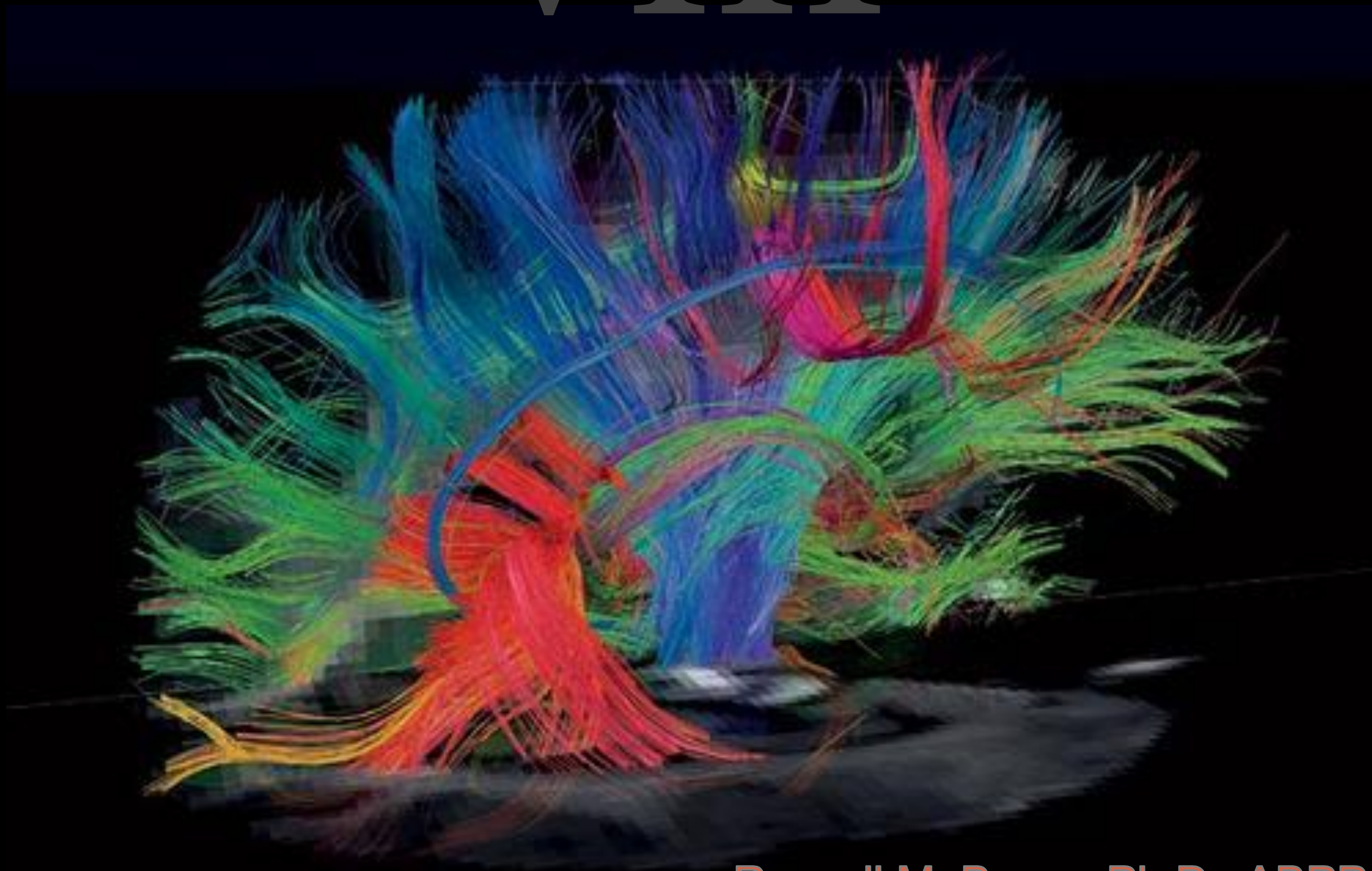
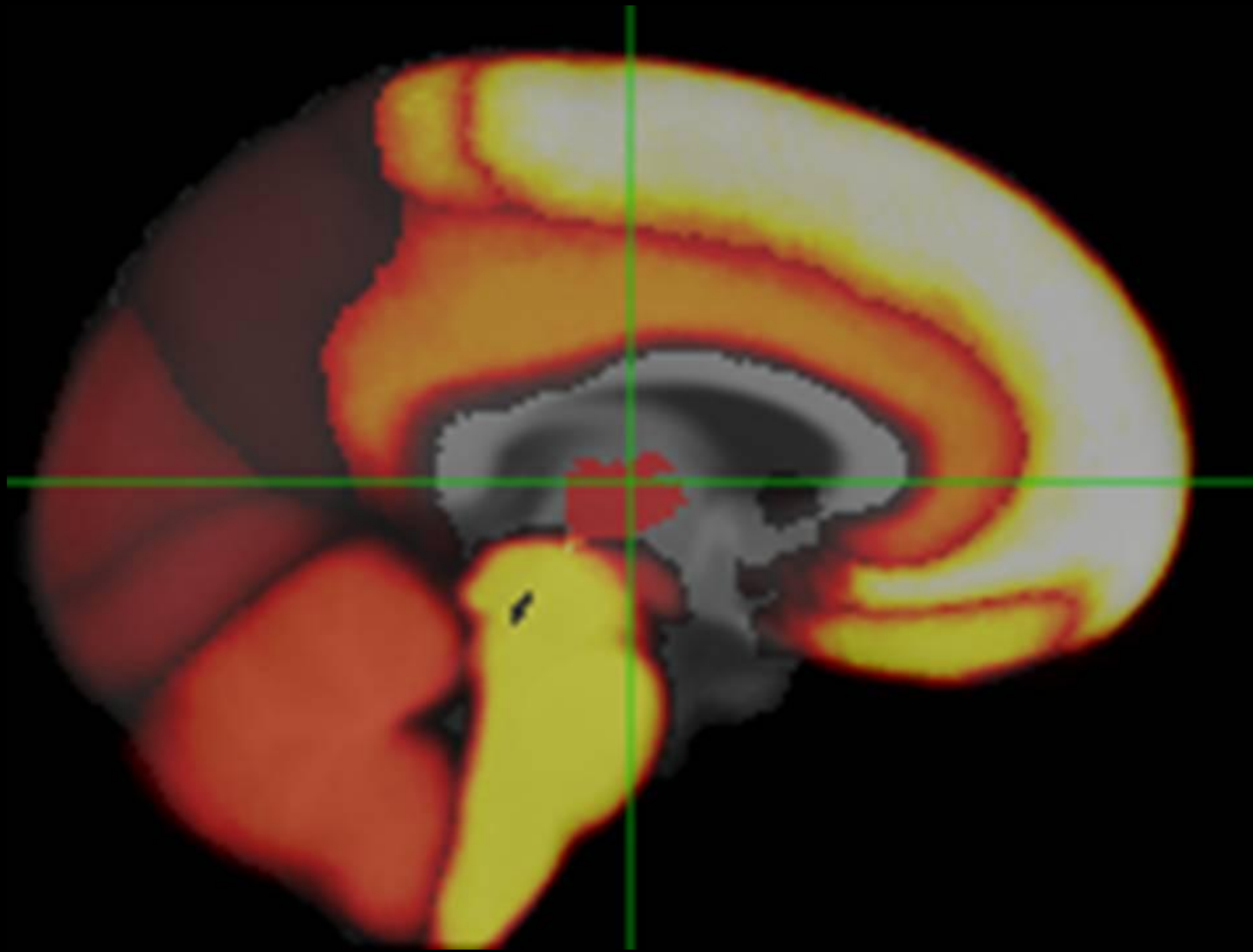
# Clinically Relevant Functional Neuroanatomy

# VIII




Russell M. Bauer, Ph.D., ABPP
University of Florida

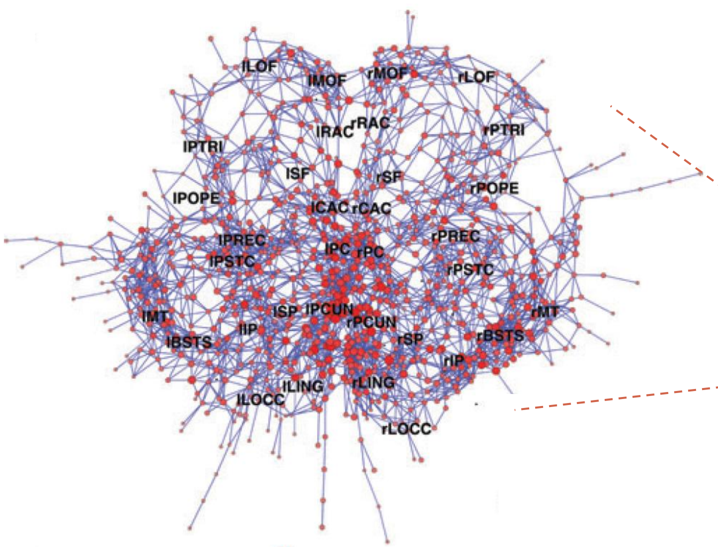
# Your Speaker

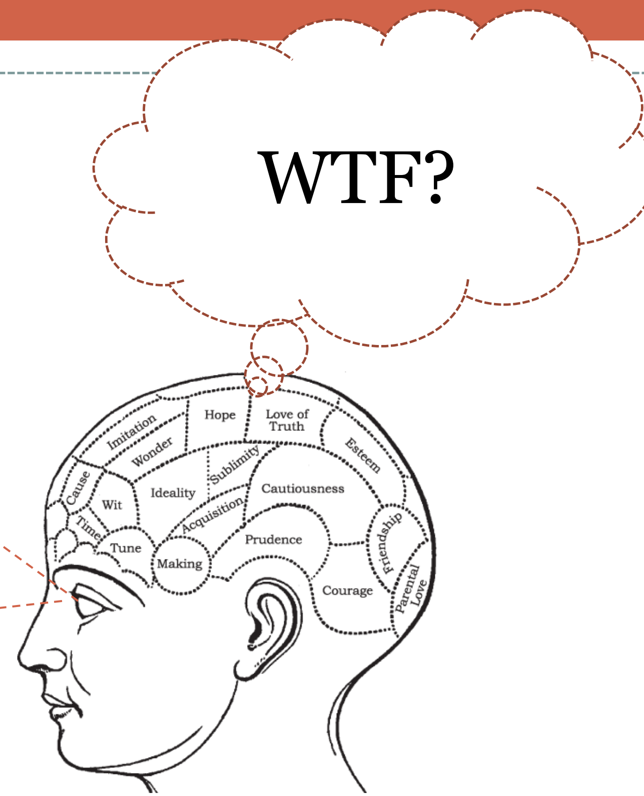


# Key Principles to be Covered in this Workshop

- Functional systems vs. Extreme Localization
- Inhibition and Excitation in Functional Connectivity
- Domain-Specificity vs. Domain Generality
- Disconnection vs. Processor Impairment

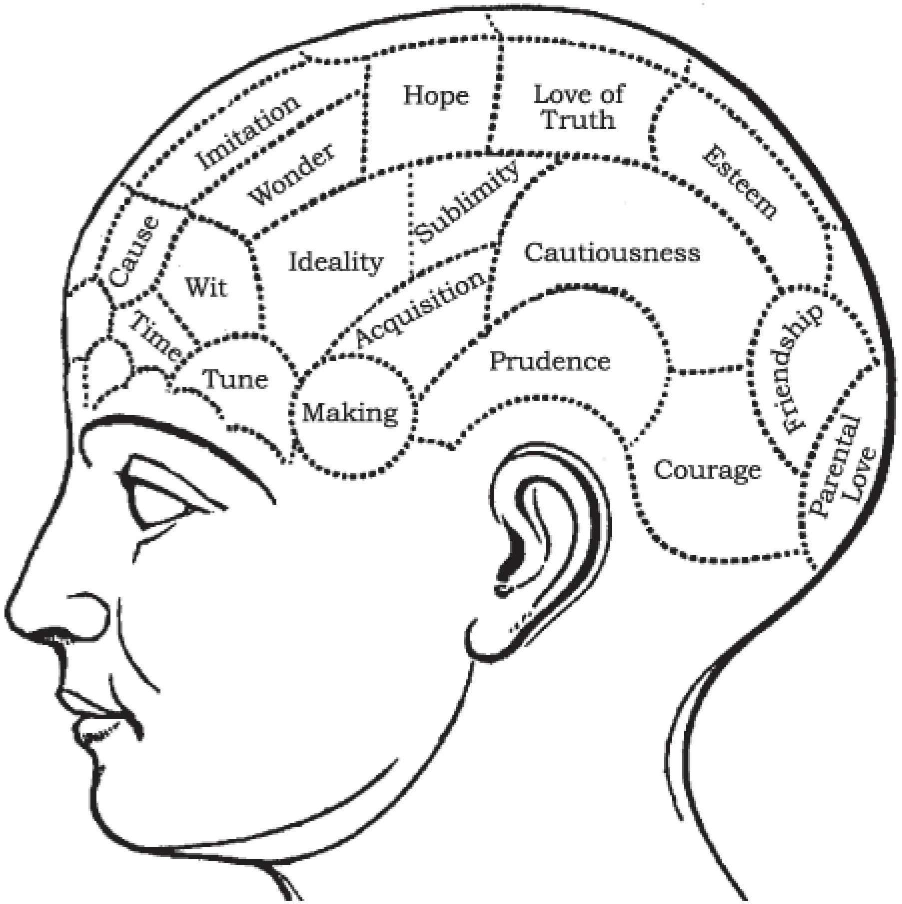
# Functional Systems vs. Extreme Localization



# Key Questions

- To what extent are complex functions localized in specialized cortical processors?
- Alternatively, to what extent are complex functions dependent on activity within distributed brain systems?
- Does one answer fit all complex functions?
- Sub-questions
    - If there are specialized processors, what do they process?
    - How do focal lesions affect such systems?




Phrenology: The Forerunner of Localizationist Theory

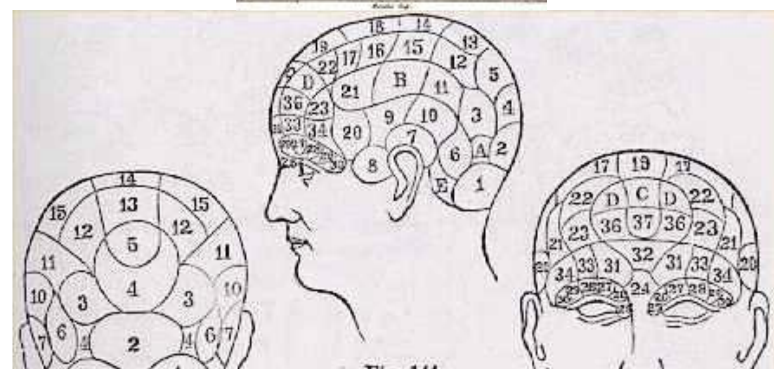



Fig. 144.

NAMES, NUMBERS,

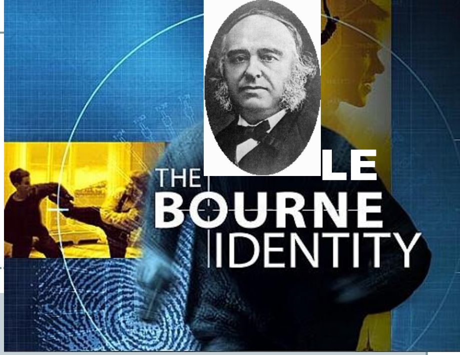
AND

LOCATION OF THE ORGANS.

1. Amativeness.
A. Conjugal Love.
2. Parental Love.
3. Friendship.
4. Inhabitiveness.
5. Continuity.
E. Vitativeness.
6. Combativeness.
7. Destructiveness.
8. Alimentiveness.
9. Acquisitiveness.
10. Secretiveness.
11. Cautiousness.
12. Approbativeness.
13. Self-Esteem.
14. Firmness.
15. Conscientiousness.
16. Hope.
17. Spirituality.
18. Veneration.
19. Benevolence.
20. Constructiveness.
21. Ideality.
B. Sublimity.
22. Imitation.
23. Mirth.
24. Individuality
25. Form.
26. Size.
27. Weight.
28. Color.
29. Order.
30. Calculation.
31. Locality.
32. Eventuality.
33. Time.
34. Tune.
35. Language.
36. Causality.
37. Comparison.
C. Human Nature.
D. Suavity.

History of Phrenology on the Web

# THE LEBORGNE IDENTITY




## The Era of Cortical Localization

- Paul Broca (1824-1880) and Monsieur Leborgne
  - Localization of expressive speech
    - Area in posterior, inferior region of the left frontal lobe
    - Lesion produces nonfluent aphasia

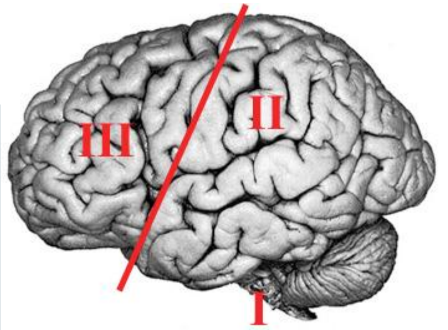
# Equipotentiality Karl Lashley (1890-1958)

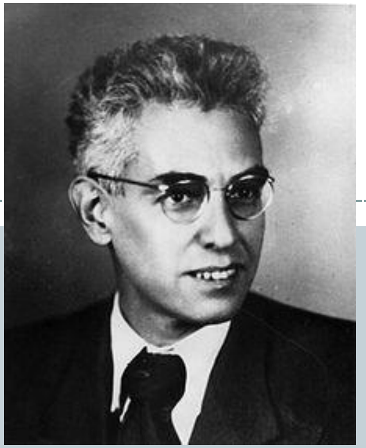
- Helped found experimental neuropsychology
- Initially searching for the “engram”, the biological locus of memory
- Rats / maze running experiments
- Formulated the <u>principle of mass action</u>
  - Extent of behavioral deficits is directly proportional to the mass of the removed tissue, doesn’t matter where from.
- Also emphasized the <u>multipotentiality</u> of brain tissue
  - Each part of the brain participated in more than one function; undamaged parts of the brain can assume function for damaged regions
  - This critical proposition is forerunner of modern notion of “neuroplasticity”

# The Brain Hierarchies of John Hughlings Jackson (1835-1911)

- Hierarchical Organization
  - Higher-level processes made up of lower-level skills
  - No such thing as a the "speech center". Rather, speech is a a higher mental function made up of smaller sub-processes: hearing, discrimination of speech sounds, fine –motor and kinesthetic control of speech movements.
    - Accounts for the diversity of clinical presentations
- An integration of localization and equipotentiality theory
  - Localizationist: each brain area has a specific function
  - Holistic: even the simplest behavior requires all levels of the nervous system.

