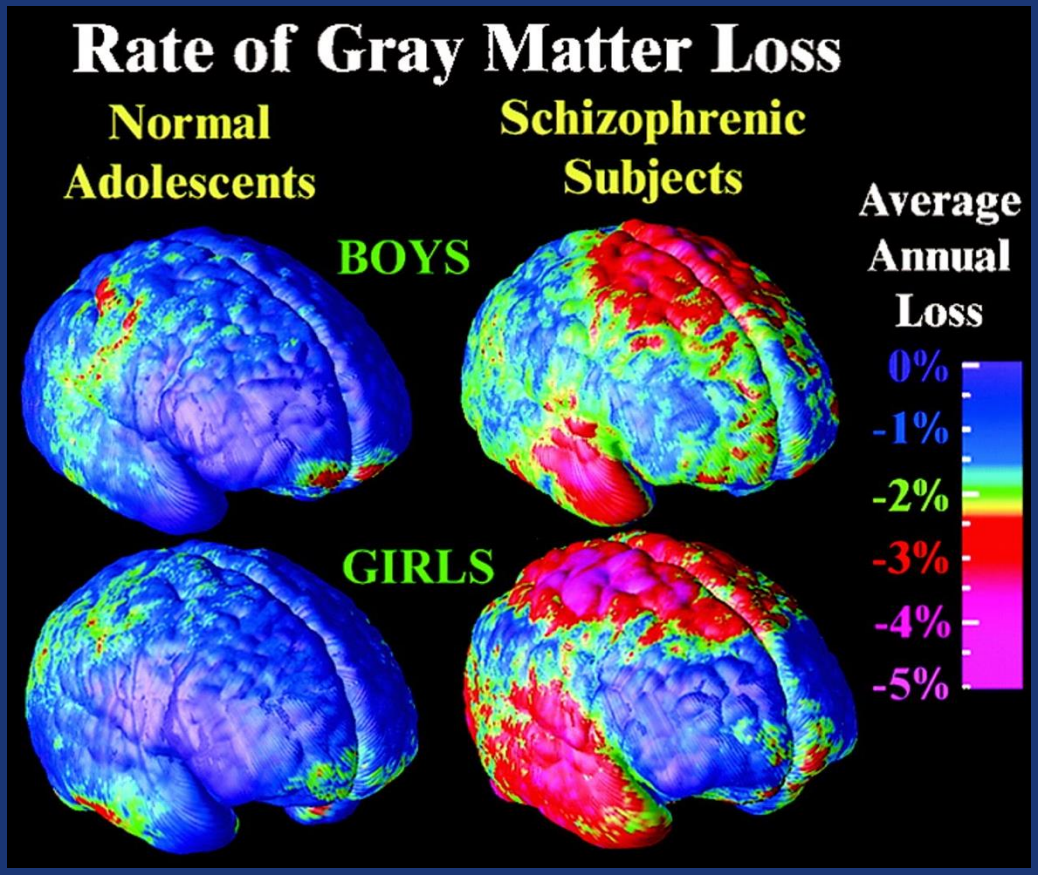
Mapping the Brain Of A Fruitfly



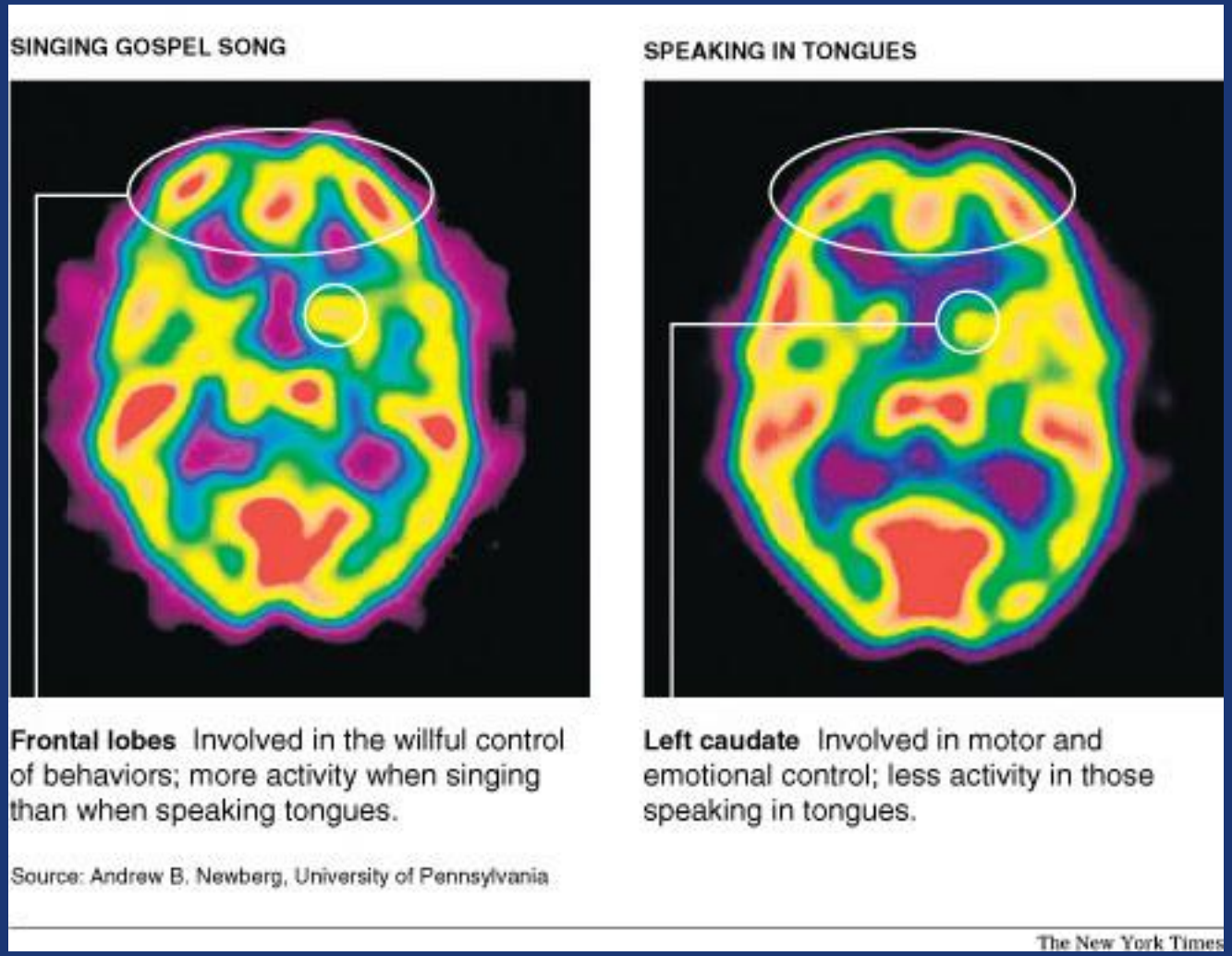
Brain Mapping Project

Fiber Tract Mapping

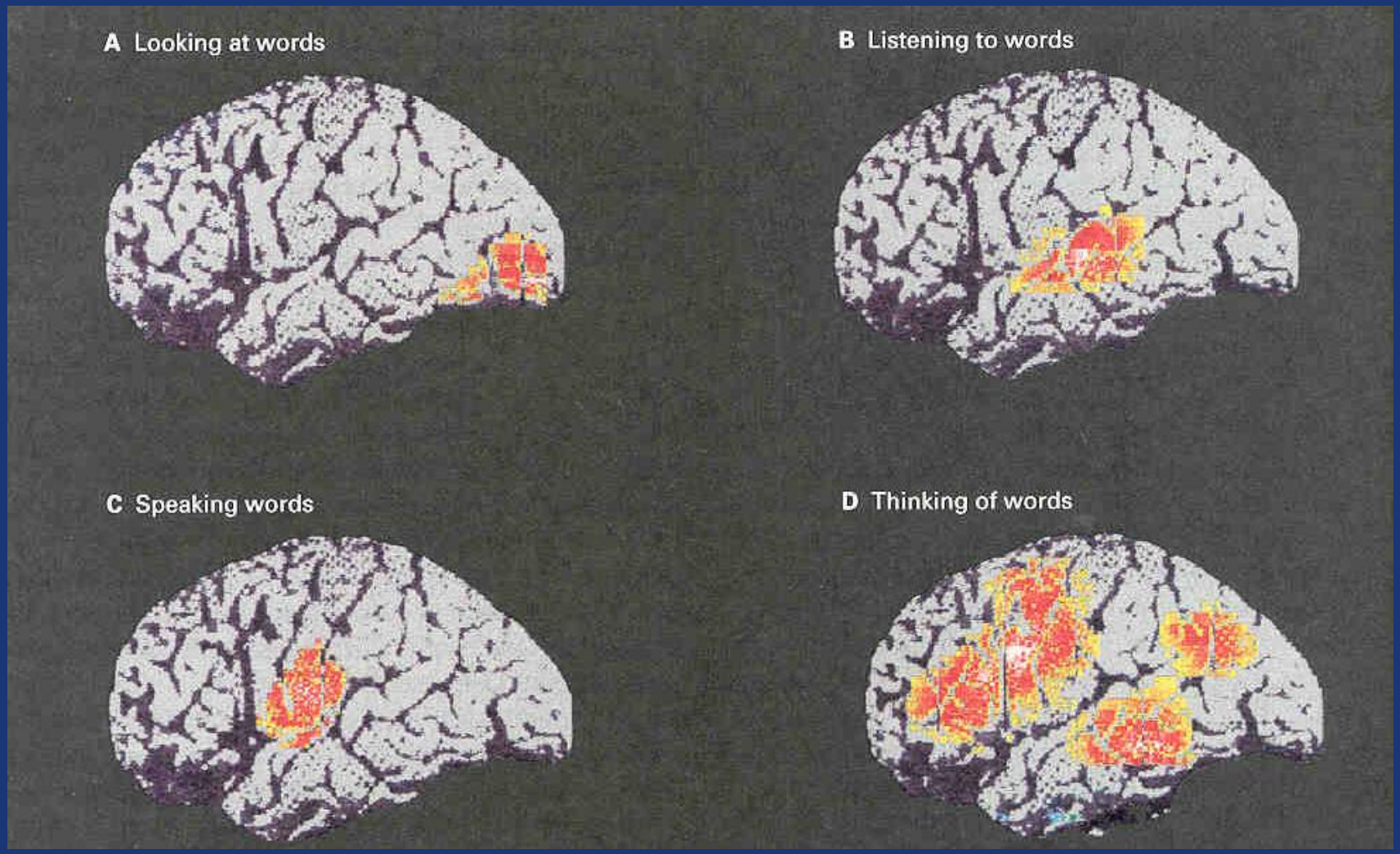
Mapping Schizophrenia



Mapping "Functional" Localization



Metabolic Assessment Of Cognitive Functions: How Does It Tie Together - Where Does The Actual Perception Occur?



Do Brain Scans Reveal Mechanisms?

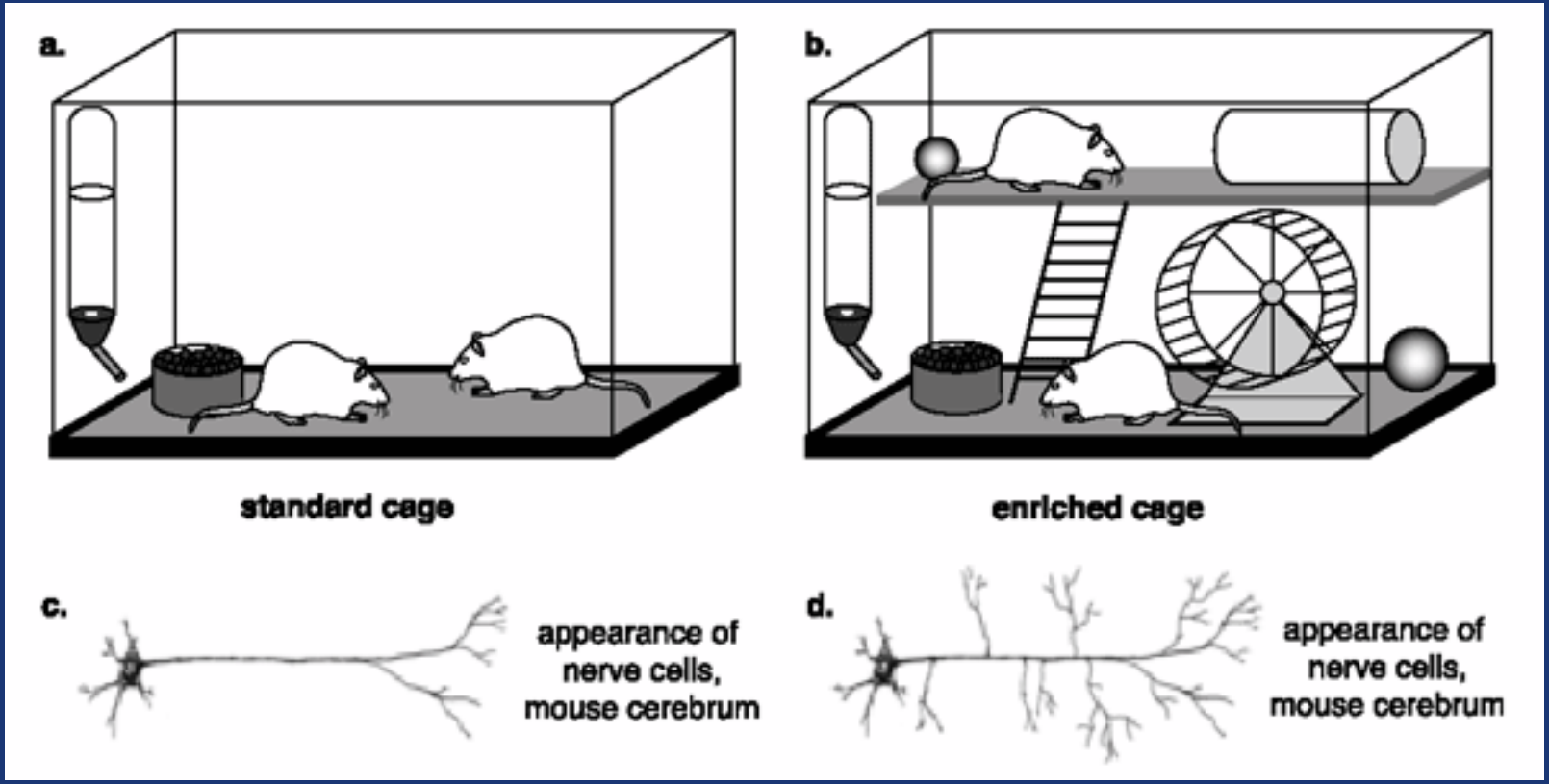
- They cannot explain recovery or sparing of function after injury.
- They **associate** brain structures with psychological and behavioral functions but *associations are not explanations*.
- The difference between phrenology and modern brain imaging is that brain scans more accurately identify brain structures that are active when someone is doing something.
- They do not provide any information on mechanisms because they do not explain how those neural networks generate behaviors that are supposedly dependent on that structure.

"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."

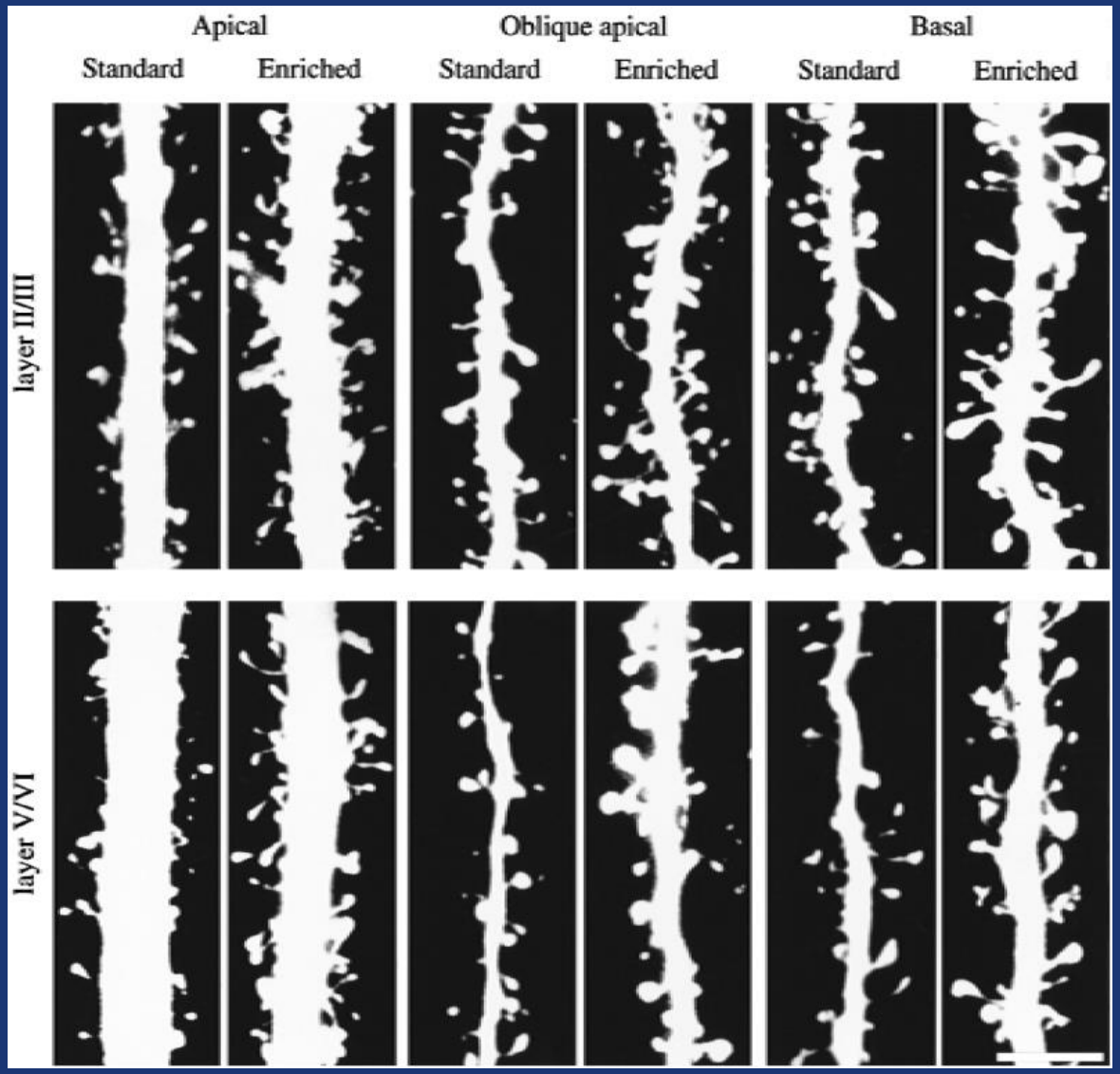
-Kuhn, T.S. "The Structure of Scientific Revolution"
2nd Edition, 1970 Univ. Chicago Press

You Don't Need A Brain Injury To See/Produce Plasticity: Environment And Experience Can Alter Cells Even In The Adult Brain

Studies From The 1950's

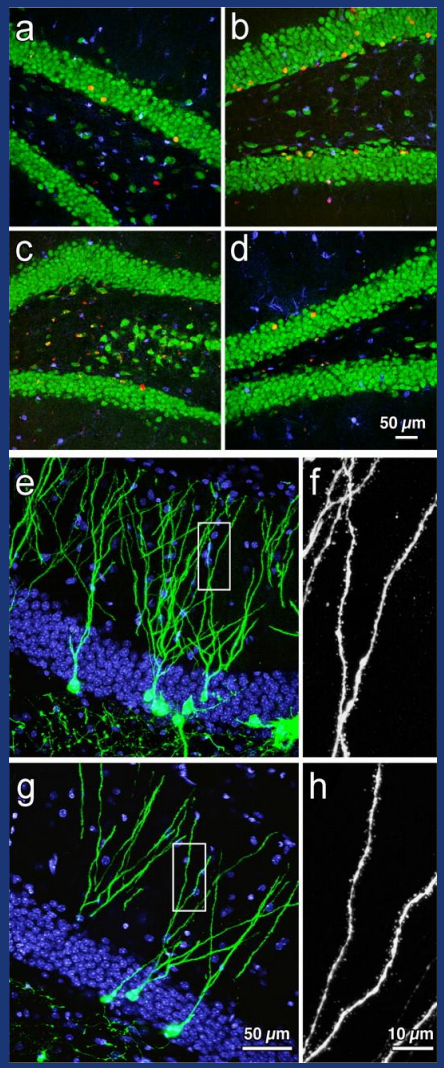


Effects Of Enrichment On Dendritic Growth



Neurogenesis Induced By Exercise In The Young And Aged Dentate Gyrus

*Note that number of new cells is very small (red dots)