# Functional System (Luria)



Aleksandr Luria (1902-1977)—Each area of the brain has a specific role and all behavior requires the interaction of three functional systems (brain working as a whole):

- I: Brainstem (arousal and muscle tone)
- II: Posterior cortex (reception, integration of sensory info)
- III: Frontal/prefrontal cortex (planning, executing, verifying behavior)

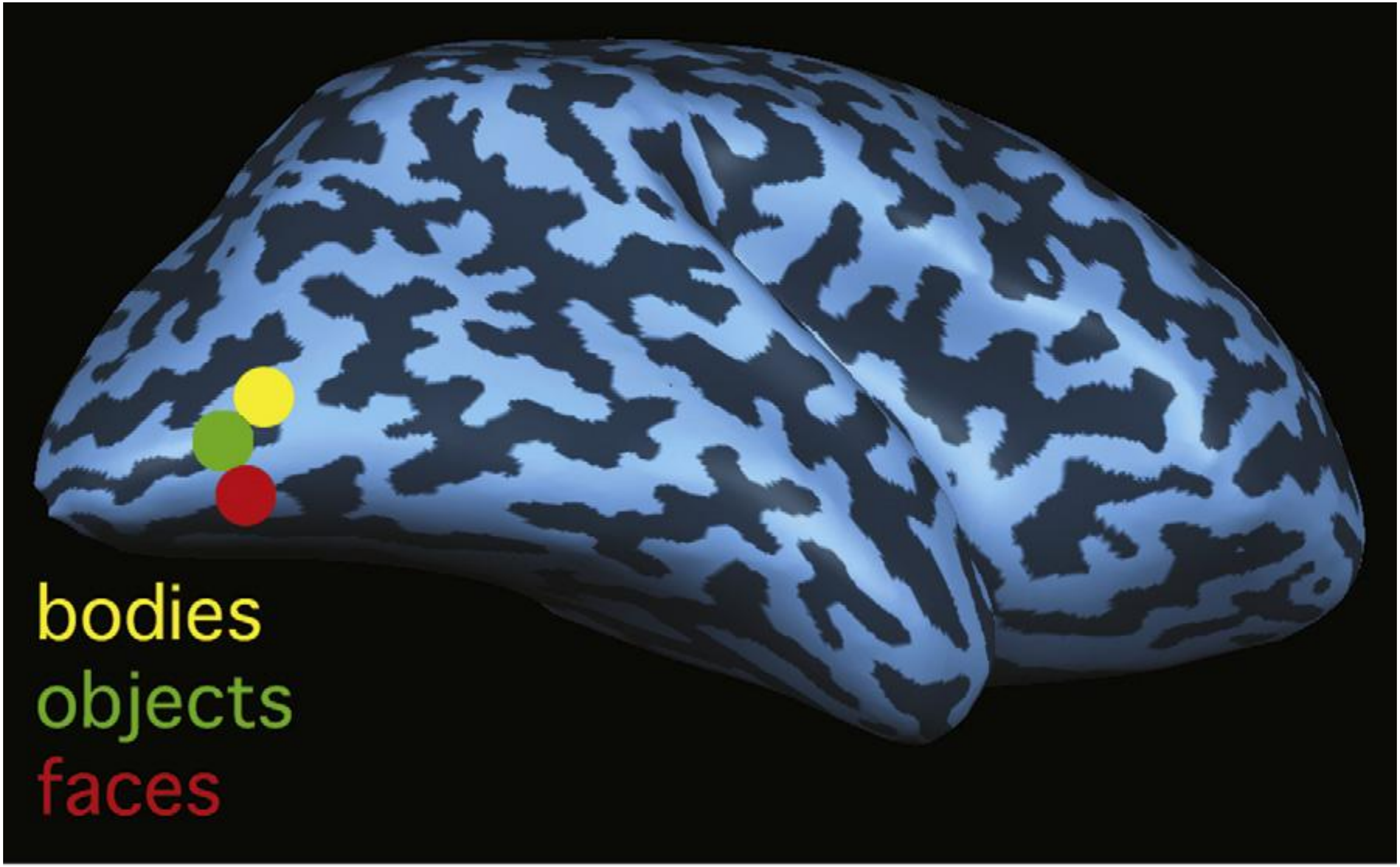
- Behavior results from integration of functional systems
  - A disruption at any stage can cause deficits
  - But also plasticity
- Pluripotentiality: any area of the brain can be involved in relatively few or many behaviors

# Contemporary Localizationist Perspectives

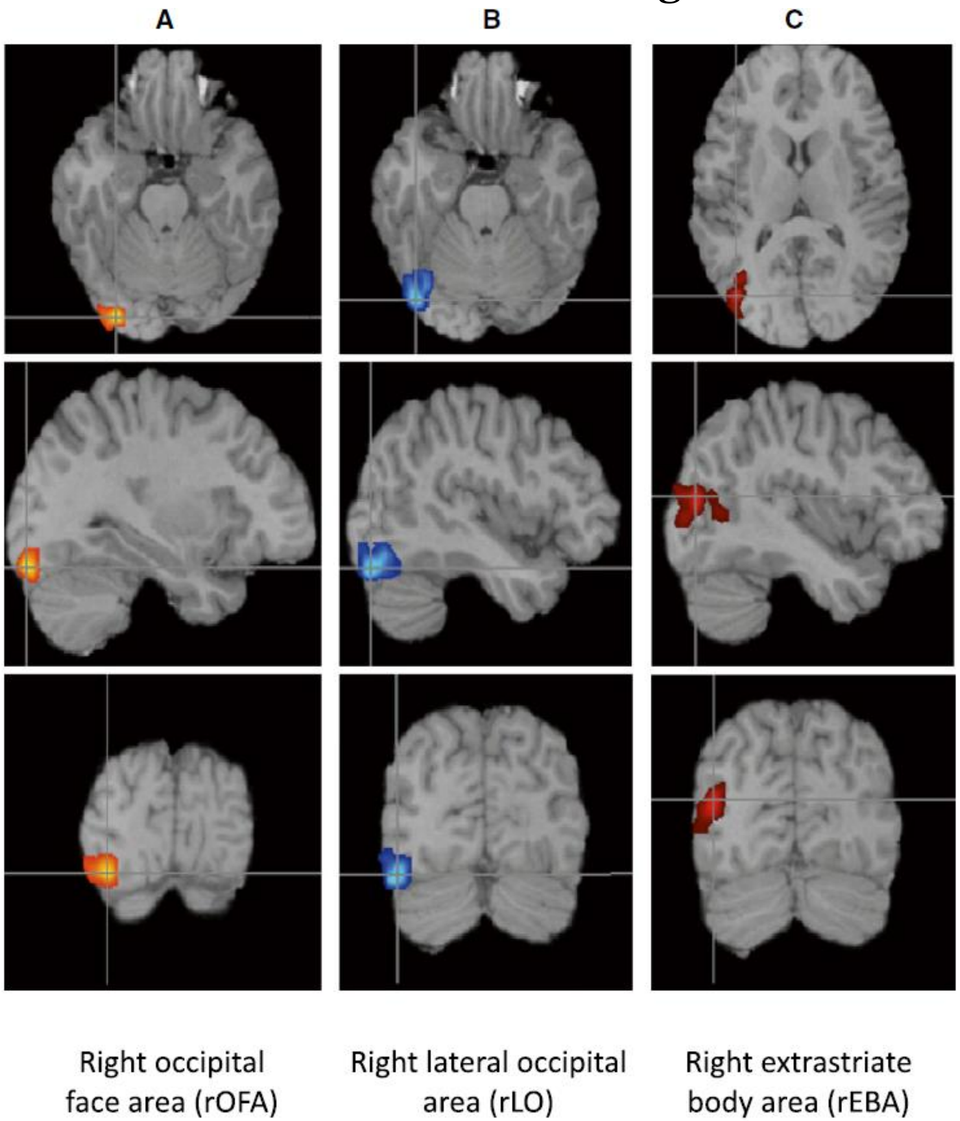
- "Modules" in the brain
  - separate innate structures which have established evolutionarily developed functional purposes
  - Characteristics of "Modules"
    - Domain specific/specialized for processing one type of information
    - Informationally encapsulated modules need not obtain broad inputs in order to operate
    - Obligatory firing, modules process in a mandatory manner
    - Fast speed, probably due to the fact that they are encapsulated (thereby needing only to consult a restricted database) and mandatory (time need not be wasted in determining whether or not to process incoming input)
    - Shallow outputs, the output of modules is very simple
    - Limited accessibility
    - Characteristic ontogeny, there is a regularity of development
    - Fixed neural architecture
    - **KEY CHARACTERISTIC: cognitive impenetrability**

# Modular Claims

- Language Module (Pinker)
  - Weak evidence
    - No one area for language
    - No clear double dissociation between language and cognition
    - Not informationally incapsulated (McGurk effect)
- Visual Modules
  - V5/hMT+ :  motion detection
  - Extrastriate Body Area (EBA): body parts
  - Parahippocampal Place Area (PPA): places and scenes
  - Fusiform Face Area (FFA):  faces


bodies
objects
faces

# Triple dissociation among faces, objects, and bodies in extrastriate cortex using TMS



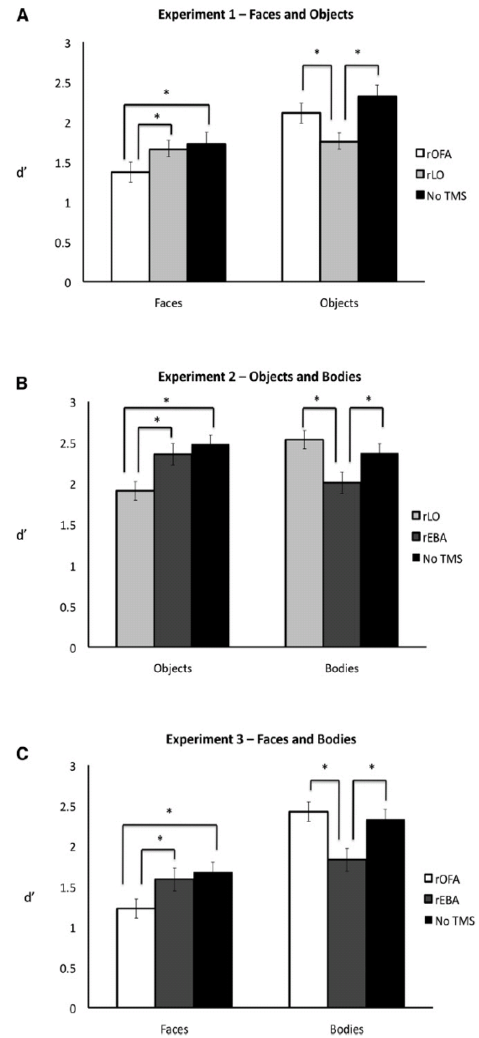
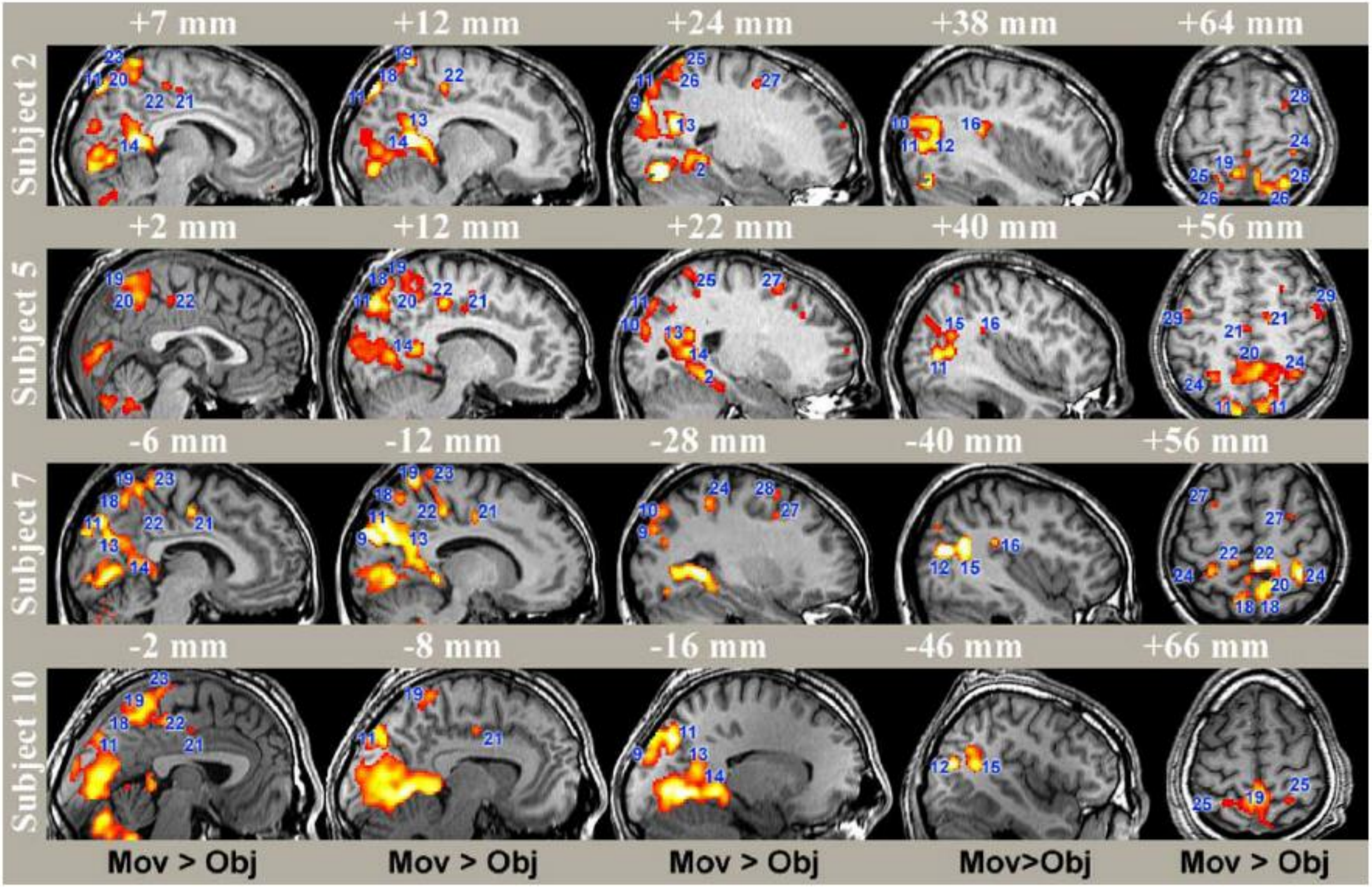




Figure 2. Results from Experiment 1, Experiment 2, and Experiment 3
In each panel, performance on two tasks is compared in three conditions: TMS to a site selective for that category, TMS to a site selective for another