van PraagH et al., J Neurosci 2005;25:8680-8685

Neurogenesis in the adult hippocampus of the monkey

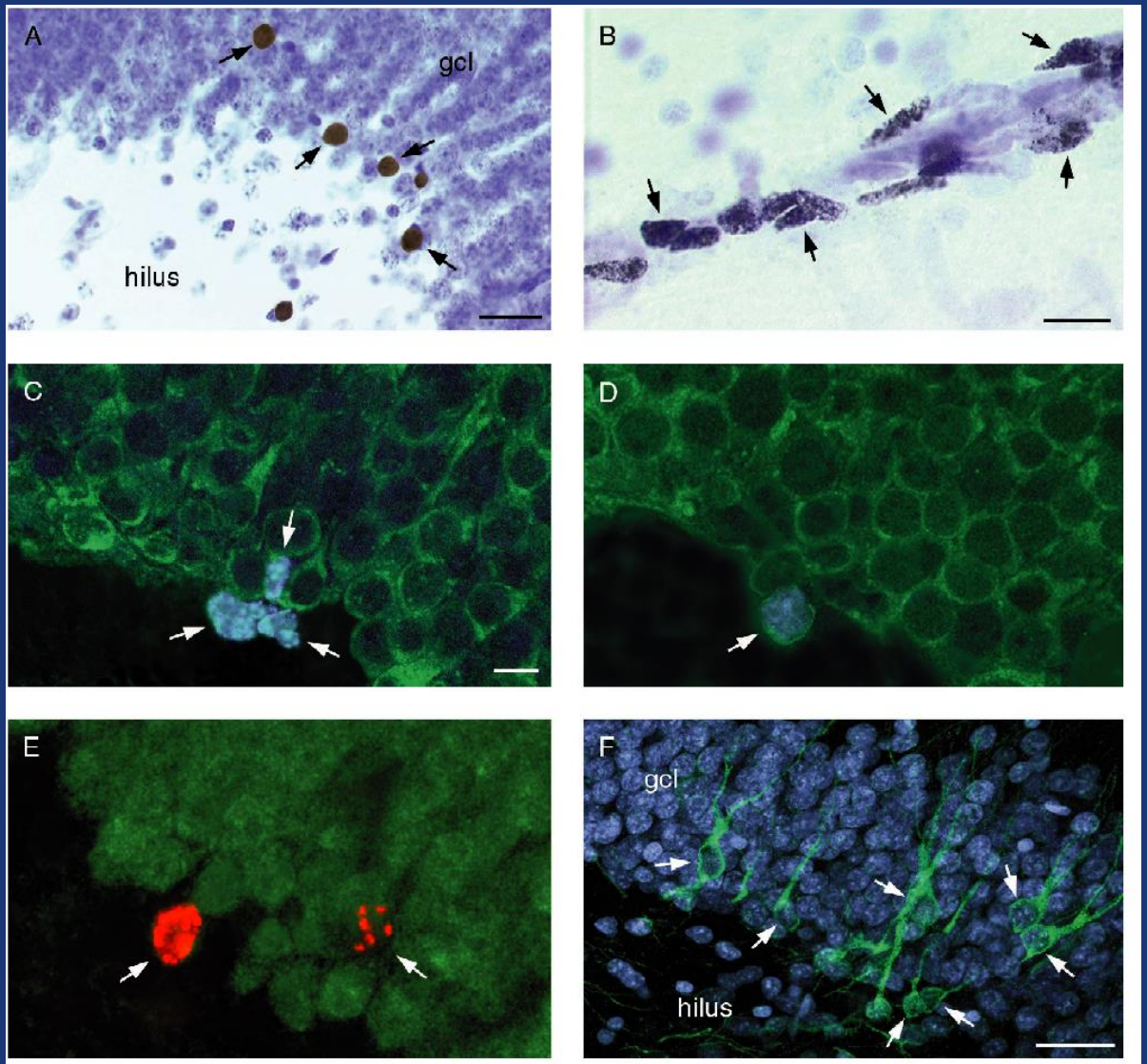


FIG. 1. Photomicrographs (*A* and *B*) and confocal laser scanning microscopic images (*C–F*) depicting new cells produced in the adult monkey brain. BrdUrd-labeled cells were observed in the granule cell layer of the dentate gyrus (*A*) (arrows) (animal 7) and in a region corresponding to the rostral 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., PNAS 96, 5263-5267, 1999

Plasticity and Repair of the Damaged Brain

What We Can Learn About Brain Injury Can help Us to Understand Brain Plasticity

Injury-induced Plasticity In The Brain

- In brain imaging studies, during localization of sounds, blind humans activate large parts of the visual cortex as well as larger regions of posterior parietal cortex—areas involved in vision in seeing patients.

- Total left brain removal in children often spares much language function, suggesting a shift to the remaining intact hemisphere, but there may be subtle deficits later in life.

- PET and fMRI demonstrate that patients with left hemisphere epilepsy have much greater language representation in the contralateral hemisphere compared to controls.

- Using a variety of imaging studies, epileptic patients also show reorganization of language functions into healthy brain tissue surrounding the damaged area.

- How does other tissue "take over function" while maintaining its own function(s)?

Re-wiring The "Connectome"?

- Early visual deprivation leads to an expansion of brain regions in the auditory or somatosensory domain and a corresponding improvement of function.
- This has been demonstrated in the superior colliculus and, most prominently, in the cerebral cortex.
- Similarly, blindness from birth in humans can cause reassignment of cortical regions from one sensory modality to another, as functional imaging studies have shown.
- The most exciting consequence of these recent studies is that sensory substitution in the blind may become a practical reality, allowing blind individuals to harness the power of crossmodal plasticity to perceive, localize and recognize objects with their auditory and tactile senses

Recovery From Subcortical Stroke: PET Activation Patterns In Patients Compared With Healthy Subjects

- Single, focalized lesions lead to depression of metabolism in the area surrounding the injury, but also to functional decreases in remote sites. One also finds changes in the hemisphere contralateral to the injury.

- In patients showing recovery of movement after stroke, rCBF changes are seen bilaterally distributed whereas in normals activation is only unilateral.

- These results demonstrate that the brain can show significant changes in multiple cortical (and subcortical) areas after local cerebral injury even if the injury is very restricted to the pyramidal tract.

Klaus-Martin Stephan and Richard Frackowiak

Can Changing Behavior Enhance Neural 'Plasticity'?

- "Behavioral treatment options can be used to restoring function and treating problematic symptoms. An example is mirror therapy, a technique used to treat phantom limb pain.

- In this situation, the patient uses a mirror to cover their amputation and focuses on watching their intact limb perform activities while imagining that both limbs are performing the same activity.

- One of the most studied rehabilitation techniques is constraint-induced movement therapy (CIMT).

- Used in patients with a stroke, the premise is that by constraining the functional limb, the affected limb is engaged in repetitive task practice and behavioral shaping".

- M. Puderbaugh; Prabhu D. Emmady. 2023

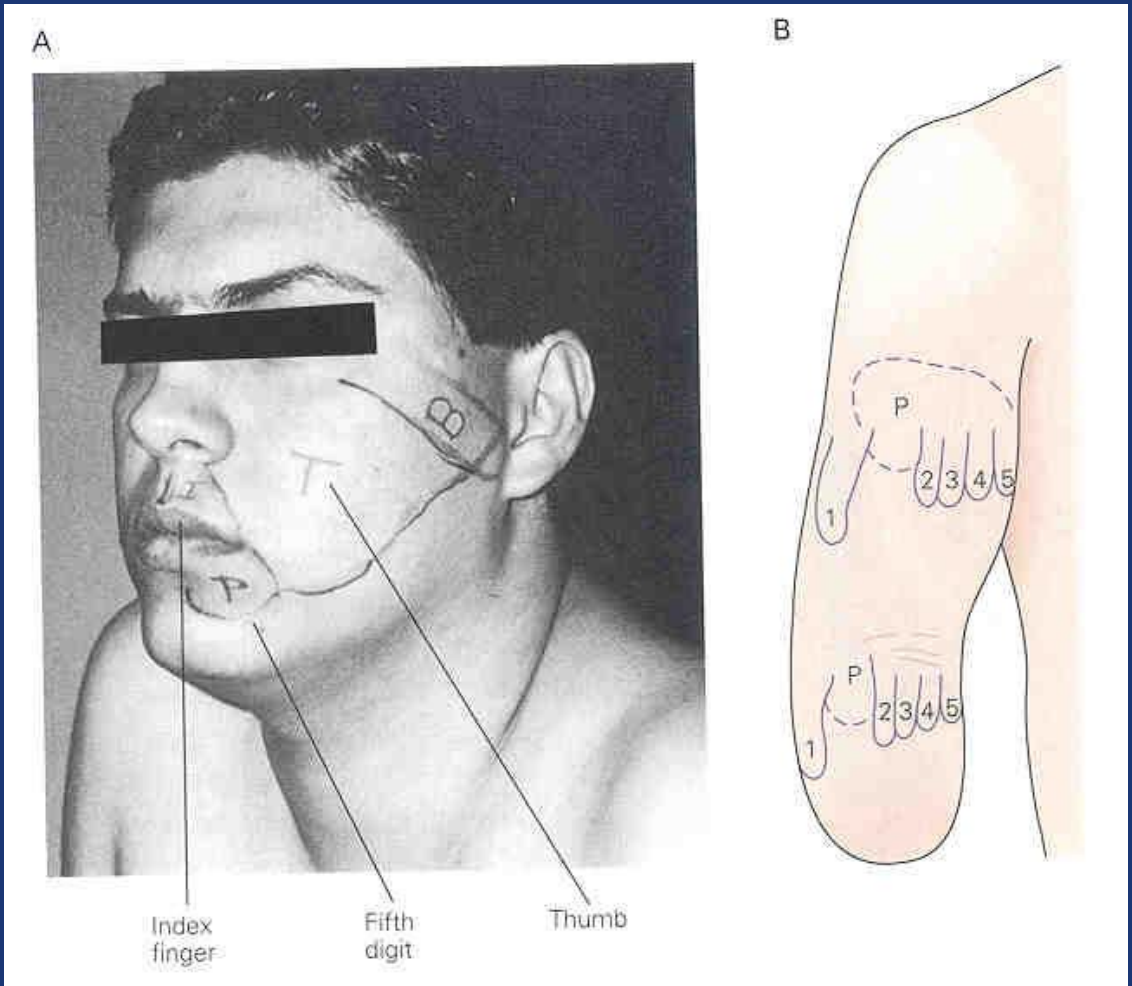
Plasticity In Phantom Limbs Induced With Mirrors

- A mirror reflection of the patient's intact hand is superimposed on the felt position of the phantom.
- When the normal hand is moved so that the phantom is perceived to move in the mirror, kinesthetic sensations emerge in the phantom. The sensation of "clenching" spasms could also be removed when the mirror was used to facilitate "opening" of the phantom hand.
- The data "suggest that there is a considerable amount of latent plasticity even in the adult human brain. The strictly modular, hierarchical model of the brain that is currently in vogue needs to be replaced with a more dynamic, interactive model."

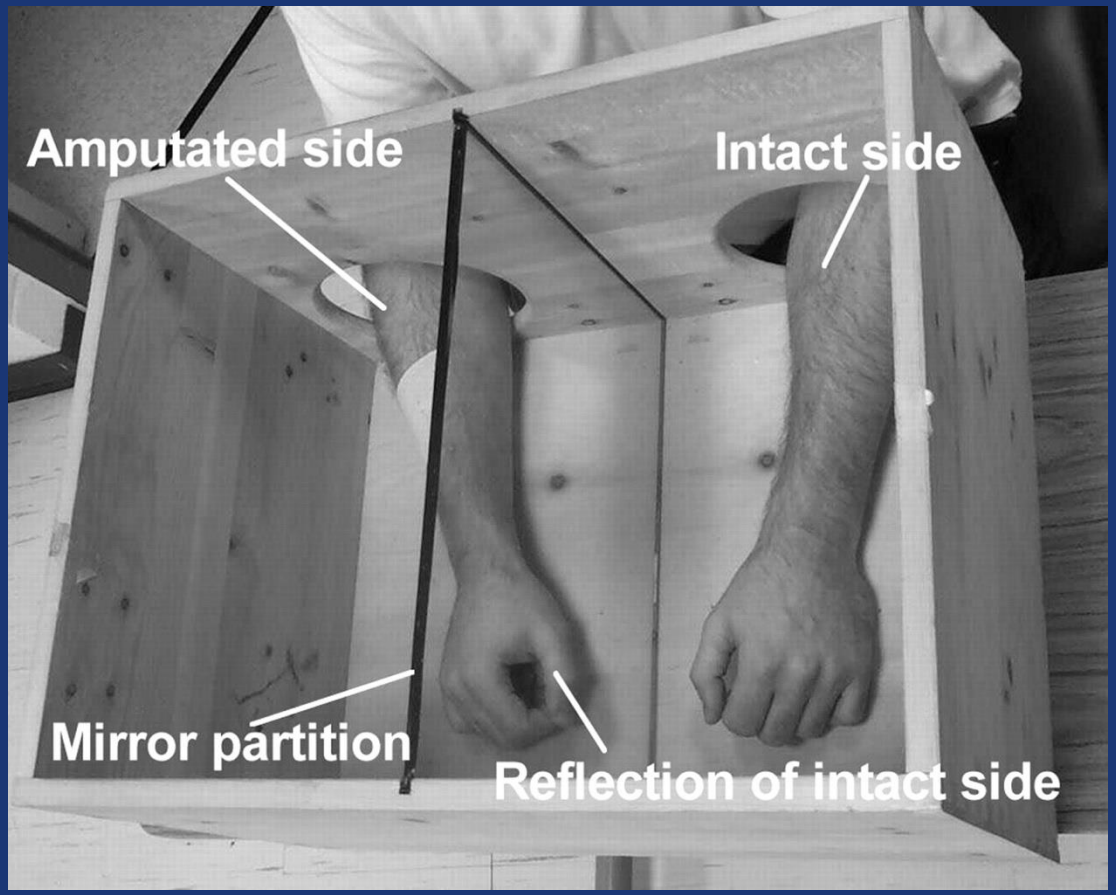
Rapid Reorganization And Re-mapping The Brain - II

- 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 individual history plays a role.

Phantom Limb Reorganization



The Mirror-box Illusion: Immediate Reorganization Of Function



Hunter, J. P. et al. Brain 2003 126:579-589; doi:10.1093/brain/awg054

BRAIN
A journal of neurolo

Conclusions

- Cortical somatosensory maps are dynamic
- Cortical maps can change (or add new)
- representational matrices
- The self-organizing capacity of sensory fields does not end early in life.

Be Careful! There's a lot of 'Hoaxes' Out There

Brain Plasticity Exercises **Neuroplasticity** Exercises - Proven **brain** training exercises to help you think faster, focus better, and remember more. Proven memory, attention, and speed exercises - train your **brain** in just minutes a day. **Brain** Health Classes. **Sponsored** Study.com
https://www.study.com/

What is **Neuroplasticity**? - Lesson | Study.com Discover Video Lessons. Worksheets. Practice Questions and More. All in One Place. Used by Over 30 Million Students & Teachers. Join Today To Find Out Why! 70,000+ effective lessons. Easy to

Scientists Agree: Meditation Is The #1 Brain Changer. So, what's the best way to build a better brain? Backed by 1000's of studies, meditation is the neuroscientific community's most proven way to upgrade the human brain.
Here we dive into **9 key brain regions** enhanced through meditation, with a focus on the massive life-transforming implication

Brain Plasticity: Understanding the **Brain's** Ability to Heal and Adapt

The Magic of NeuroPlasticity: Scientists Agree: Meditation Is The #1 Brain Changer. So, what's the best way to build a better brain? Backed by 1000's of studies, meditation is the neuroscientific community's most proven way to upgrade the human brain. Here we dive into **9 key brain regions** enhanced through meditation, with a focus on the massive life-transforming psiHand helps overcome stroke recovery plateaus. Explore **brain**-activated therapy—supporting arm...

Neuroplasticity: How our brains are wired for change: The MindBody Food Institute. 100% online. Flexible and soft-paced. Affordable payments. Holistic Life Coach, Mind-body practicioner, somatic pain practicioner.n

The Marketing Of Brain Plasticity

Plasticity in a Bottle?

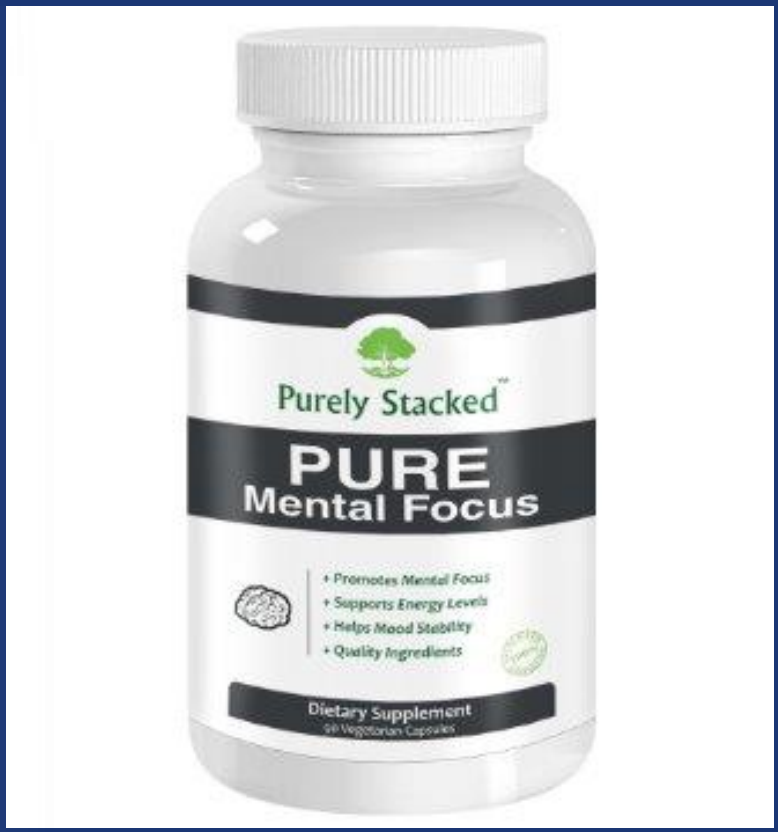
Top 10 Brain Supplements

1. Alpha Focus
2. Cerebral Charge
3. Neuro HD
4. MedixSelect Cresceo
5. MRM Neuro-Max II
6. FutureBiotics ThinkFast
7. ProSupps I-Focus
8. TheraBotanics Cebria
9. Vitazen CogniZen
10. Truetoniqs Brain Toniq

The Hard Sell

- Alpha focus has jumped to the top ranking in every category.
- It is specifically designed to boost memory focus, reduce mental focus and support healthy brain function.
- Alpha focus helps your brain naturally increase its potential and immediately improves function.
- Alpha focus jump-starts your mental focus.
- The natural ingredients smooth enural pathway to give razor-sharp focus without negative side effects.

Neuroplasticity In A Bottle



Remaining Issues in Plasticity and Recovery Research and Theory

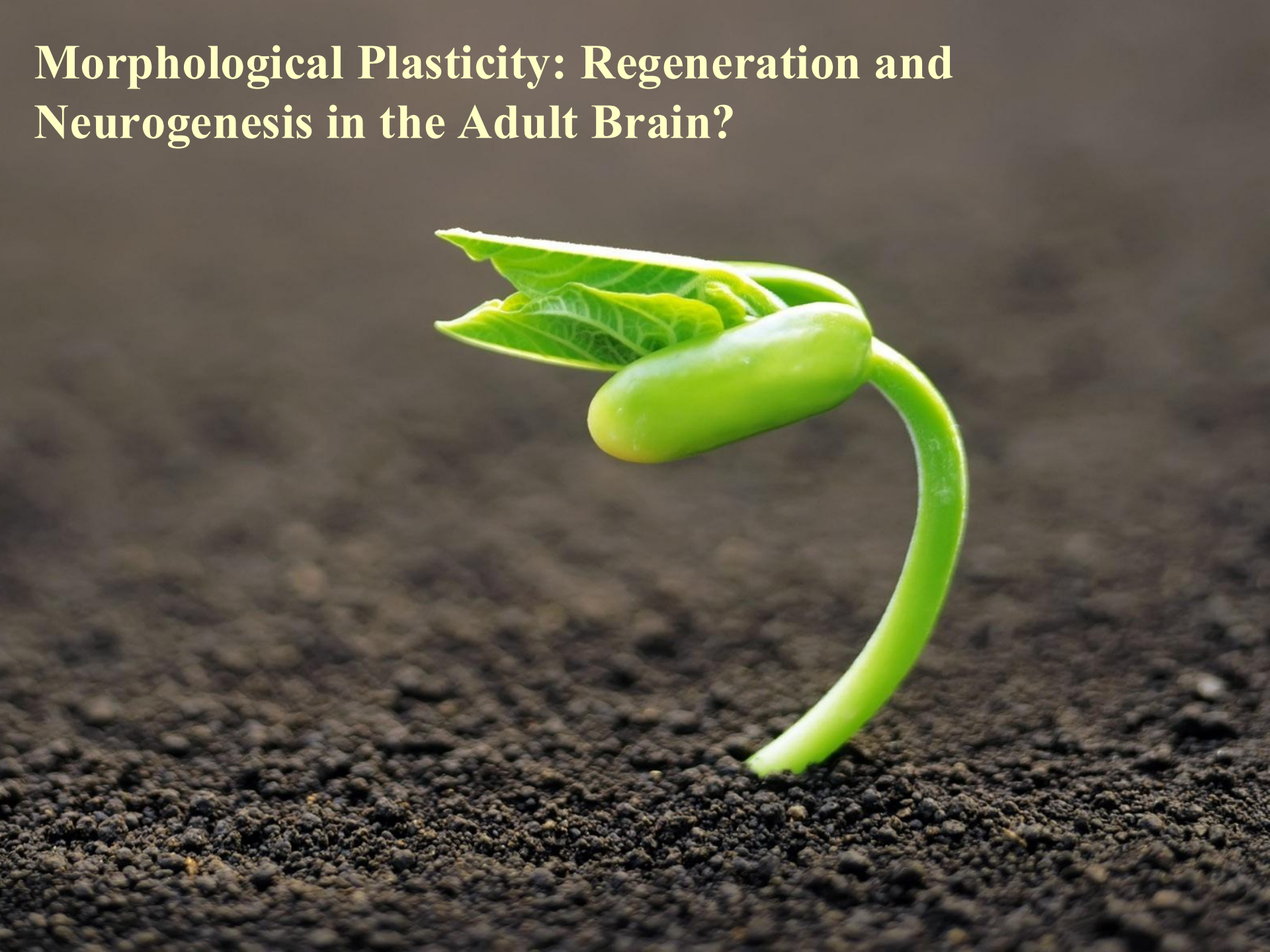
- Glial and stem cells: what are their roles in the repair process?
- Genes and receptors: what are their roles in inducing factors that enhance repair and recovery?
- To what extent is the whole brain reorganized after injury and during repair?
- What age and gender factors contribute to recovery?

Conclusions

- There are now multiple opportunities for brain repair and functional rehabilitation, including:
  - pharmacological, genomic and proteomic manipulations
  - transplants of stem cells and glia
  - neurogenesis
  - direct stimulation
  - behavioral training
  - enriched environment
  - robotics
  - and others to be discovered
- *Functional* recovery is likely to be dependent on the context of the injury and involve multiple physiological processes.
- History, gender, training and experience of the patient can influence the extent and type of cerebral reorganization.

End

Morphological Plasticity: Regeneration and Neurogenesis in the Adult Brain?