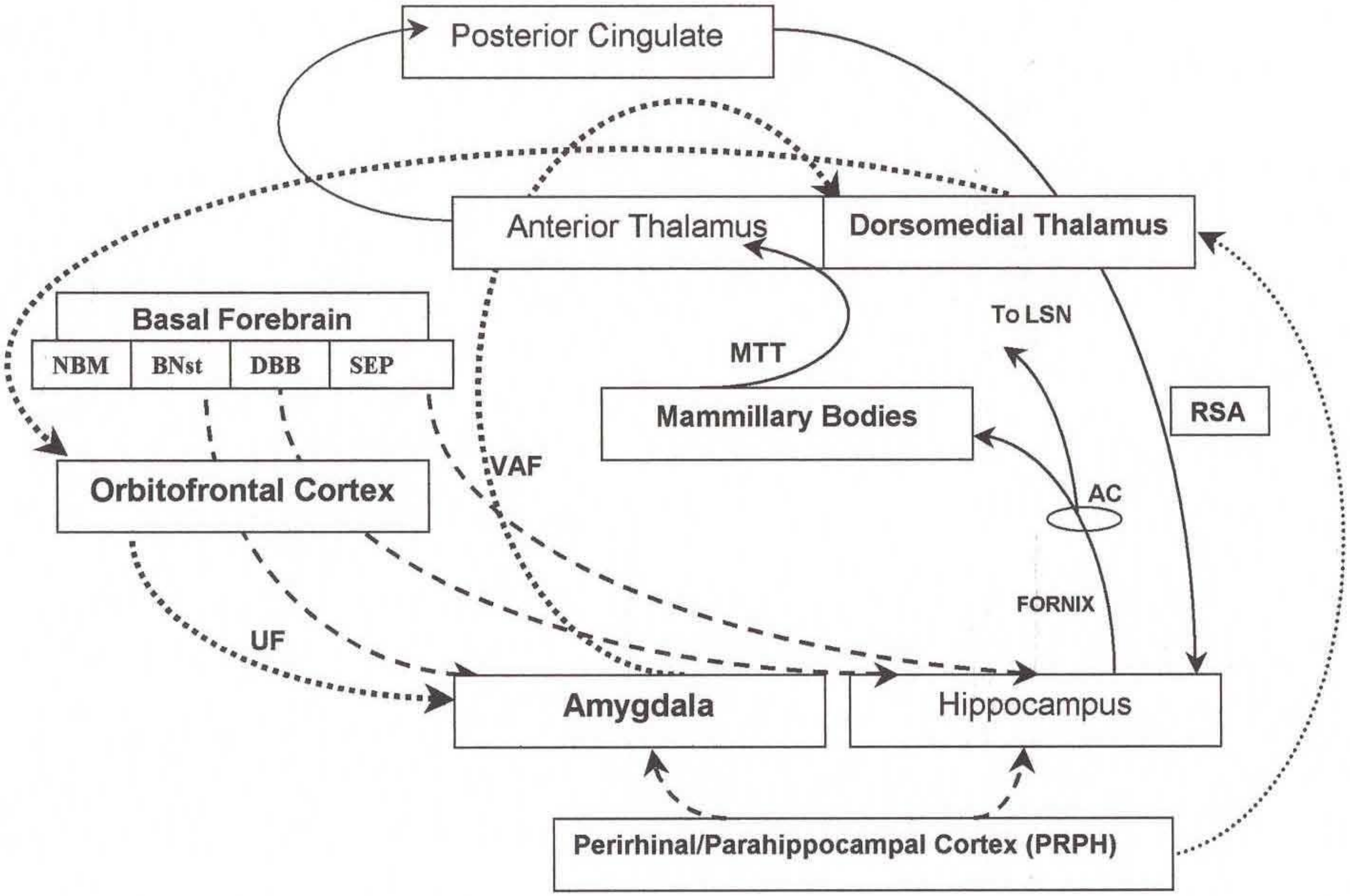
Pitcher et al., (2009), *Current Biology*

Stiers, et al. (2006) *Neuroimage* suggests motion-sensitive *stream*, not module

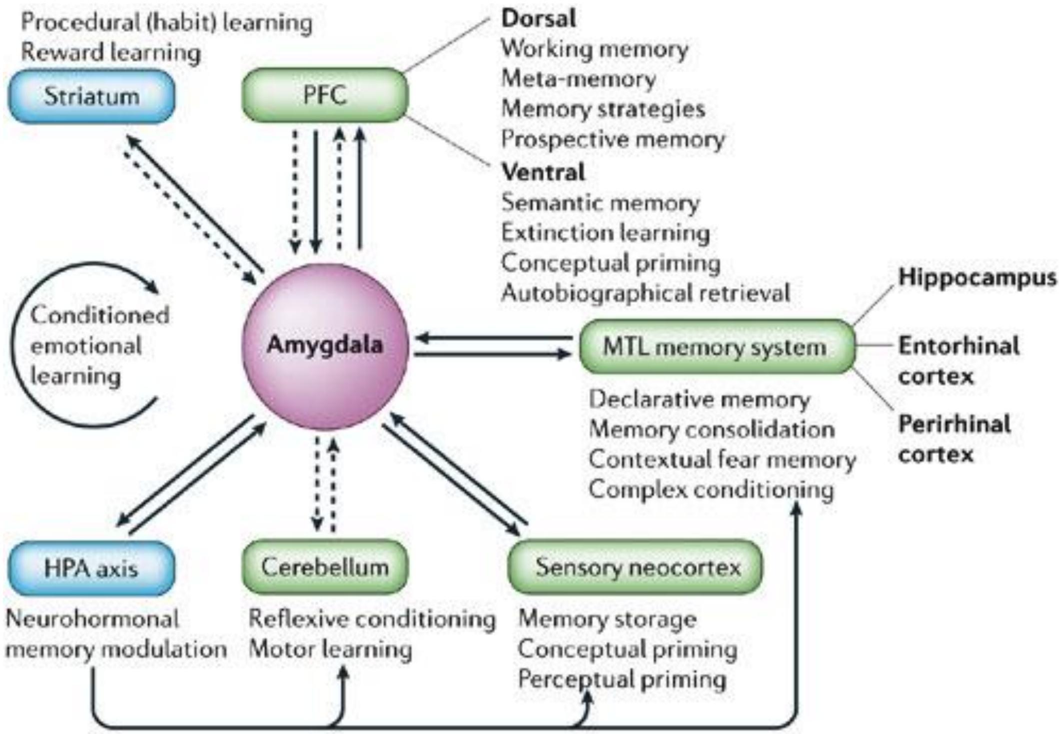


# Functional Systems Perspectives

- Distributed system for memory
  - Medial Temporal lobe/Hippocampal/Amygdala circuits
  - Diencephalon
  - Basal Forebrain
- Attention
  - Posterior v. Anterior attentional systems
  - Subcortical structures in attention
- Language
  - Perisylvian language system
  - Subcortical structures in language




Integrated Circuitry Linking Temporal, Diencephalic, and Basal Forebrain Regions

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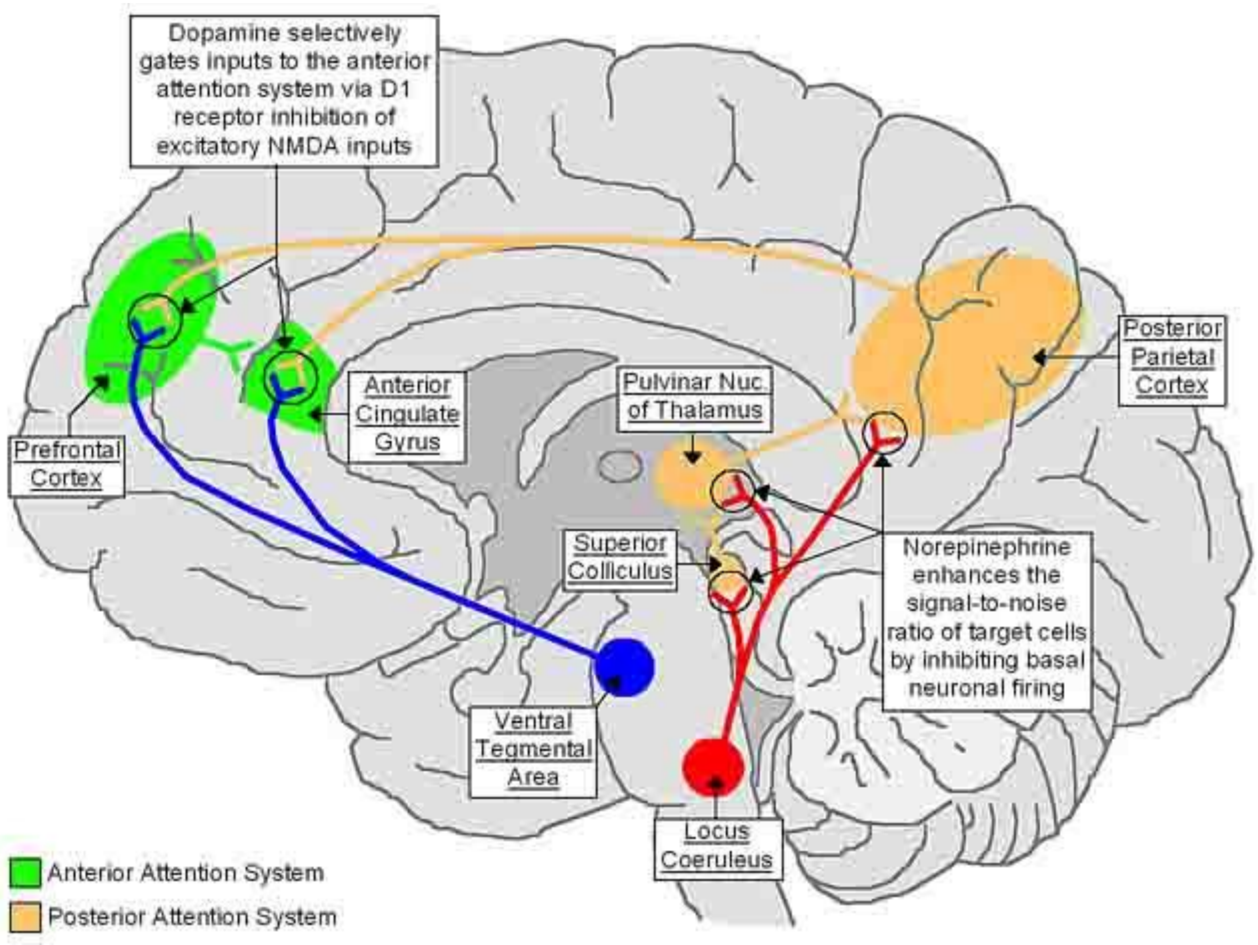
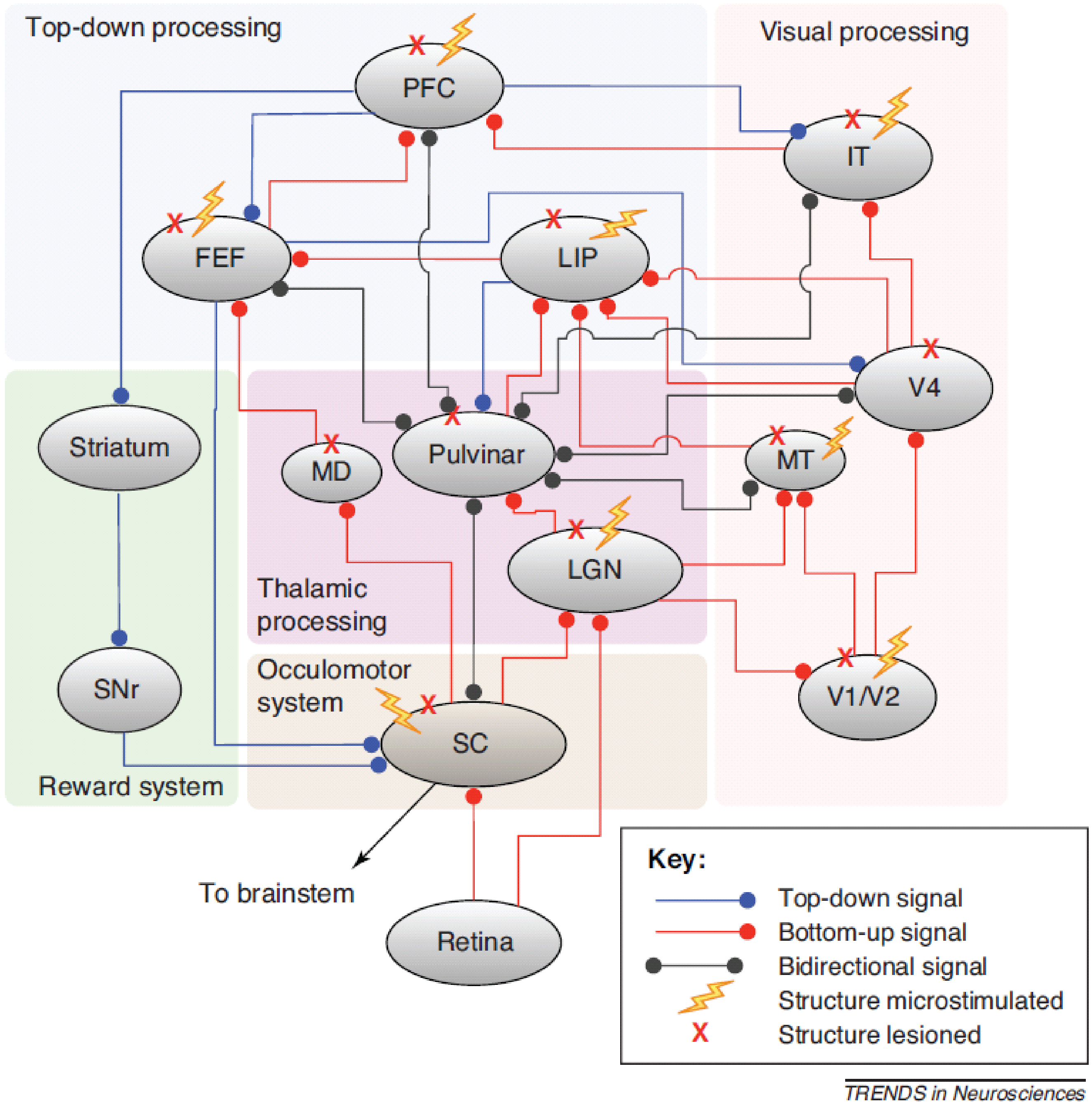
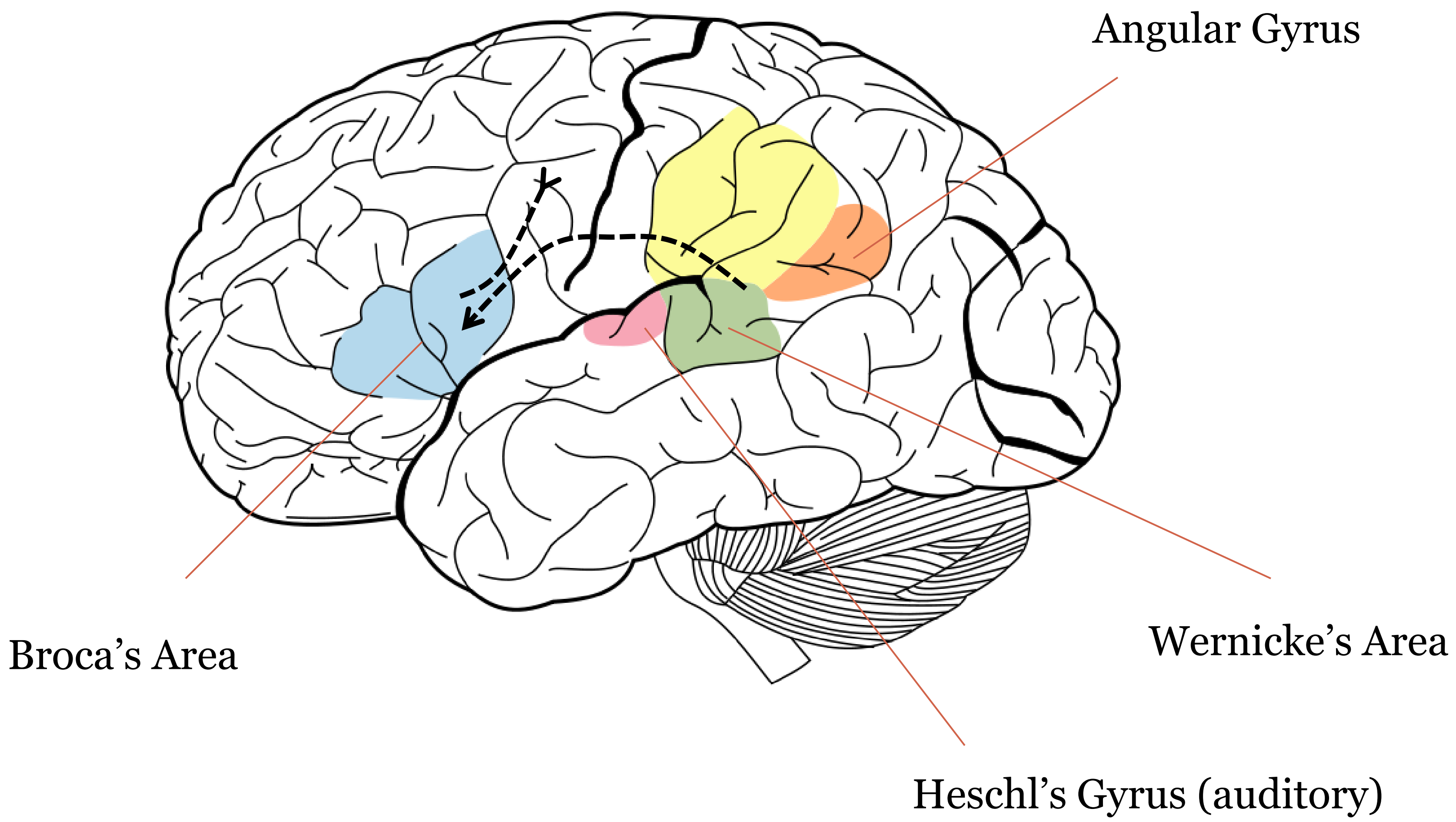
# Anterior and Posterior Attentional Systems





Top-down processing
Visual processing
PFC
IT
FEF
LIP
V4
Striatum
Pulvinar
MD
MT
LGN
Thalamic processing
SNr
Occulomotor system
SC
V1/V2
Reward system
To brainstem
Retina
Key:
Top-down signal
Bottom-up signal
Bidirectional signal
Structure microstimulated
X
Structure lesioned
TRENDS in Neurosciences