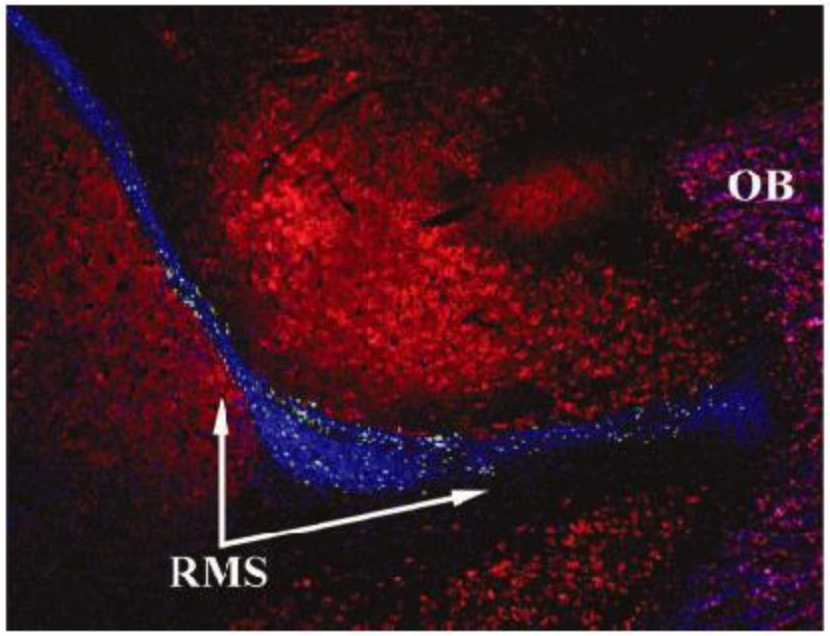


Working Hypotheses about Anatomical Recovery

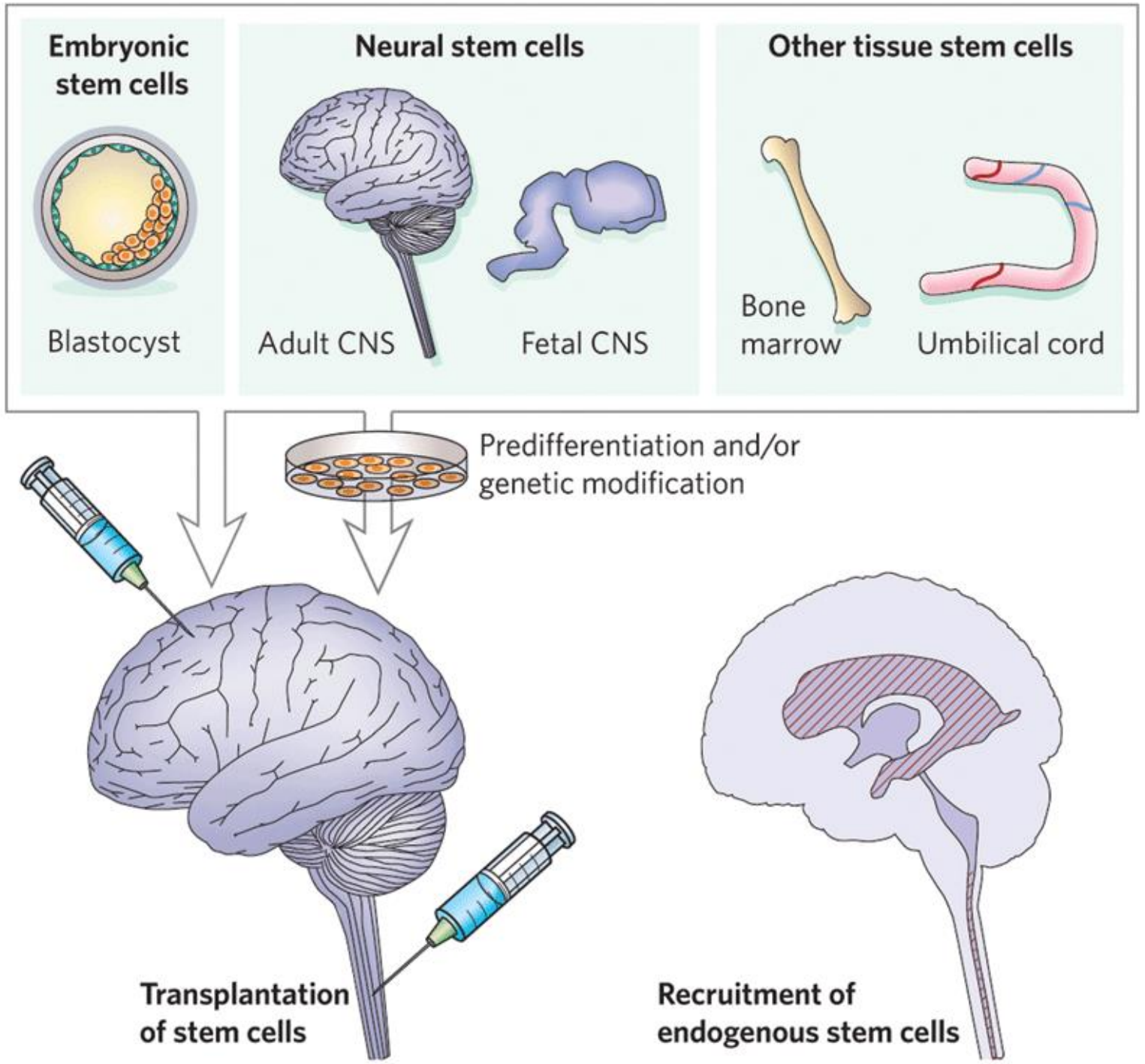
- Neuronal sprouting and regeneration may directly mediate recovery (but rarely seen to be functional in adult brain—if ever).
- Neurogenesis in adults (although limited) may re-establish functional connections and enhance recovery.
- Transplanted fetal, genetically modified, neural or progenitor cells may be used to mediate functional recovery.

New Neurons in the Adult Brain

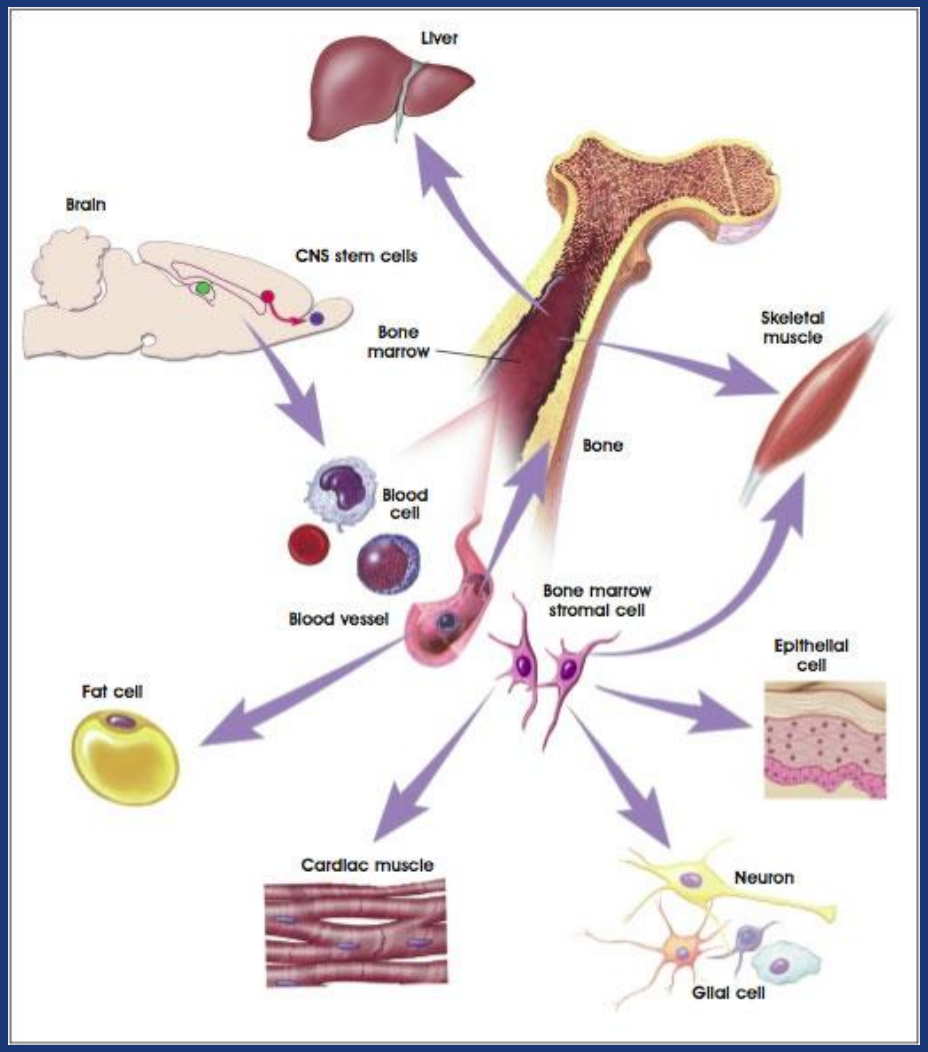
Fig. 2. Adult forebrain neurogenesis. A sagittal section of the adult mouse forebrain [with mature neurons labeled for NeuN (a neuronal antigen) in red] shows neuronal precursors labeled with bromodeoxyuridine (green) migrating along the rostral migratory stream (RMS; blue Hoechst stain) toward their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



Is There a Future for Stem Cell Therapy in Restoring Brain Functions?


Embryonic stem cells
Blastocyst
Neural stem cells
Adult CNS
Fetal CNS
Other tissue stem cells
Bone marrow
Umbilical cord
Predifferentiation and/or genetic modification
Transplantation of stem cells
Recruitment of endogenous stem cells