# Examples of Functional Systems

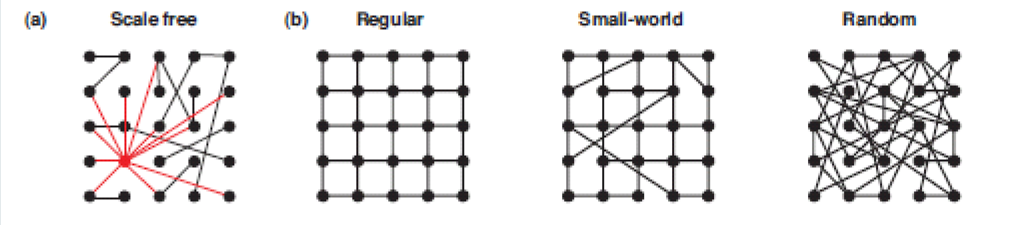


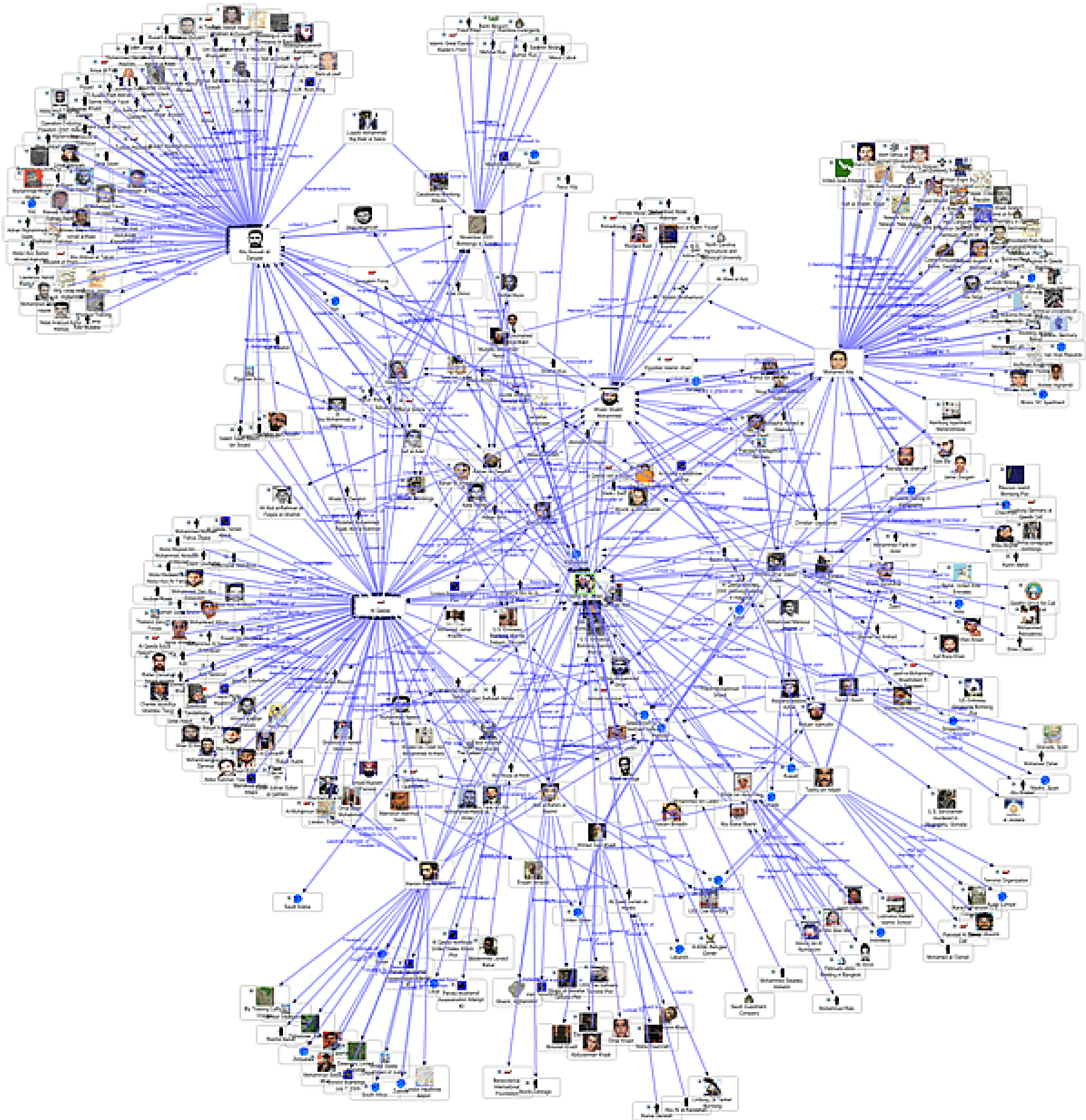
# So….

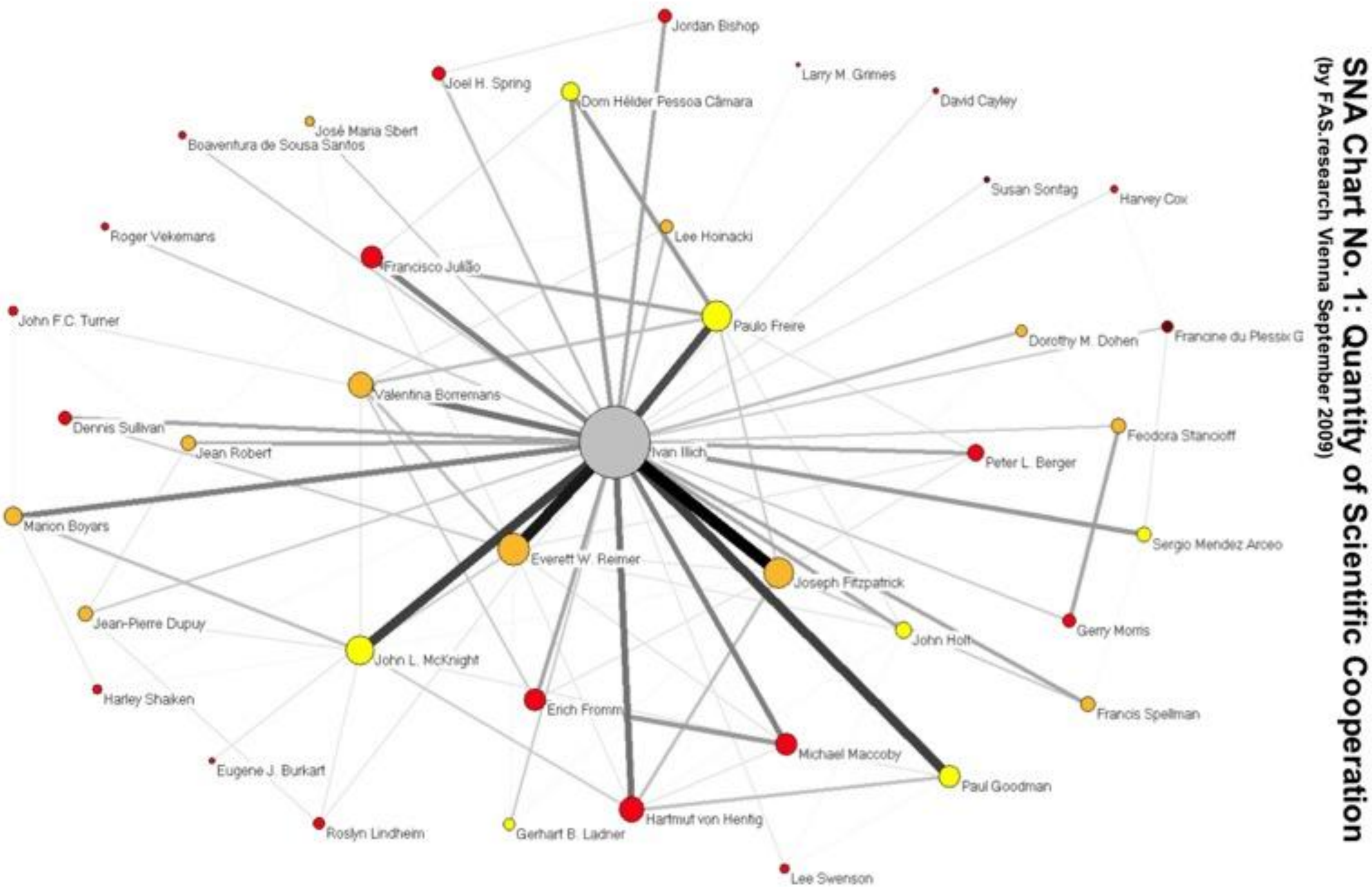
- If modules exist to handle specific evolutionarily based neuropsychological functions, how are they connected with other brain systems in which the output of those modules is important?
- And…if distributed brain systems exist to handle complex functions like memory, language, and attention, how do they operate from a network perspective?
- Functions of a cortical area defined by:
  - Intrinsic properties (e.g., laminar organization)
  - Connectivity

# Network Neuroscience

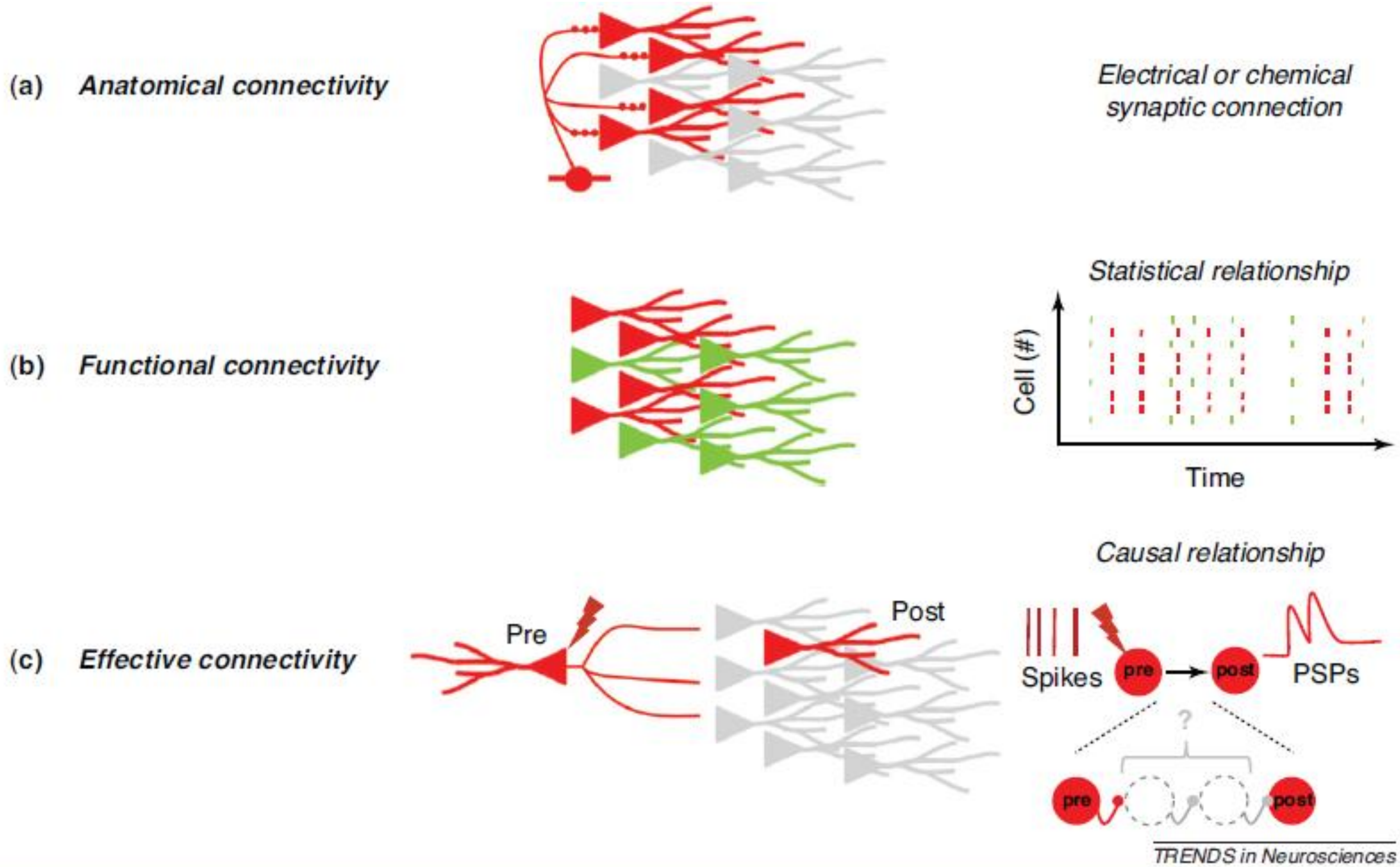
- Emerging interdisciplinary science concerned with the study of networks
- Key features:  nodes and connections
- Examples
  - Internet modeling
  - Social networking and team science
- Network analysis vs. network modeling
- Types of networks






SNA Chart No. 1: Quantity of Scientific Cooperation
(by FAS.research Vienna September 2009)
Jordan Bishop
Larry M. Grimes
Joel H. Spring
Dom Hélder Pessoa Câmara
David Cayley
José Maria Sbert
Boaventura de Sousa Santos
Susan Sontag
Harvey Cox
Lee Hoinacki
Roger Vekemans
Francisco Julião
Paulo Freire
John F.C. Turner
Dorothy M. Dohen
Francine du Plessix G
Valentina Borremans
Dennis Sullivan
Jean Robert
Ivan Illich
Feodora Stancioff
Peter L. Berger
Marion Boyars
Sergio Mendez Arceo
Everett W. Reimer
Joseph Fitzpatrick
Jean-Pierre Dupuy
Gerry Morris
John Holt
John L. McKnight
Harley Shaiken
Erich Fromm
Francis Spellman
Michael Maccoby
Eugene J. Burkart
Paul Goodman
Hartmut von Hentig
Roslyn Lindheim
Gerhart B. Ladner
Lee Swenson

# Three Concepts of "Connectivity" Used to Describe Neural Networks




Feldt, et al., *TINS,* (2011)

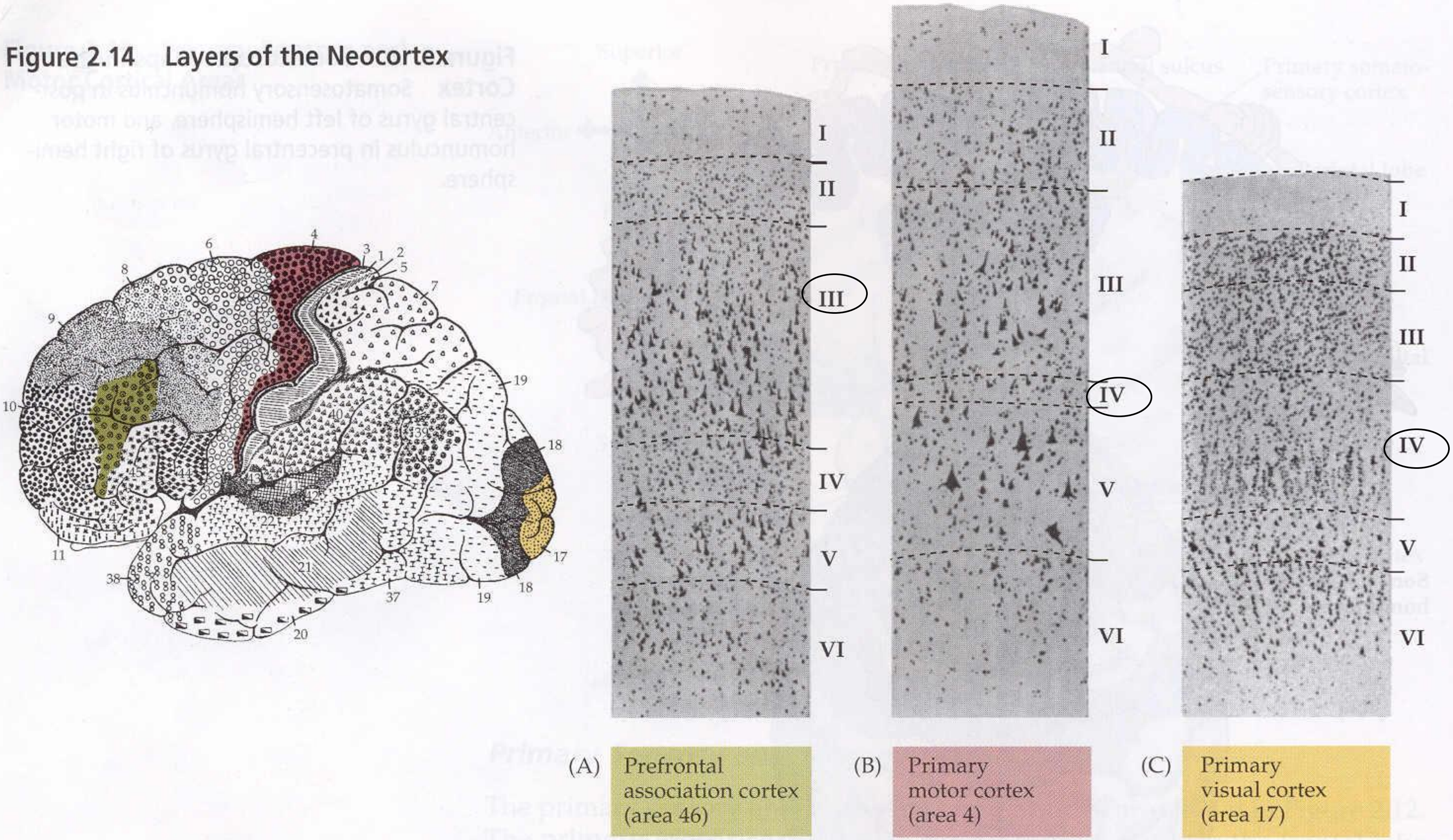
# Cortical Regions are DEFINED by Connectivity Patterns
(you can tell a lot about someone by looking at their friends)

**TABLE 2.3** Cell Layers of the Neocortex

| LAYER | NAME | ALTERNATIVE NAME | MAIN CONNECTIONS |
|---|---|---|---|
| I | Molecular layer | | Dendrites and axons from other layers |
| II | Small pyramidal layer | External granular layer | Cortical–cortical connections |
| III | Medium pyramidal layer | External pyramidal layer | Cortical–cortical connections |
| IV | Granular layer | Internal granular layer | Receives inputs from thalamus |
| V | Large pyramidal layer | Internal pyramidal layer | Sends outputs to subcortical structures (other than thalamus) |
| VI | Polymorphic layer | Multiform layer | Sends outputs to thalamus |