Various Stem Cell Possibilities



Stem Cells Originate in Different Brain Structures

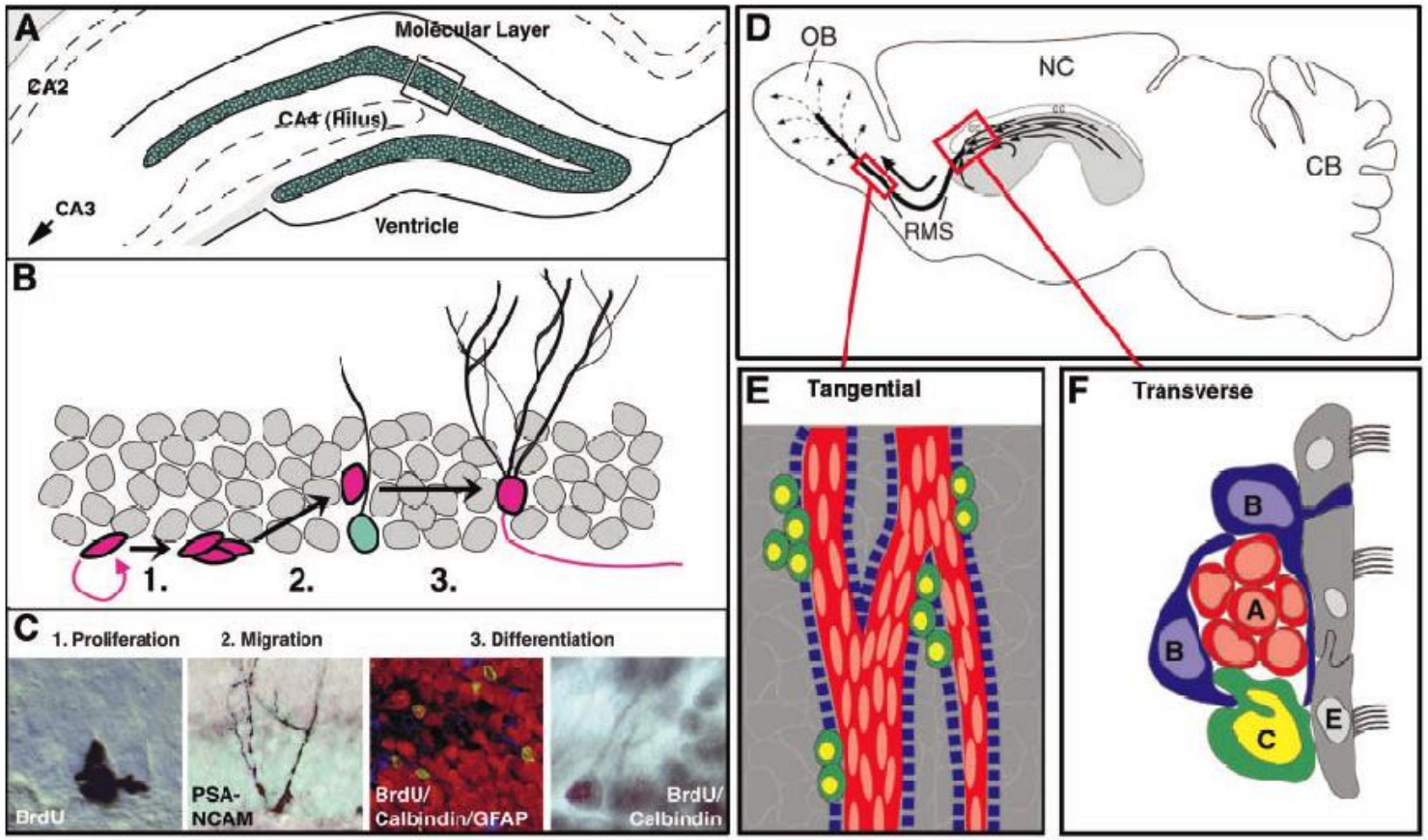
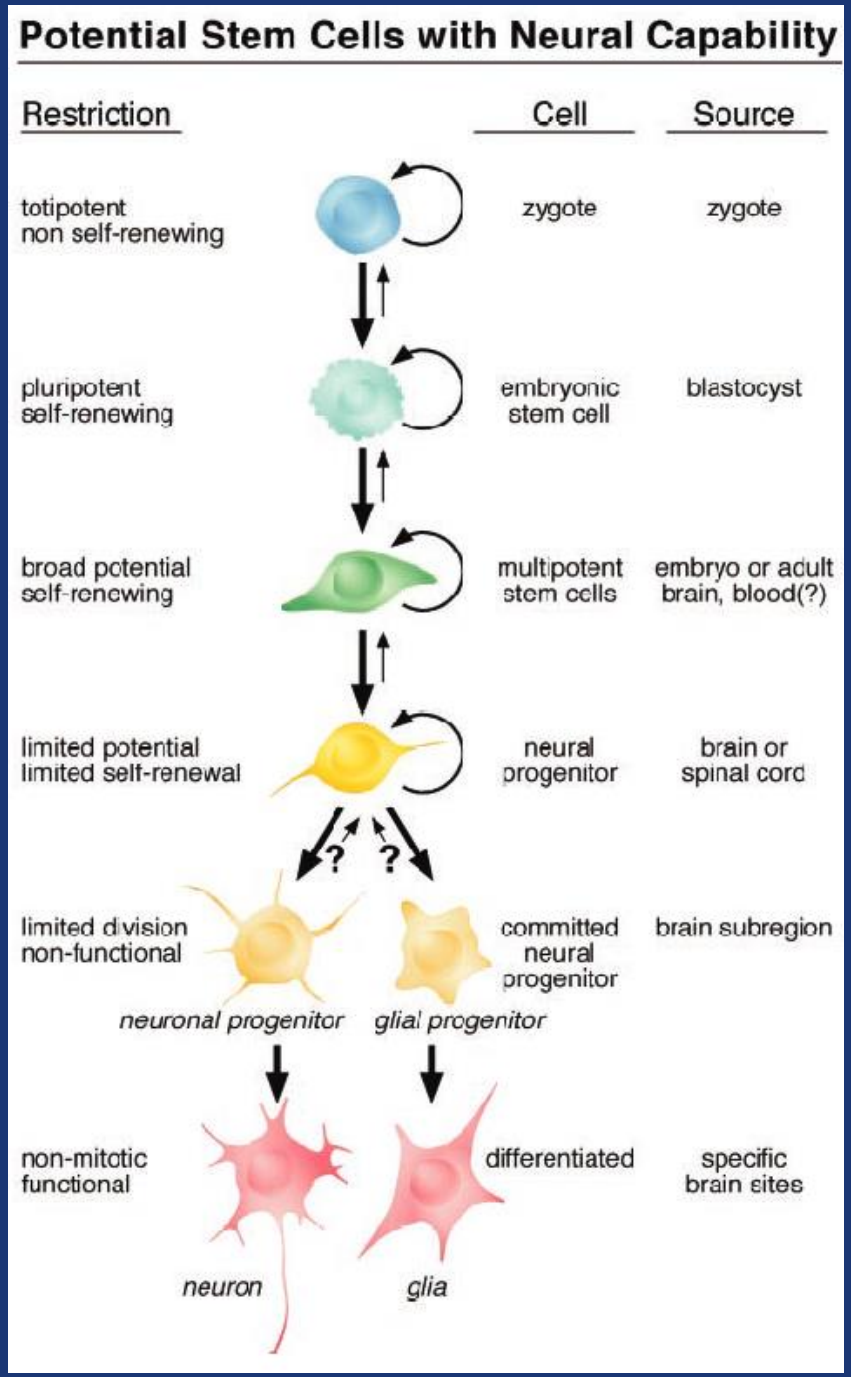


Fig. 3. Examples of the origin and migratory pattern of the stem cells observed in situ in (**A** through **C**) the adult dentate gyrus and (**D**) the subependymal RMS. The box in (A) indicates the granule cell layer illustrated in (B). The numbers in (B) refer to the three steps shown in (C). OB, 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.

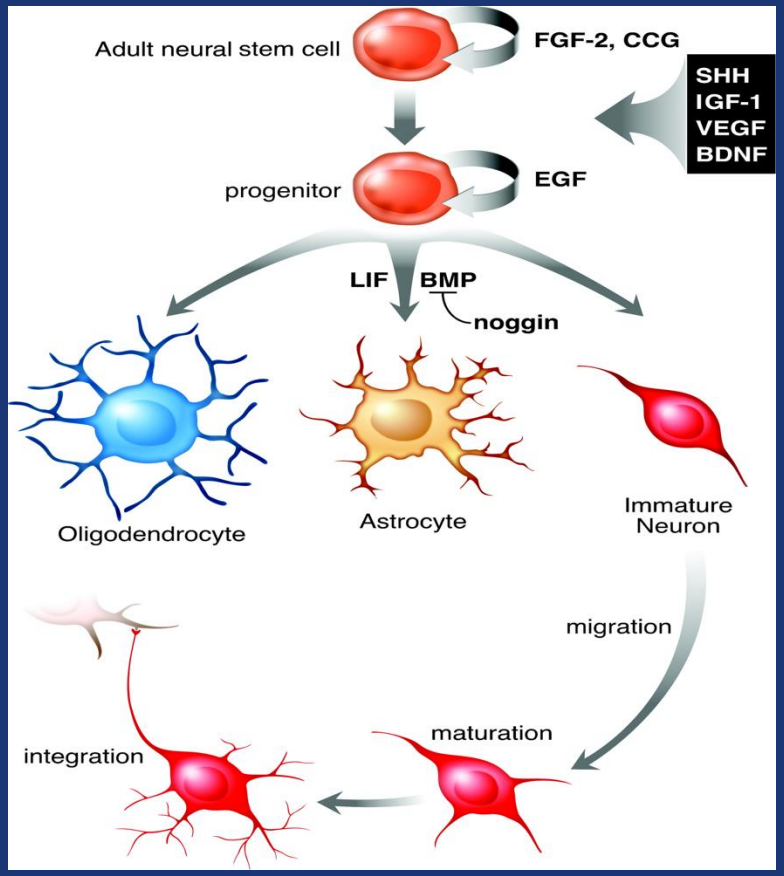
Gage (2000) Scence 287:1433-38.

in theory stem cells could assume different structures and functions in the brain

but what if they don't?



Trophic Factors Affecting Stem-Cell Development



Functional Requirements for Generated New Cells in Adaptive Plasticity

- must be able to modify adult brain function in a *beneficial* way (e.g. not produce seizures*)
- must show *normal* neuronal activity (synaptic and axonal) and integrate into neuronal circuits
- should enhance learning and memory, not impair it
- must *mature and survive* over a period of time
- should *enhance recovery* of function, not prevent or distort it

* *Epilepsy causes a large increase in hippocampal neurogenesis*

Can Transplanted Stem Cells Assume Different Functions?

- Stem cells can migrate from their birthplace, from the site of implantation, or from the site of injury.
- Functional recovery after implantation does not depend on cells transforming into neurons—they may maintain their original identity.
- They may or may not integrate with host tissue.
- They could become tumors. All tumors start with stem cells.
- Glial cells also enhance recovery without forming new connections.

Clinical trials with intrastriatal transplantation of human fetal mesencephalic tissue, rich in dopaminergic neurons, in Parkinson's disease (PD) patients show that cell replacement can work and in some cases induce major, long-lasting improvement.

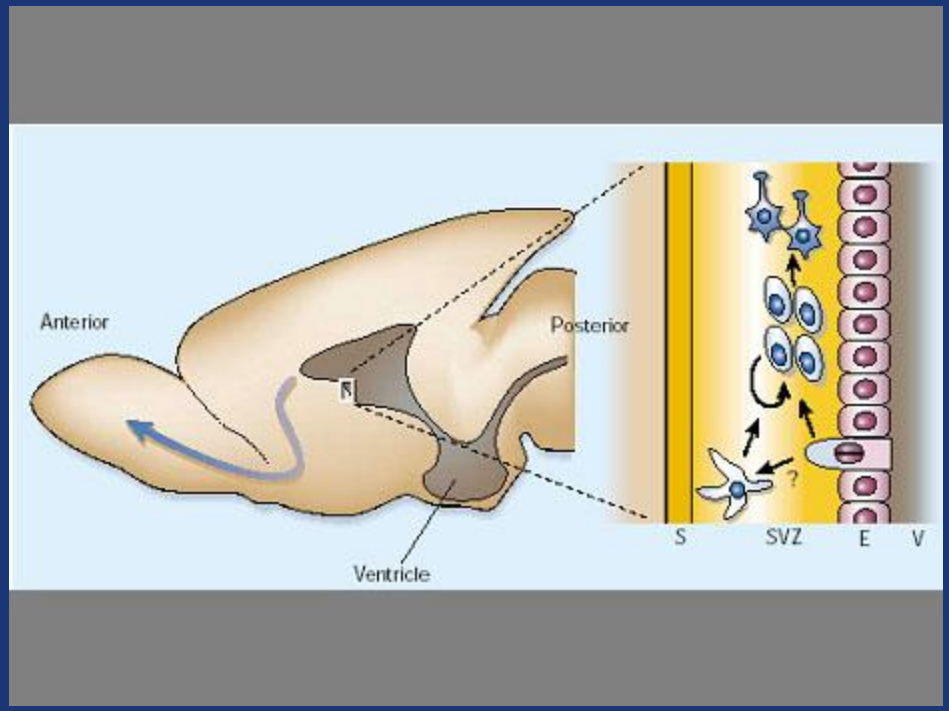
However, owing to poor tissue availability, this approach can be applied in very few patients, and standardization is difficult, leading to wide variation in functional outcome.