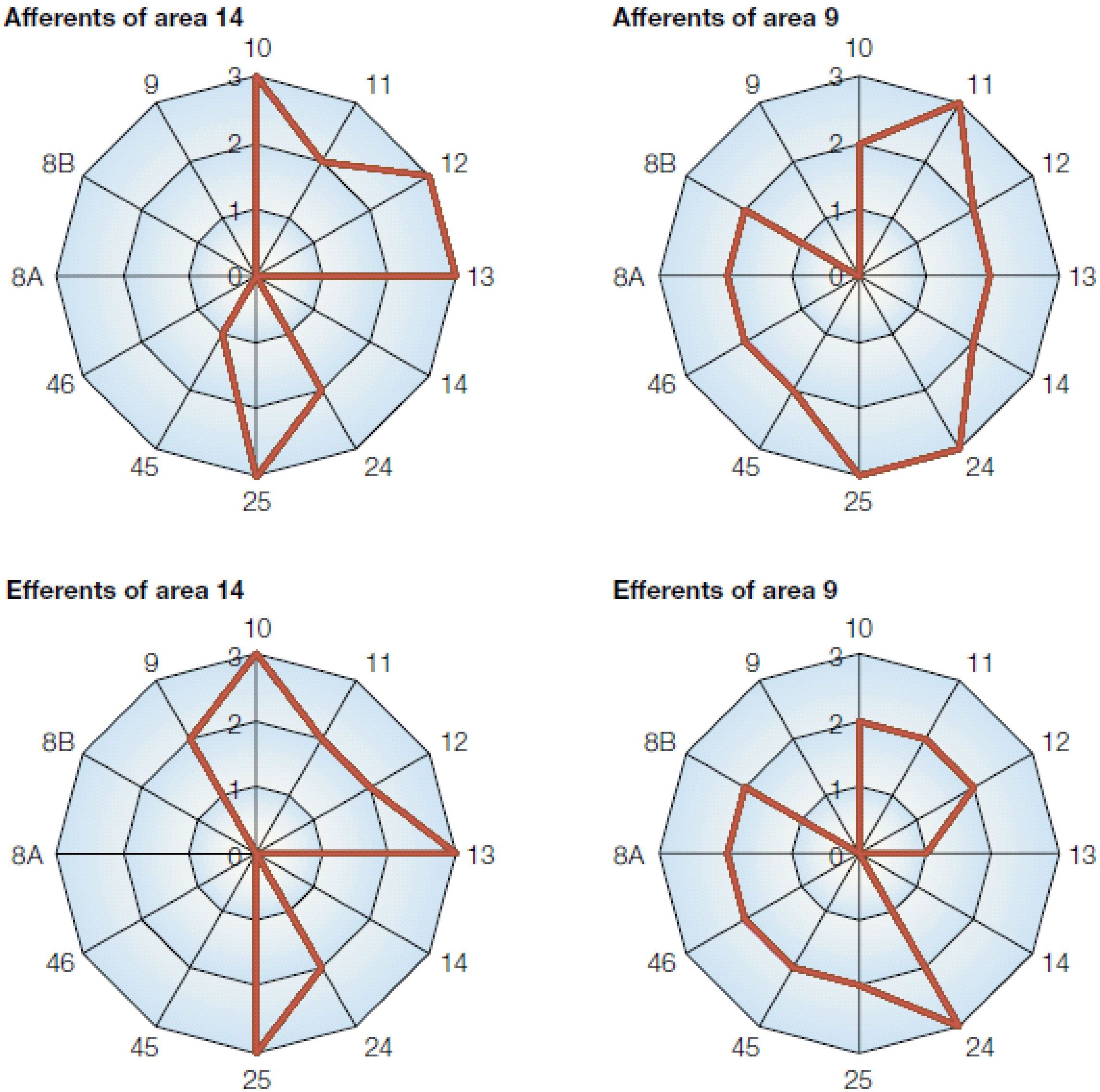
*Blumenfeld, 2002*

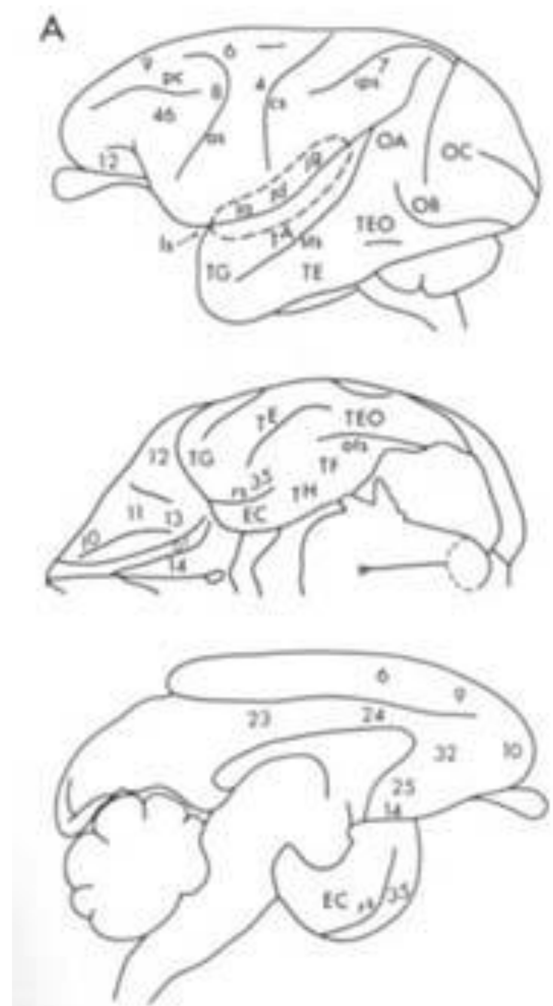
**Figure 2.14 Layers of the Neocortex**




*Blumenfeld, 2002*

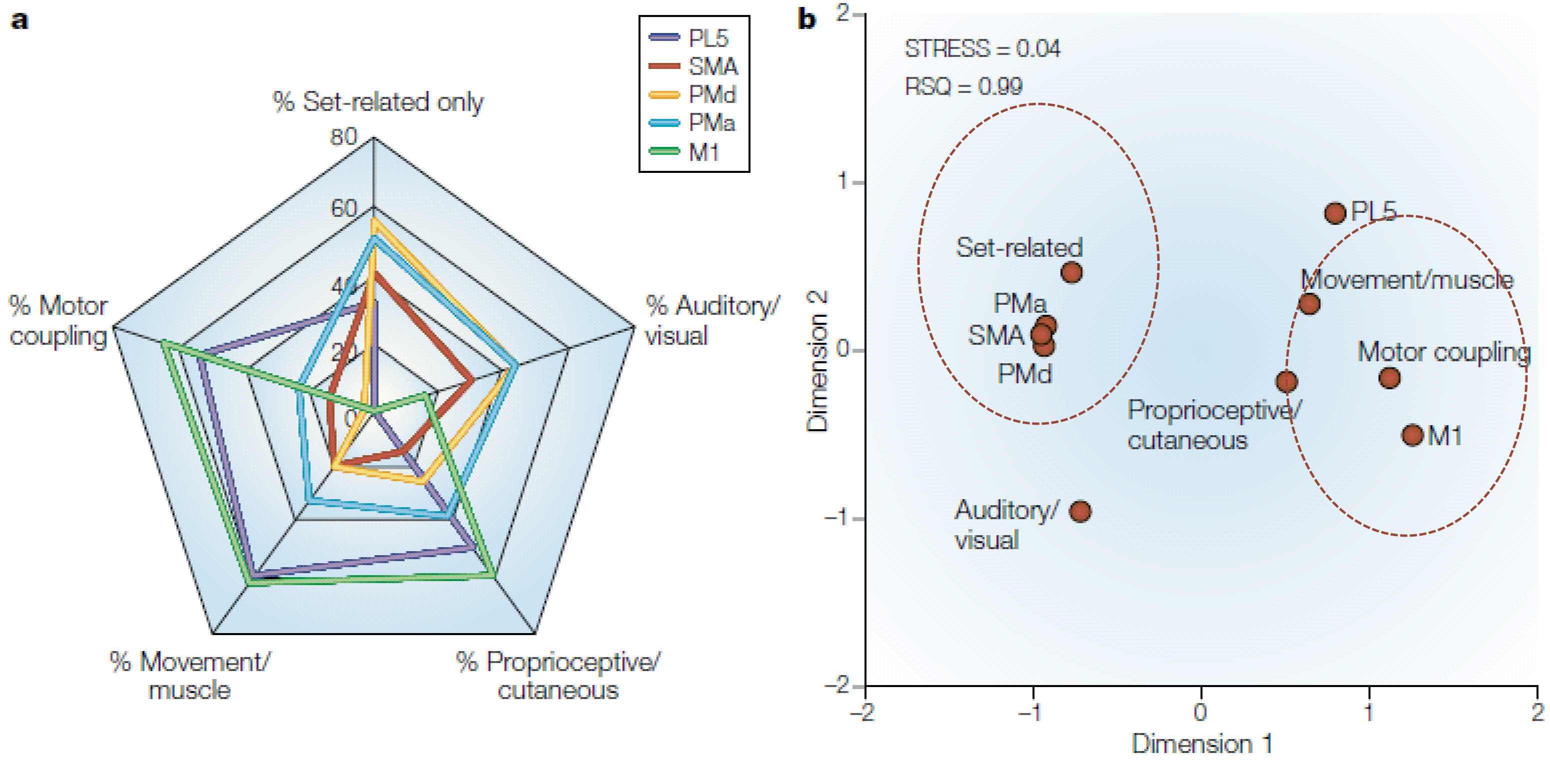
# ***Connectional*** Fingerprints of Two Prefrontal Cortical Areas




Passingham, Steffan, & Kotter, *Nature Rev Neurosci*, (2002) – uses CoCoMac

# ***Functional*** Fingerprints of Five Cortical Motor Areas




Functional fingerprint

Multidimensional Scaling

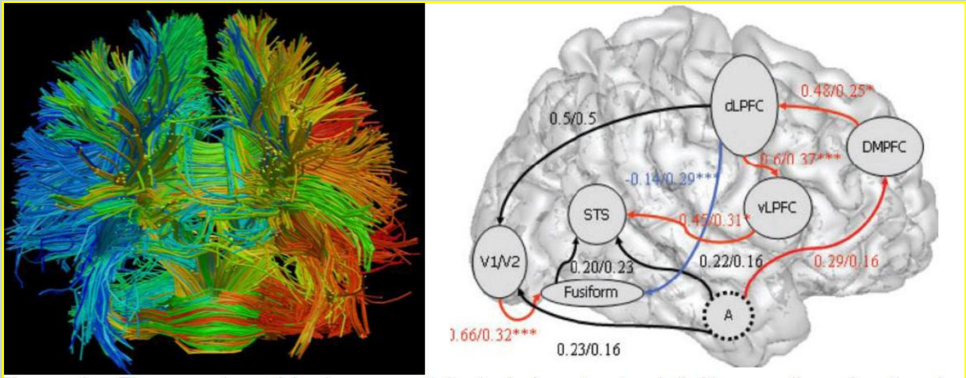
Passingham, Steffan, & Kotter, *Nature Rev Neurosci,* (2002)

# Passingham, Steffan, & Kötter (2002)

- Each cytoarchitectonic area has a unique connectional fingerprint (e.g., prefrontal, premotor)
- Area "families" share a resemblance in their connections
- The proportion of cells that fire in association with different tasks or task events differs between areas; areas have their own functional fingerprints.
- Differences between these functional fingerprints are determined by the extrinsic and intrinsic connections of these areas.
- Imaging is a useful tool that could allow formal tests of the relationship between functional and anatomical fingerprints.

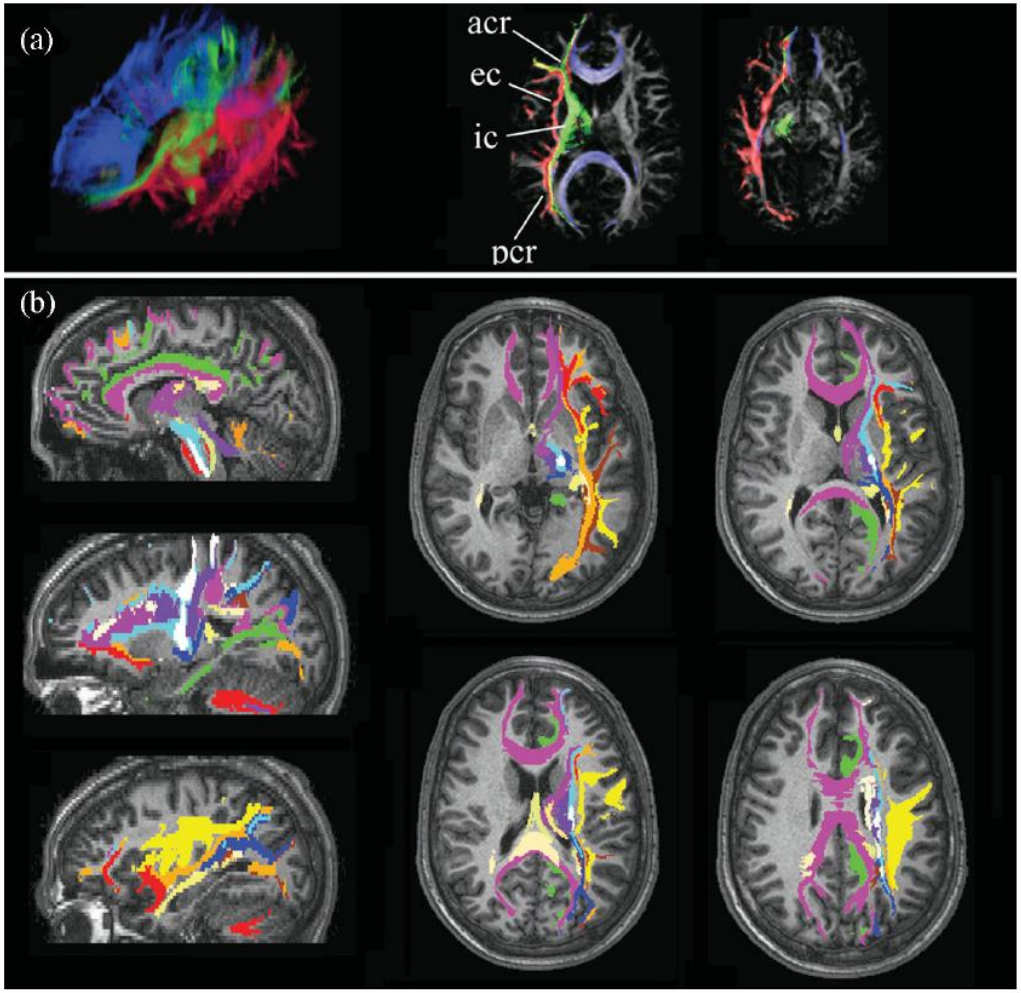
# Connectivity Analysis

- Anatomic
  - DTI
- Functional
  - rTMS
  - fMRI
- Neurotropic viruses
- Key results
  - Maps of human structural connectivity ("connectome")
  - Structural connectivity predicts functional connectivity
  - Development of "resting state" models of functional systems
  - Can model, through computed network dynamics, effects of 'lesions'




igure 1: The mapping of brain connectivity includes structural (left) as well as functional right) neuroimaging approaches.

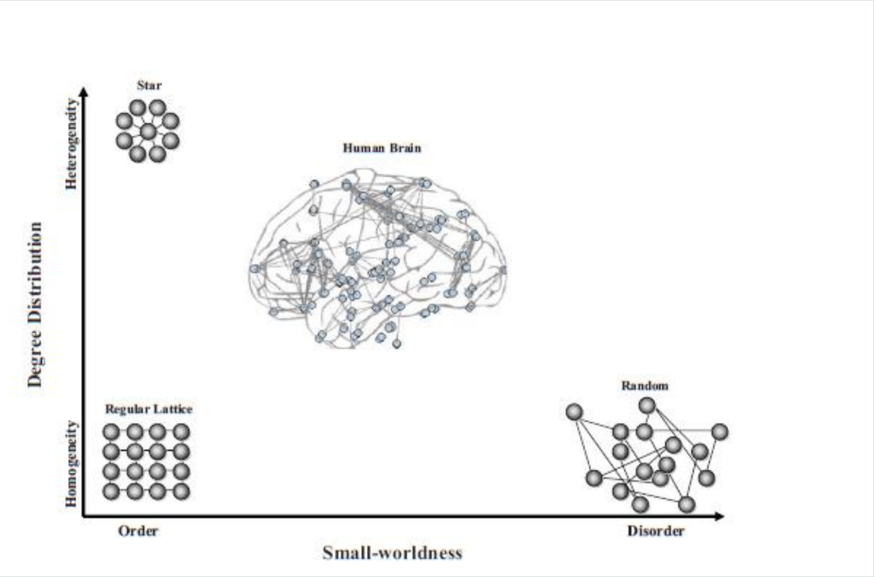
# FIG 8 – white matter tractography



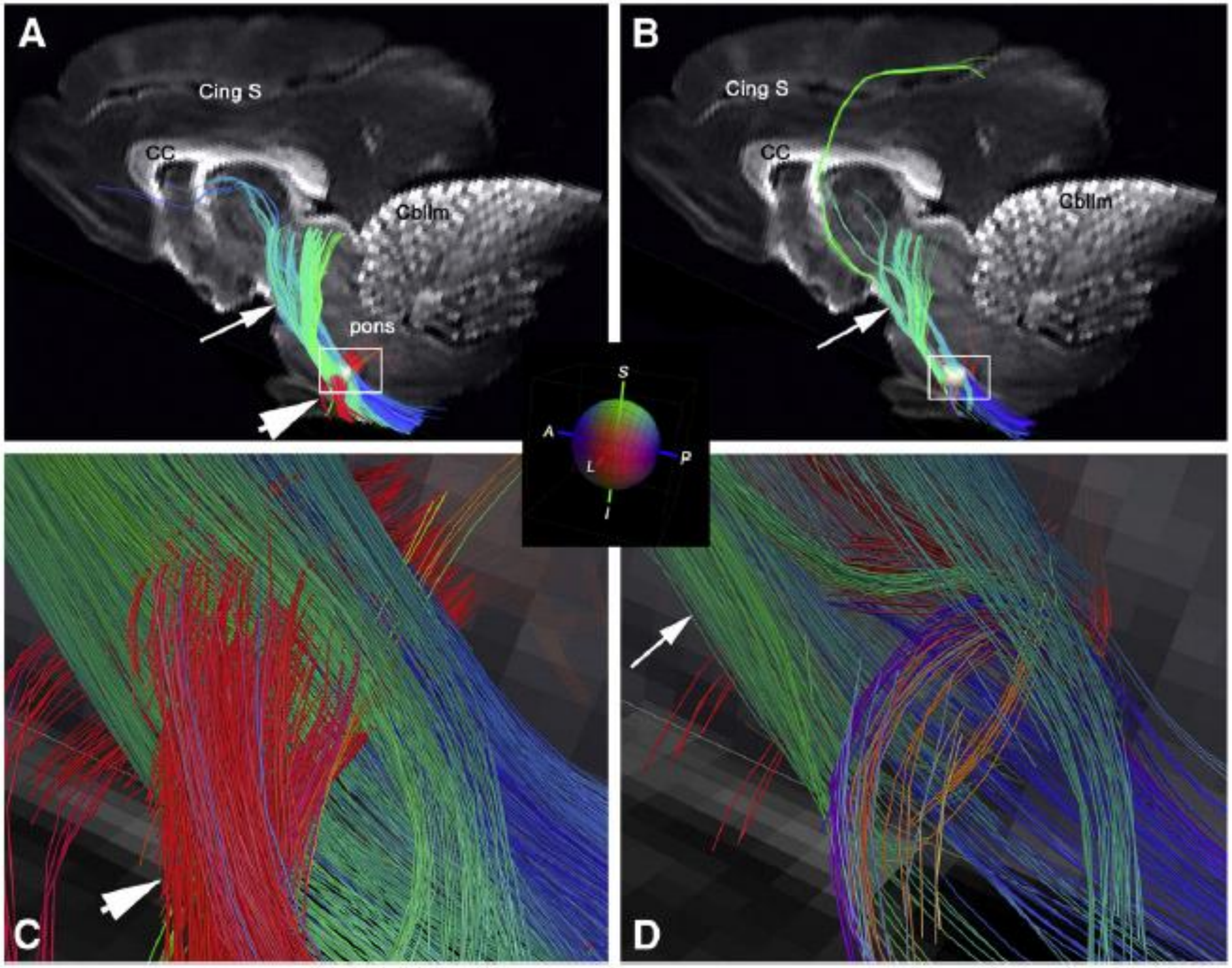

Lazar, *NMR in Biomedicine*, 2010

# DTI and the Connectome: Key Results

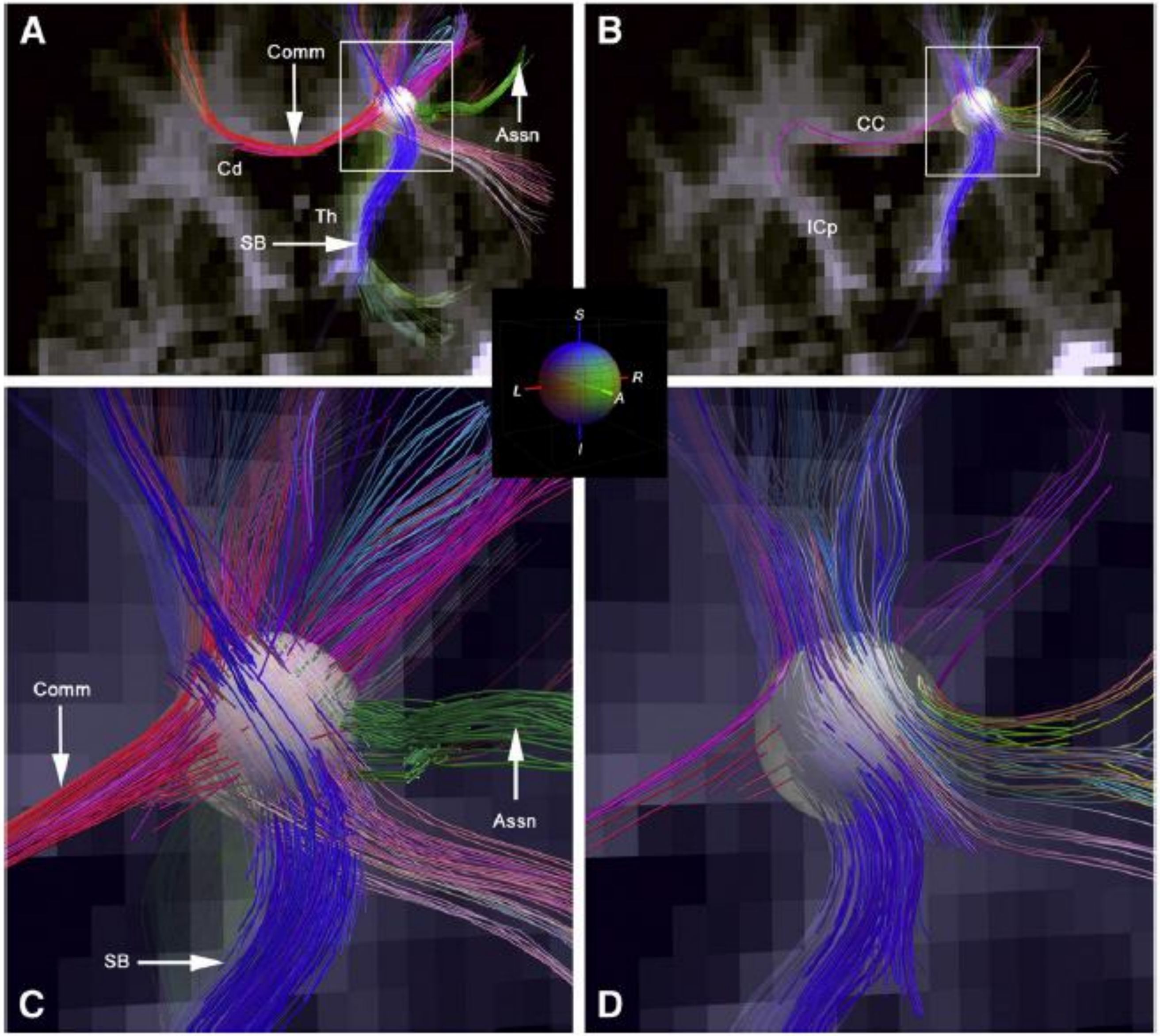
- Small-worldness
- Modularity
- Heterogenous degree distribution (presence of highly interconnected “hubs”)



Diffusion Spectrum Imaging　　Diffusion Tensor Imaging



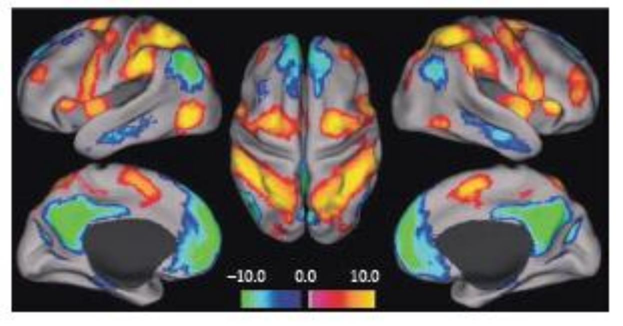

Wedeen, Wang, Schmahmann, et al., *Neuroimage*, 2008




Wedeen, et al., *Neuroimage*, 2008

# Resting State Networks (RSN)

- Reproducible, distributed patterns of neural activity during "rest"
- Originally thought to reflect "self-referential" thought, but also occur under anaesthesia and sleep, when no self-referential activity is occurring
- Evolving concept:  reflects anatomical connectivity and functional dynamics
- Example:  "Default mode network"
- DMN – anatomic network "hubs"




Deco, Jirsa, and McIntosh (2011)

# Resting State Networks of the Brain

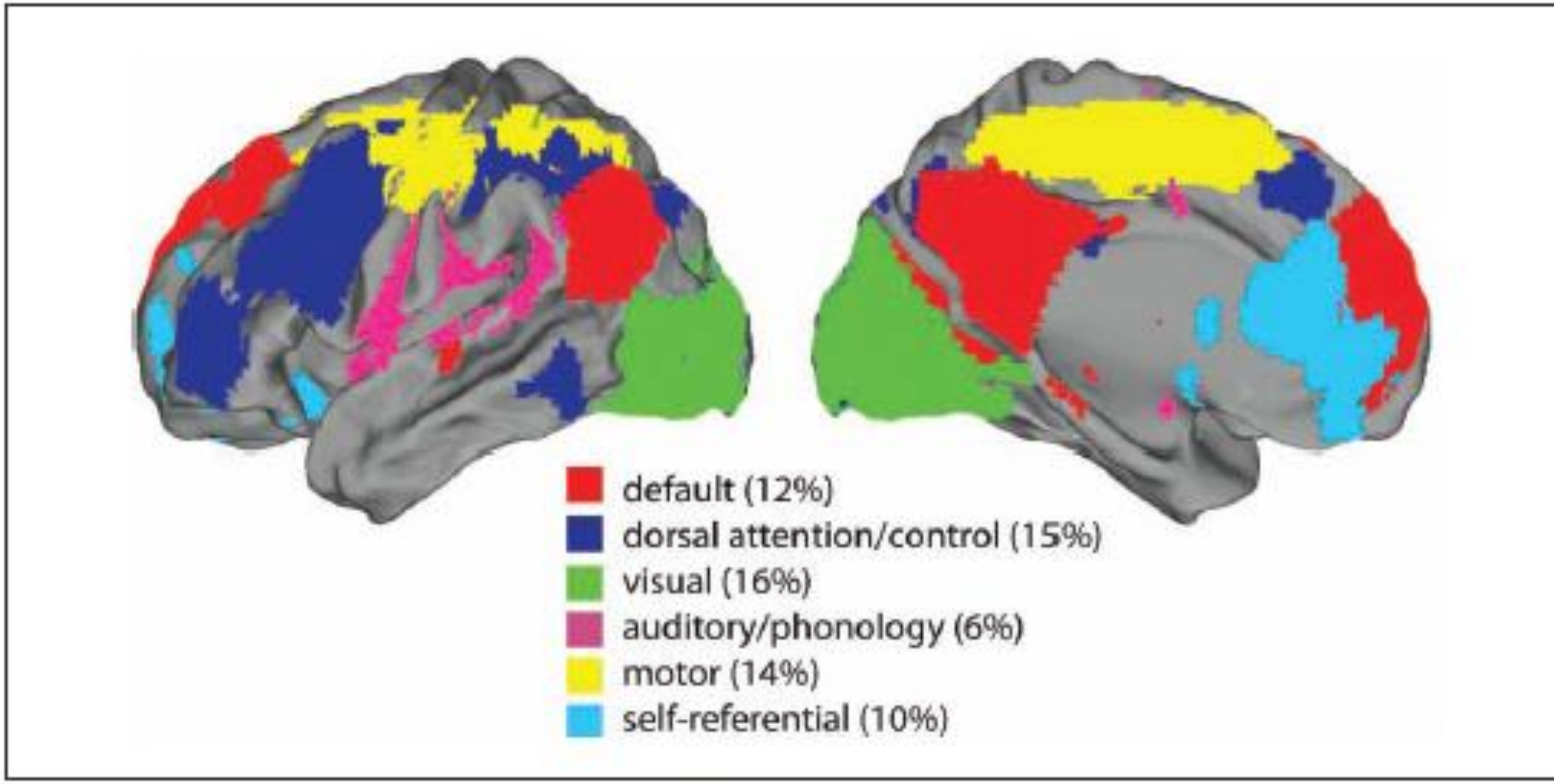
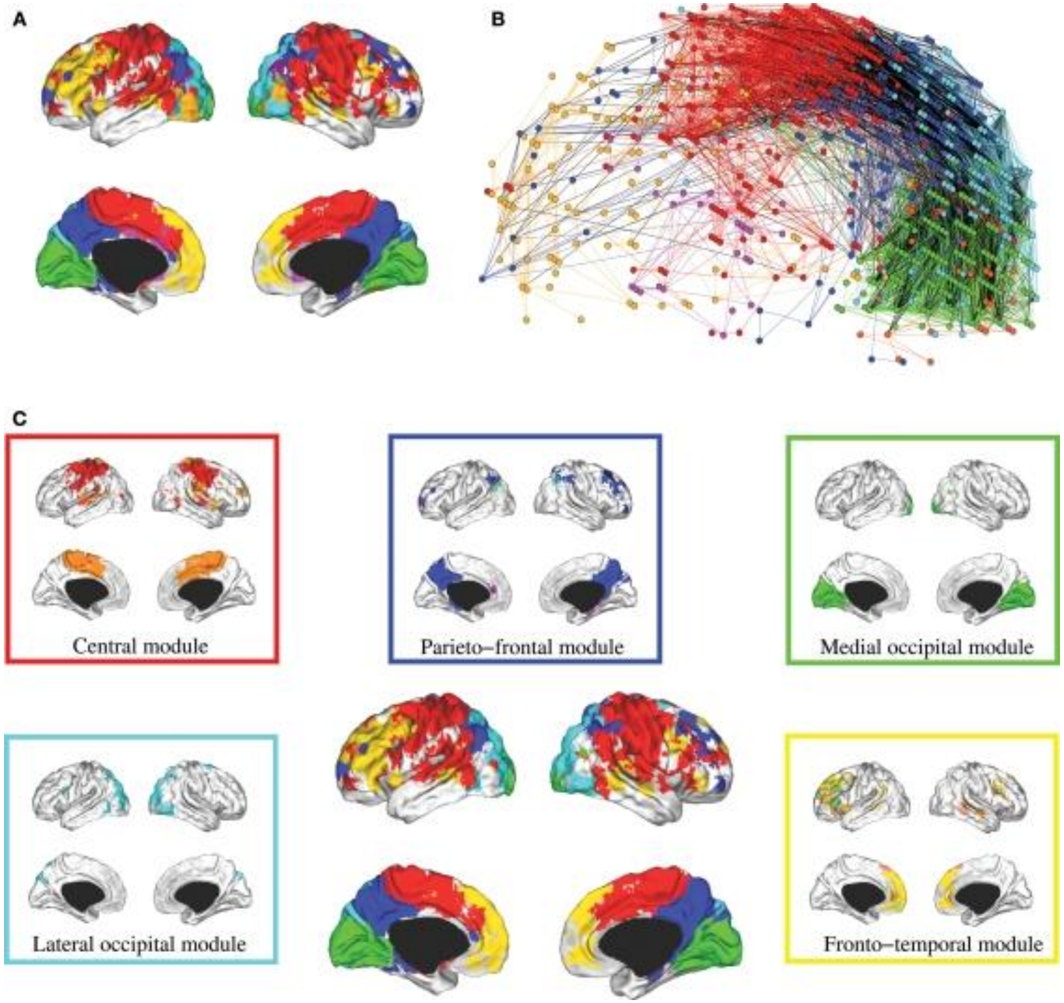



**Figure 2.** Different identified resting state networks (RSN) onto the same atlas brain covering about 66% of the total brain volume. These RSN are somato-motor, visual occipital and auditory temporal, and several associative networks covering fronto-temporal-parietal cortices (dorsal attention, default, language, and control).