(Is a placebo effect possible?)

Philos Trans R Soc Lond B Biol Sci. 2015 370:1680

Treatment of Parkinson's disease using cell transplantation

Some Pros and Cons of Stem Cell Transplants in Brain Repair



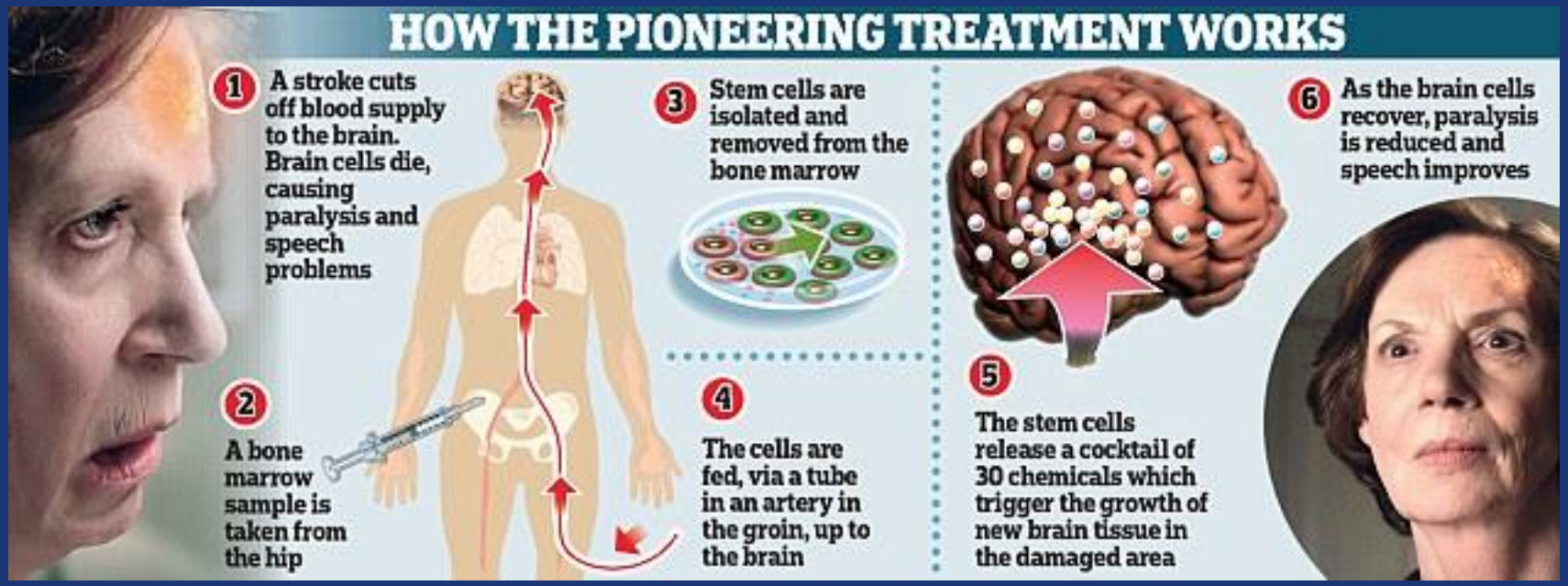
The Marketing Side of Stem Cells

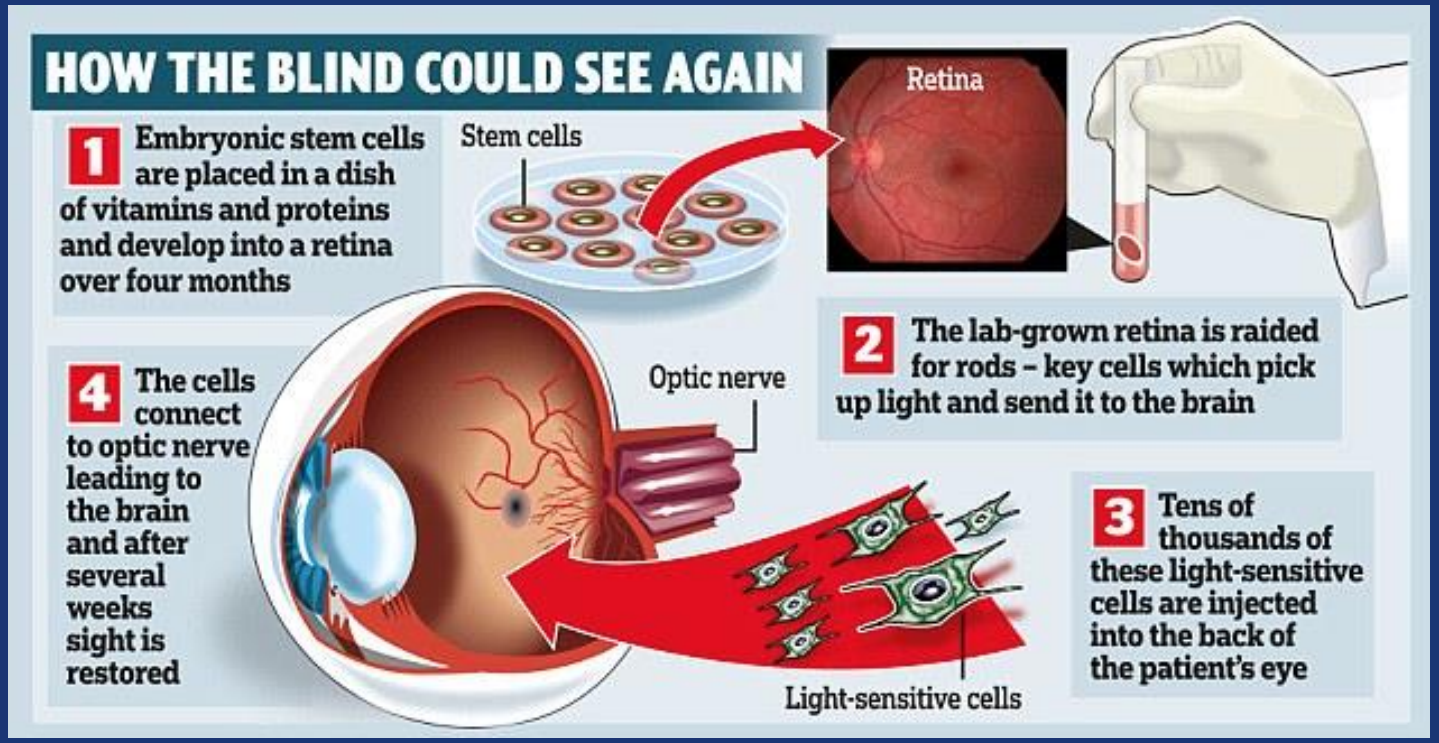
How Well Do They Work?

MONDAY, April 7, 2014 (HealthDay News)

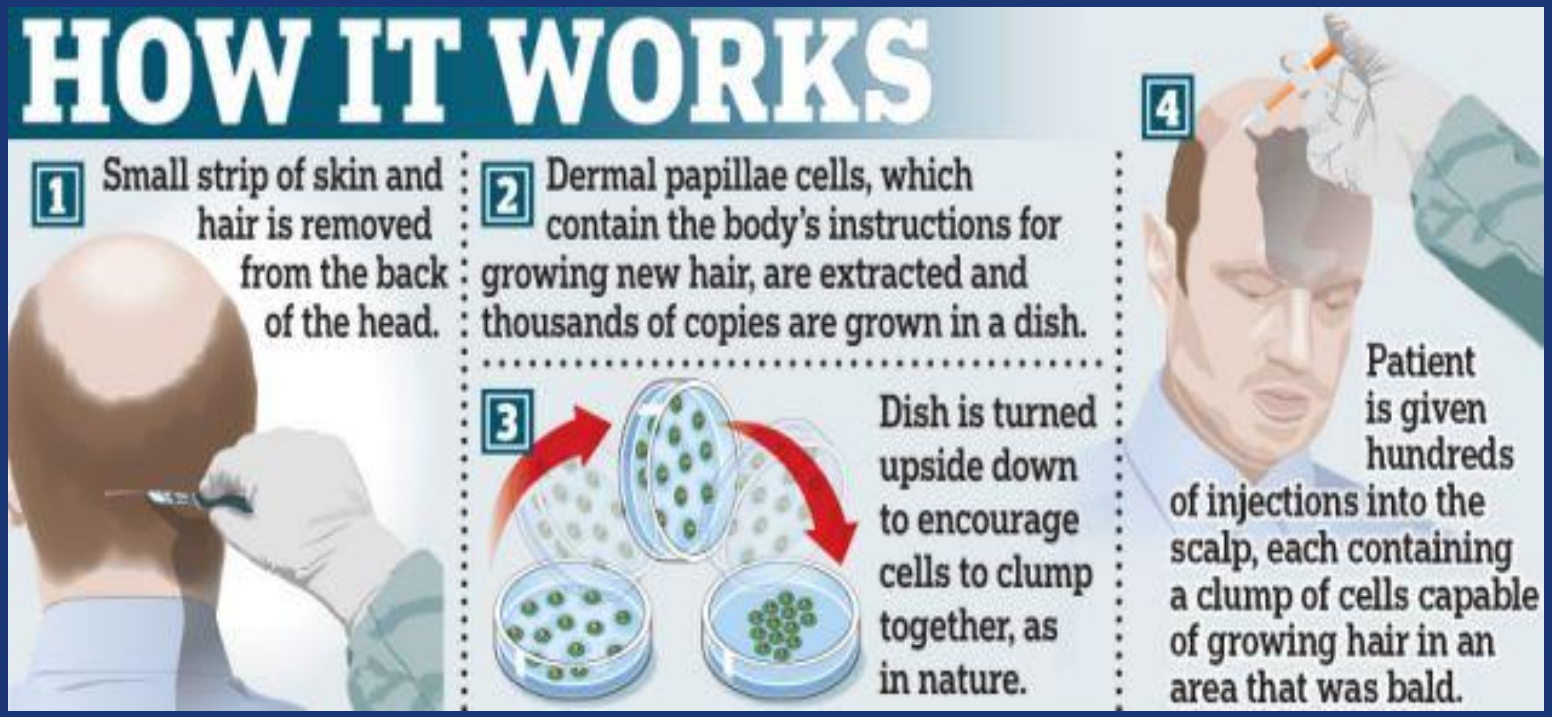
In an early test, researchers report they've safely injected bone marrow stem cells into the brains of 18 patients who had suffered strokes. And two of the patients showed significant improvement.

BTW: That's about a 10% success rate!