Deco, Jirsa, and McIntosh (2011)

# Hierarchical Modularity in Human Brain Networks using resting state fMRI

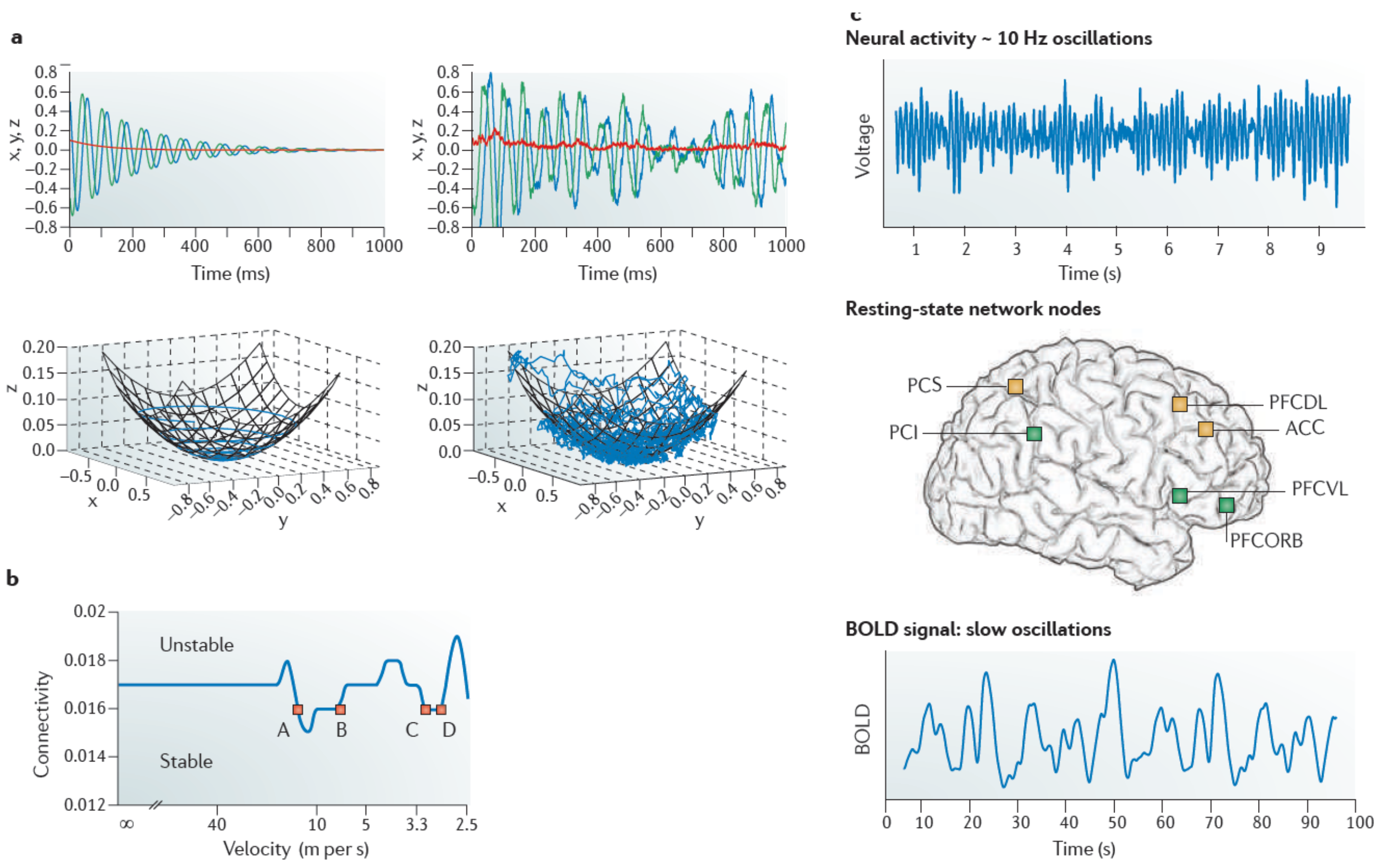



Note: Simon's "near decomposition" – balance of integration and parcellation – an adaptive feature

| Module description | # Nodes | Connector nodes | Provincial hubs | Connector hubs | Sub-modules | Size of sub-modules |
|---|---|---|---|---|---|---|
| Central (sensorimotor) | 239 | 8 | 1 | 4 | 11 | 115, 96, 8, 4, 3 *(2)*, 2 *(5)* |
| Parieto-frontal (default/attention) | 138 | 10 | 1 | 0 | 10 | 115, 3 *(5)*, 2 *(4)* |
| Medial occipital (primary visual) | 132 | 3 | 0 | 0 | 1 | 132 |
| Lateral occipital (secondary visual) | 101 | 7 | 0 | 1 | 1 | 101 |
| Fronto-temporal (symbolic) | 89 | 0 | 2 | 3 | 24 | 19, 8, 6, 5 *(2)*, 4, 3 *(6)*, 2 *(12)* |

Meunier, et al., *Front Neuroinformatics,* 2009

# Resting State Networks Emerge from a Dynamic Network of Noise, Anatomic Connectivity, and Time Delays

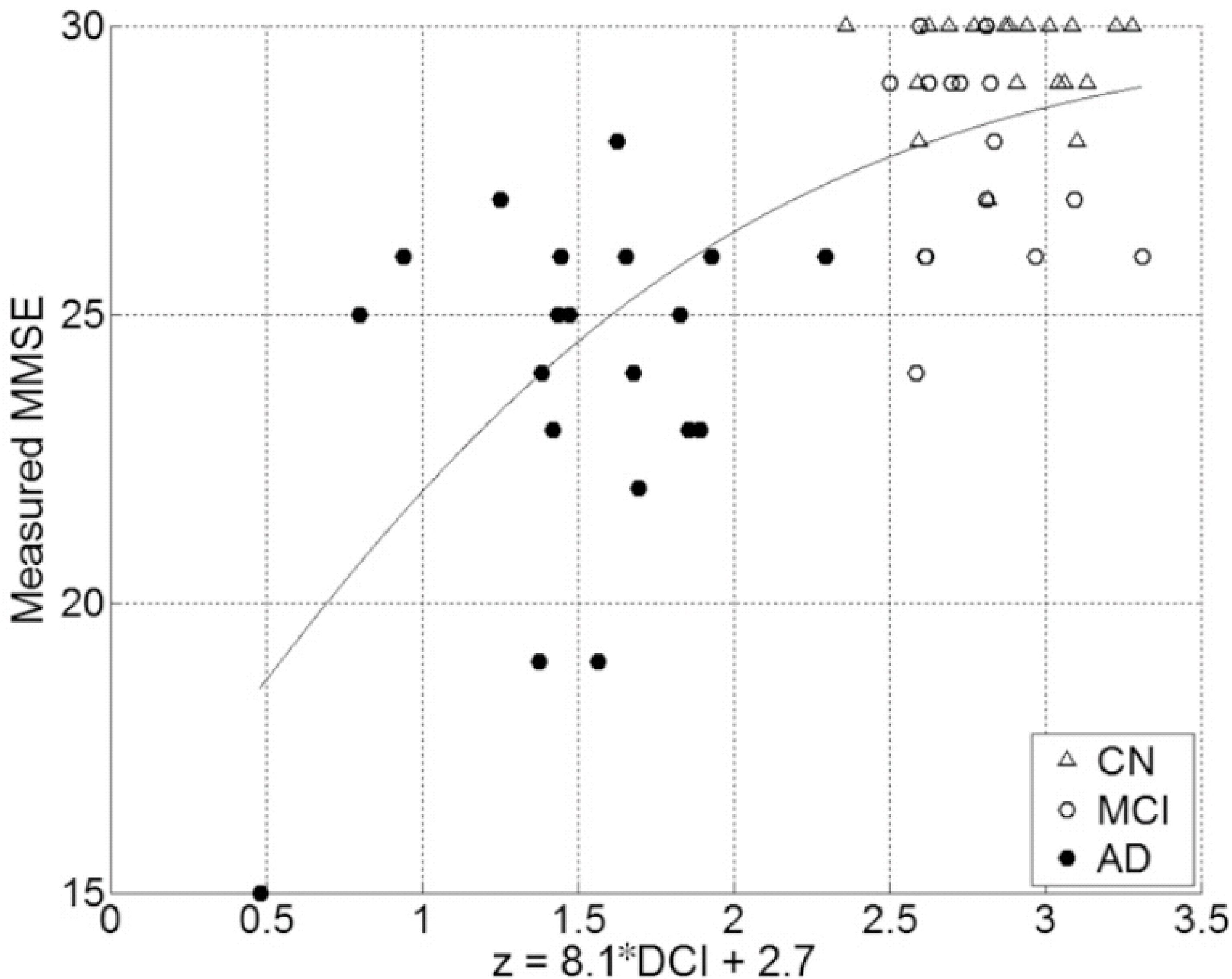



Deco, Jirsa, and McIntosh (2011)

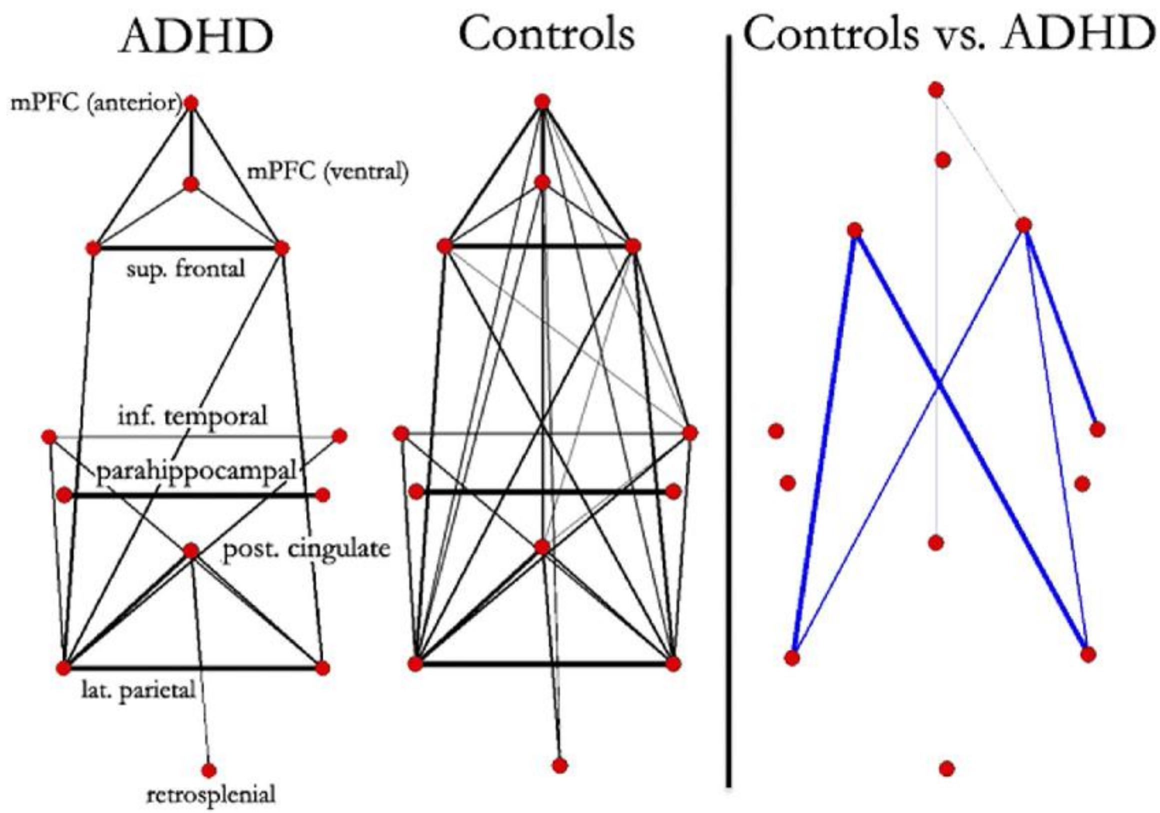
# Implications

- RSN's have functional value
  - RSN variability predicts trial-by-trial cognitive function
  - Noise drives network dynamics; anatomic connections determine what configuration emerges
- Brain networks have 'small-world' architecture
  - In presence of noise, system will visit this architecture on its own
  - Brain is thus able to visit different network configurations that will likely be useful in novel contexts or impending stimuli
- May be possible to account for aspects of pathology through biomarkers of disordered RSN activity
  - Recent research interest in RSN in brain disease

# Resting State Functional Connectivity and MMSE in MCI and AD



# DMN Connectivity Reduced in ADHD



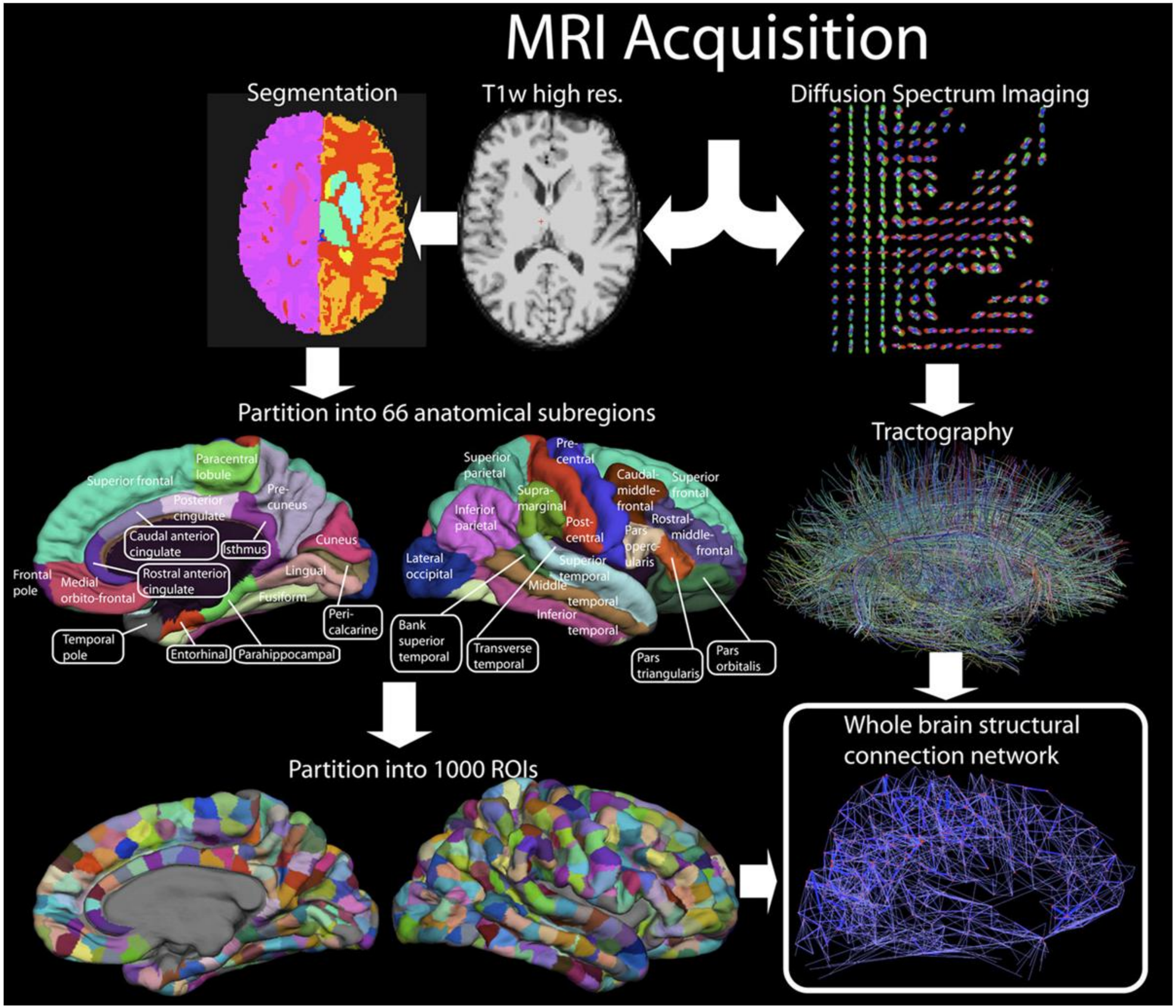

Fair, et al, *Biol Psychiat,* 2010

# DMN Activation/Connectivity Related to Cognitive/Neuropsychiatric D/O

**Table 1**
A summary of empirical findings of altered DMN activity in individuals with mental disorders

| Mental disorder | Measure | Task | DMN deactivation | | Connectivity | | Anti-correlation | DMN function |
|---|---|---|---|---|---|---|---|---|
| | | | Anterior | Posterior | DMN | TPN | | |
| Alzheimer's disease | | | | | | | | |
| Greicius et al. (2004) | fMRI-ICA | SM | – | – | ↓ | – | – | – |
| Rombouts et al. (2005) | fMRI-ICA | WM | ↓ MCI & C | MCI < C | – | – | – | – |
| Buckner et al. (2005) | See text | WM | – | – | – | – | – | PCC at risk of atrophy |
| Wang et al. (2006) | fMRI-ROI | RS | – | – | ↓ | – | – | – |
| Firbank et al. (2007) | MRI-FA | RS | – | – | ↓ | – | – | Effect of global atrophy |
| He et al. (2007) | fMRI-ReHo | RS | – | – | ↓ PCC | – | – | PCC related to MMSE |
| At risk of Alzheimer's | | | | | | | | |
| Sorg et al. (2007) (MCI) | fMRI-ICA, ROI | RS | ↓ | ↓ | ↓ | – | – | – |
| Bai et al. (2008) (MCI) | fMRI-ReHo | RS | – | – | ↓* | – | – | *Controlled for atrophy, age |
| Persson et al. (2008) (APOE4) | fMRI-ROI | Semantic | ↓ | ↓ | – | – | – | – |
| Schizophrenia | | | | | | | | |
| Liang et al. (2006) | fMRI-parcellation | RS | – | – | ↓ | – | – | – |
| Bluhm et al. (2007) | fMRI-ROI | RS | – | – | ↓* | – | – | *Related to +ve symptoms |
| Garrity et al. (2007) | fMRI-ICA | Oddball | ↑* | – | – | – | – | *Related to +ve symptoms |
| Zhou et al. (2007) | fMRI-ROI | RS | – | – | ↑ | ↑ | ↑ | – |
| Pomarol-Clotet et al. (2008) | fMRI-ICA | WM | ↓MPFC* | – | – | – | – | *Unrelated to performance |
| Depression | | | | | | | | |
| Greicius et al. (2007) | fMRI-ICA | RS | – | – | ↑* | – | – | *Related to refractoriness |
| Anxiety | | | | | | | | |
| Zhao et al. (2007) | fMRI-ROI | EPT | ↓ | ↑ | – | – | – | MPFC related to anxiety |
| Epilepsy | | | | | | | | |
| Laufs et al. (2007) (no control) | EEG & fMRI | RS | ↓* | ↓* | – | – | – | *Related to IED in TLE |
| Lui et al. (2008) (GS, PS, C) | fMRI-GLM | RS | – | – | ↓ PCC* | – | – | *GS patients only |
| ASD | | | | | | | | |
| Cherkassky et al. (2006) | fMRI-ROI | RS | Non-sig | Non-sig | ↓ | – | – | – |
| Kennedy et al. (2006) | fMRI-ROI | Stroop | ↓ | ↓ | – | – | – | – |
| Kennedy and Courchesne (2008) | fMRI-ROI | RS | – | – | ↓* | Non-sig | ↓ | *Specifically MPFC |
| ADHD | | | | | | | | |
| Tian et al. (2006) | fMRI-ROI | RS | – | – | ↑ | – | – | – |
| Cao et al. (2006) | fMRI-ReHo | RS | – | – | ↓ | – | – | – |
| Castellanos et al. (2008) | fMRI-ROI | RS | – | – | ↓ | – | ↓ | – |
| Uddin et al. (2008a) | fMRI-NeHo | RS | – | – | ↓* | – | – | *Specifically PCC |
| Helps et al. (2008) | DC-EEG | RS | – | – | ↓ | – | – | – |