HOW THE PIONEERING TREATMENT WORKS
1 A stroke cuts off blood supply to the brain. Brain cells die, causing paralysis and speech problems
2 A bone marrow sample is taken from the hip
3 Stem cells are isolated and removed from the bone marrow
4 The cells are fed, via a tube in an artery in the groin, up to the brain
5 The stem cells release a cocktail of 30 chemicals which trigger the growth of new brain tissue in the damaged area
6 As the brain cells recover, paralysis is reduced and speech improves


HOW THE BLIND COULD SEE AGAIN
1 Embryonic stem cells are placed in a dish of vitamins and proteins and develop into a retina over four months
Stem cells
Retina
2 The lab-grown retina is raided for rods – key cells which pick up light and send it to the brain
3 Tens of thousands of these light-sensitive cells are injected into the back of the patient's eye
4 The cells connect to optic nerve leading to the brain and after several weeks sight is restored
Optic nerve
Light-sensitive cells

Stem Cells for Hair Loss



Skin Type: All

Glymed Cell Science Stem Cell Power Serum Description:

Glymed Cell Science Stem Cell Power Serum is a highly developed formula

Contains 4 intense peptide boosters to help encourage new cell growth and improve aging skin fibroblasts, which increase collagen production.

This serum is designed to hold an instant power surge, resetting the aging skin at a cellular level.

Glymed Cell Science Stem Cell Power Serum Features & Benefits:

Helps reverse damage from Ultraviolet radiation.

Tightens, smoothes & lifts skin within days.

How To Use Glymed Cell Science Stem Cell Power Serum:

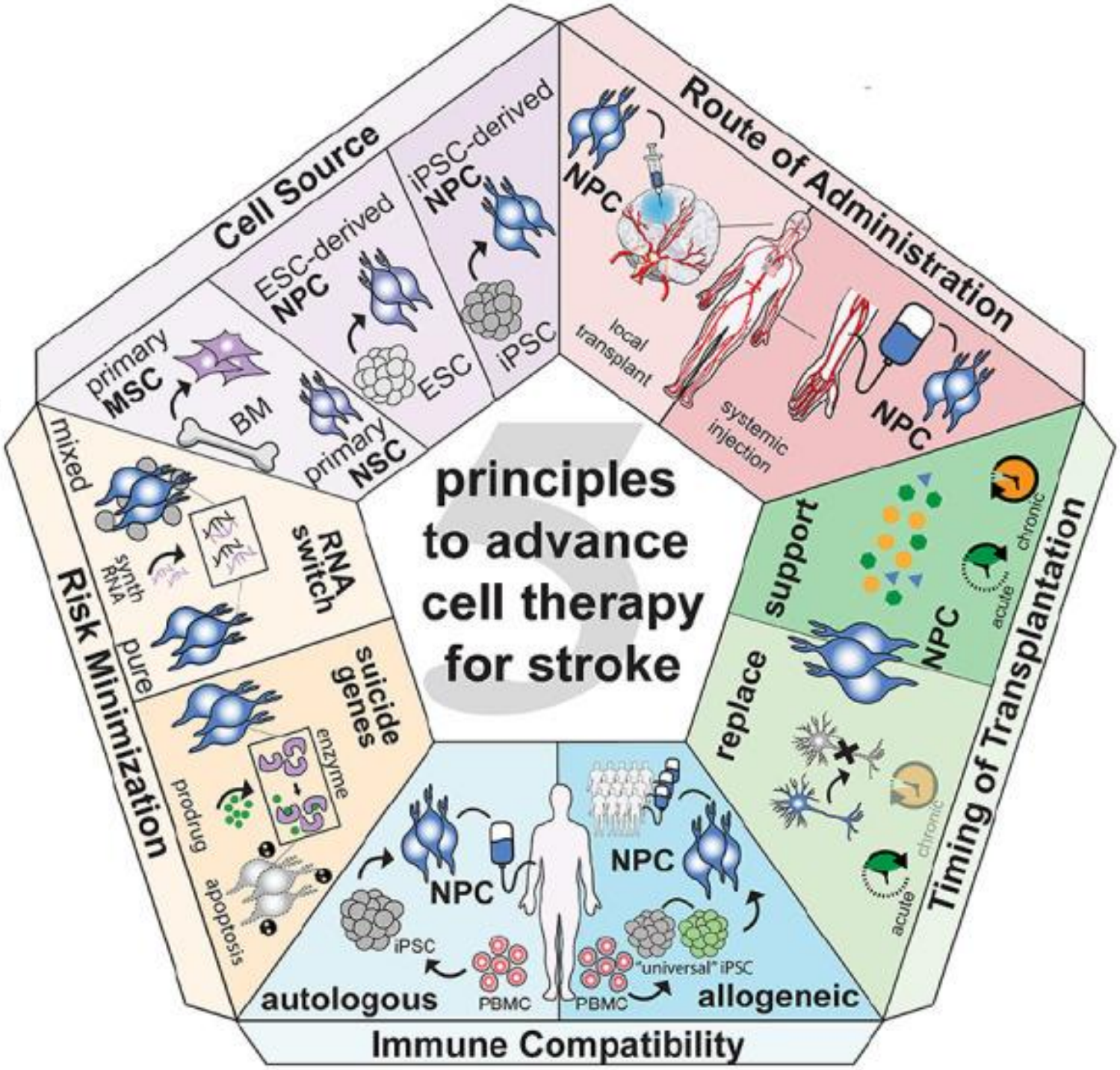
Apply 2 to 4 drops and massage into clean skin. For best results, use daily to protect skin.

Welcome to StemGenex®
a U.S. Leader in Stem Cell Therapy

- At StemGenex, we are able to offer patients access to cutting-edge *adipose stem cell therapy* for each of the degenerative diseases seen below.
- By exclusively utilizing Stem Cell Centers of Excellence we offer patients access to stem cell treatments with a level of quality and patient-centric care that simply cannot be found elsewhere. These stem cell clinics and treatment centers utilize board-certified surgeons in accredited surgical centers along with our own PhD neuroscientist setting forth and refining stem cell processing protocols.
- https://stemgenex.com

- Rats were treated intravenously with stem cells or saline 30 minutes after a stroke. At 24 hours after stroke the stem cell treated rats showed a better functional recovery. By two weeks these animals had near normal scores in the tests.
- This improvement was seen even though the stem cells did not appear to migrate to the damaged area of brain.
- The treated rats also had higher levels of biomarkers implicated in brain repair, including the growth factor VEGF.

BioMed Central's Stem Cell Research & Therapy, 2013


principles to advance cell therapy for stroke
Cell Source
primary MSC
BM
ESC-derived NPC
ESC
iPSC-derived NPC
iPSC
primary NSC
Route of Administration
NPC
local transplant
systemic injection
NPC
Timing of Transplantation
support
NPC
acute
chronic
replace
NPC
acute
chronic
Immune Compatibility
autologous
NPC
iPSC
PBMC
allogeneic
NPC
"universal" iPSC
PBMC
Risk Minimization
RNA switch
mixed
synth RNA
pure
suicide genes
enzyme
prodrug
apoptosis

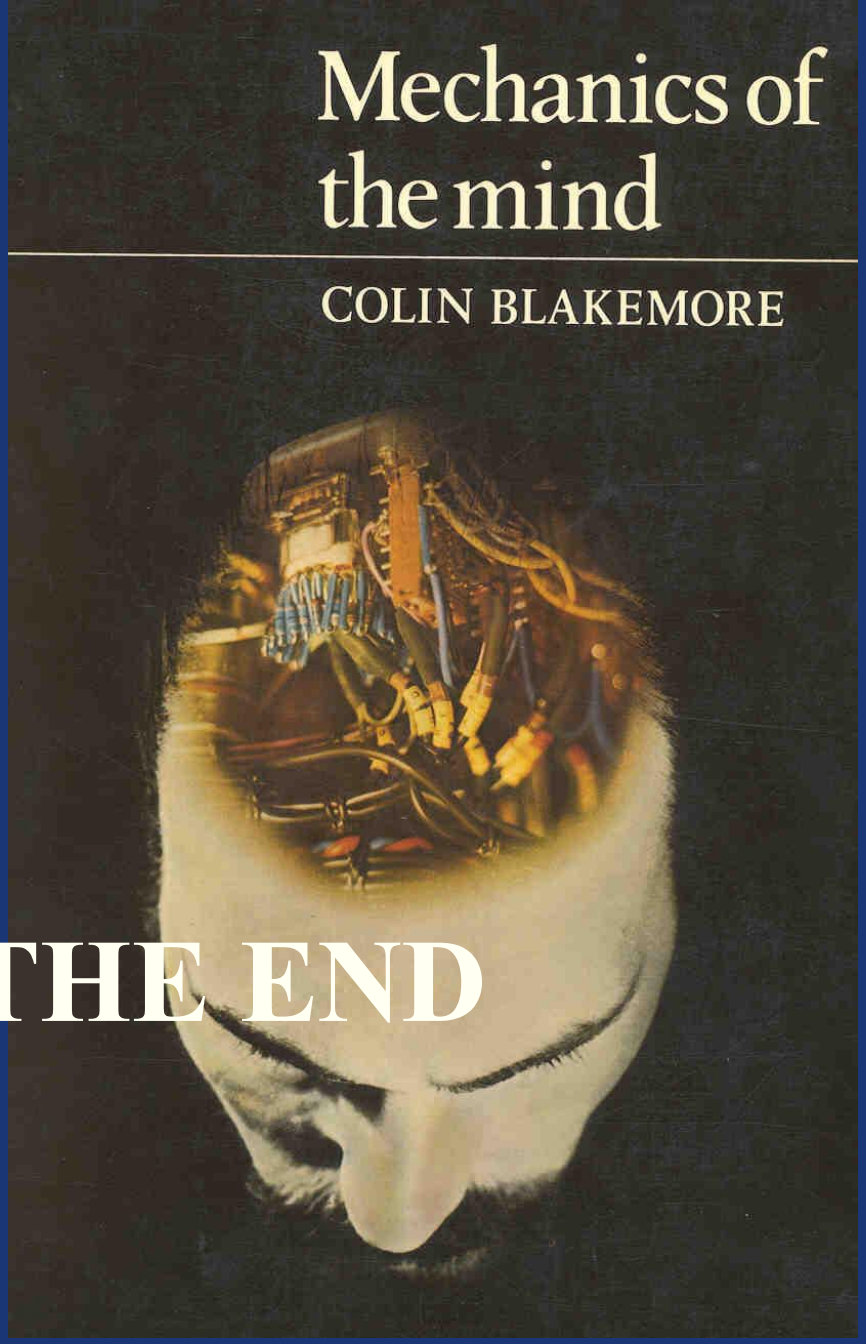
Remaining Issues in Plasticity and Recovery Research and Theory

- Glial and stem cells: what are their roles in the repair process?
- Genes and receptors: what are their roles in inducing factors that enhance repair and recovery?
- To what extent is the whole brain reorganized after injury and during repair?
- What age and gender factors contribute to recovery?

Conclusions

- There are now multiple opportunities for brain repair and functional rehabilitation, including:
  - pharmacological, genomic and proteomic manipulations
  - transplants of stem cells and glia
  - neurogenesis
  - direct stimulation
  - behavioral training
  - enriched environment
  - robotics
  - and others to be discovered
- *Functional* recovery is likely to be dependent on the context of the injury and involve multiple physiological processes.
- History, gender, training and experience of the patient can influence the extent and type of cerebral reorganization.

NOW REALLY: THE END



- Matt Puderbaugh; Prabhu D. Emmady.