Broyd, et al., *Neurosci Biobehav Rev*, 2009

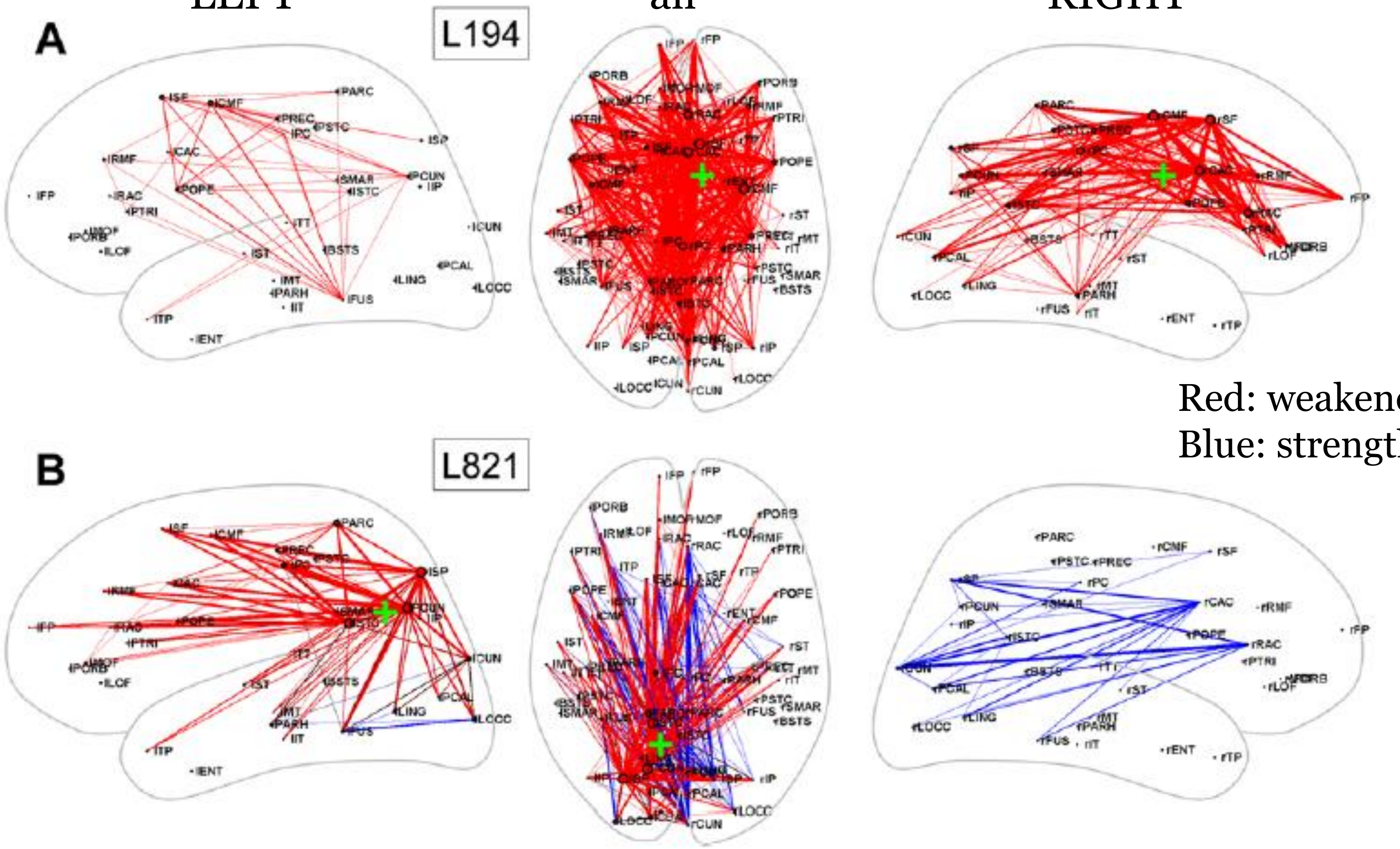

MRI Acquisition
Segmentation
T1w high res.
Diffusion Spectrum Imaging
Partition into 66 anatomical subregions
Tractography
Superior frontal
Paracentral lobule
Posterior cingulate
Pre-cuneus
Caudal anterior cingulate
Isthmus
Cuneus
Frontal pole
Medial orbito-frontal
Rostral anterior cingulate
Lingual
Fusiform
Peri-calcarine
Temporal pole
Entorhinal
Parahippocampal
Superior parietal
Pre-central
Caudal-middle-frontal
Superior frontal
Supra-marginal
Inferior parietal
Post-central
Pars operc-ularis
Rostral-middle-frontal
Lateral occipital
Superior temporal
Middle temporal
Inferior temporal
Bank superior temporal
Transverse temporal
Pars triangularis
Pars orbitalis
Whole brain structural connection network
Partition into 1000 ROIs

# Computational Lesion Modeling (Alstott, et al, 2009)

- A complement to the classic "lesion" method
- Basic approach
  - Derive structural dataset from diffusion imaging
  - Model neural dynamics based on connection strengths (physiological)
  - Lesion network one of two ways:
    - Random node deletion with successive recomputation – focused on "central" nodes
    - Localized area deletion – all nodes in specified area
  - Alstott et al. (2009) lesioned cortical midline, TP cortex, frontal cortex, and sensory-motor cortex

# Cortical Midline Lesions

LEFT | all | RIGHT



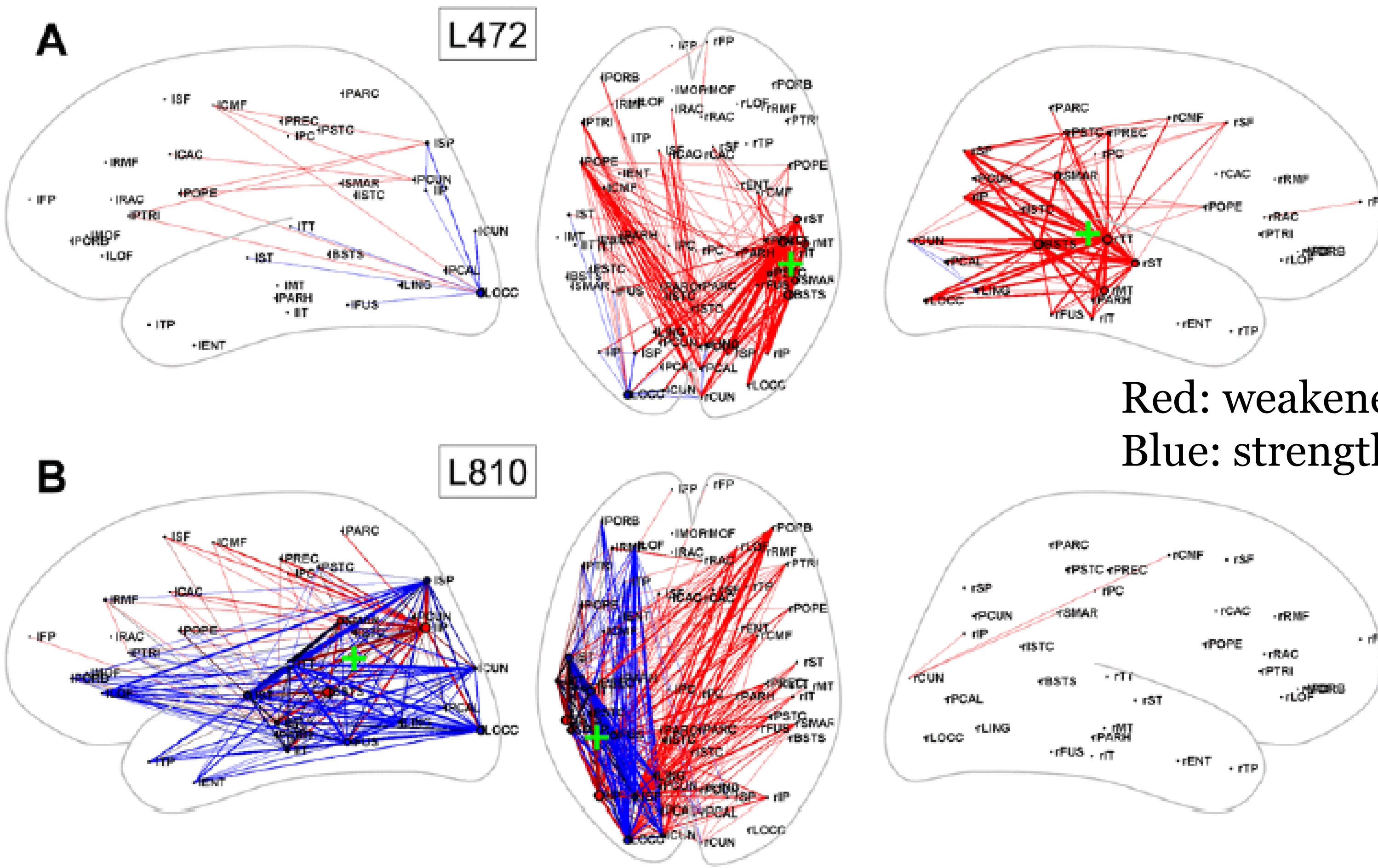

Red: weakened
Blue: strengthened

**Figure 4. Dynamic effects of lesions along the brain's midline.** (A) L194. (B) L821. In this plot, as well as in Figures 5, 6 and S1, a dorsal view of the brain (middle panel) and two lateral views of the left hemisphere (left panels) and the right hemisphere (right panels) are shown. The middle panel plots all significantly different functional connections, while the left and right panels only show significantly different functional connections within the left and right hemispheres, respectively. The 998 ROI z-score FC matrix was aggregated to 66 subregions, and pathways between these 66 subregions are plotted if at least 10% of their constituent connections linking ROI pairs are significantly changed ($|z|>3.3$) as a result of the lesion. Pathways are plotted in red or blue, if their coupling has been weakened or strengthened, respectively. The approximate lesion center is marked with a green "+".
doi:10.1371/journal.pcbi.1000408.g004

Alstott, et al, *PLoS Comput Biol*, 2009

## Temporo-parietal Lesions

LEFT | all | RIGHT




Red: weakened
Blue: strengthened

**Figure 5. Dynamic effects of lesions near the temporo-parietal junction.** (A) L472. (B) L810. For plotting conventions see legend to Figure 4.

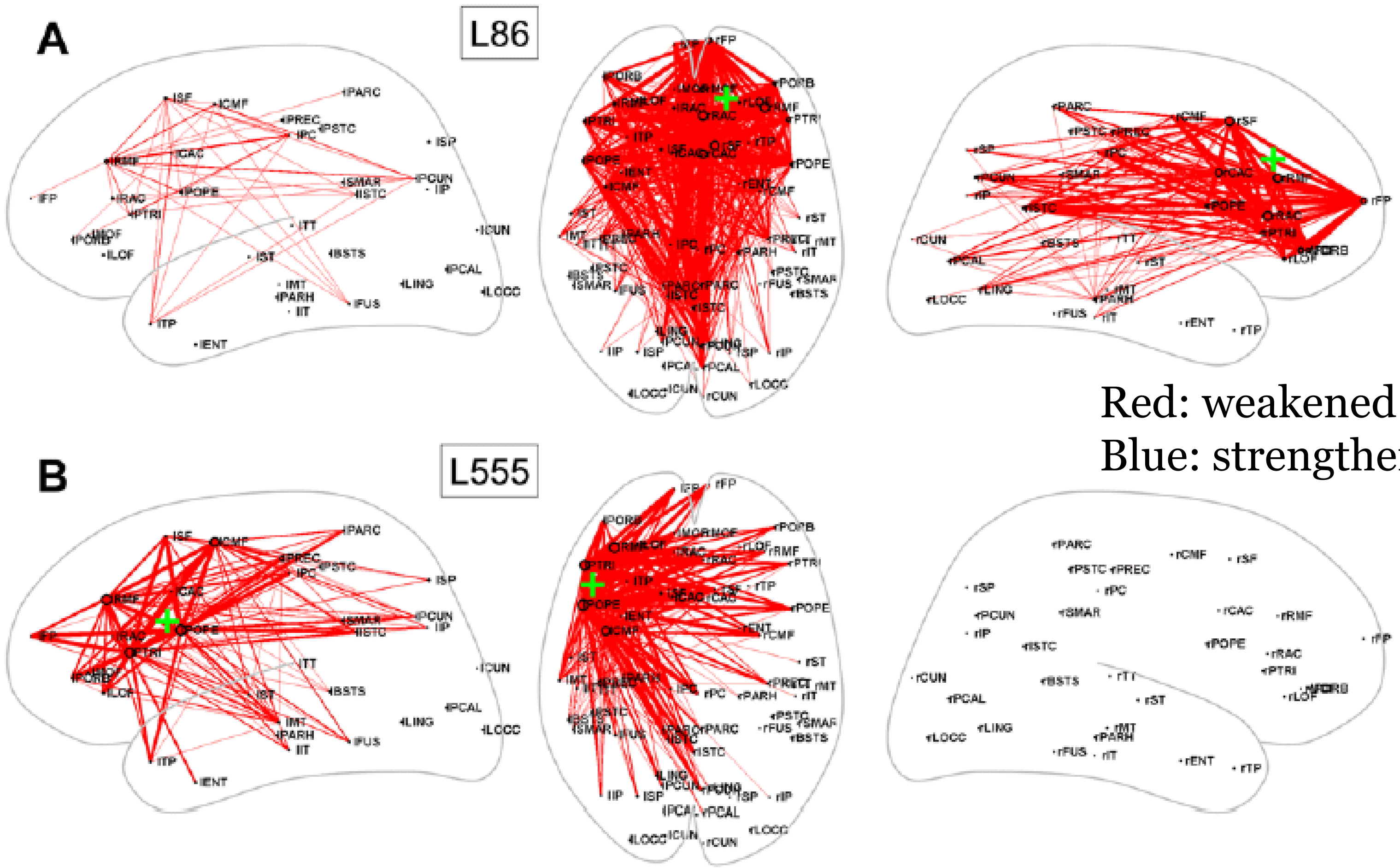
Alstott, et al, *PLoS Comput Biol*, 2009

# Frontal Lesions

LEFT

all

RIGHT

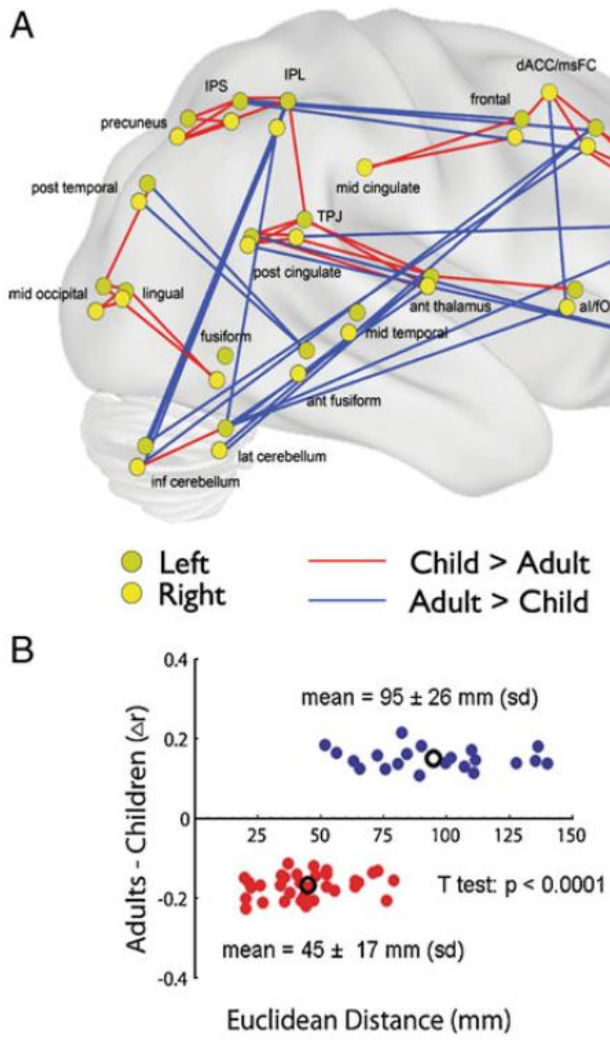



Red: weakened
Blue: strengthened

**Figure 6. Dynamic effects of lesions in frontal cortex.** (A) L86. (B) L555. For plotting conventions see legend to Figure 4.

Alstott, et al, *PLoS Comput Biol*, 2009

# Connectivity Analysis in Development

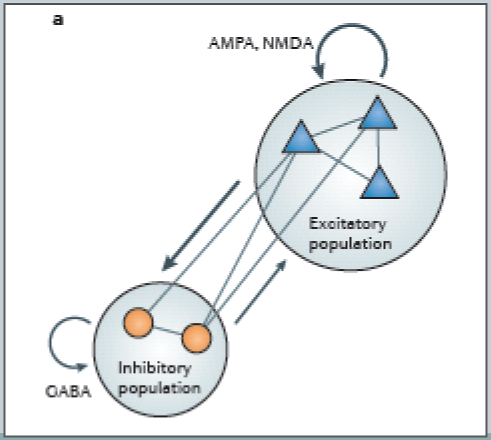



Vogel, Power, Petersen, and Schlaggar, *Neuropsychol Rev,* 2010

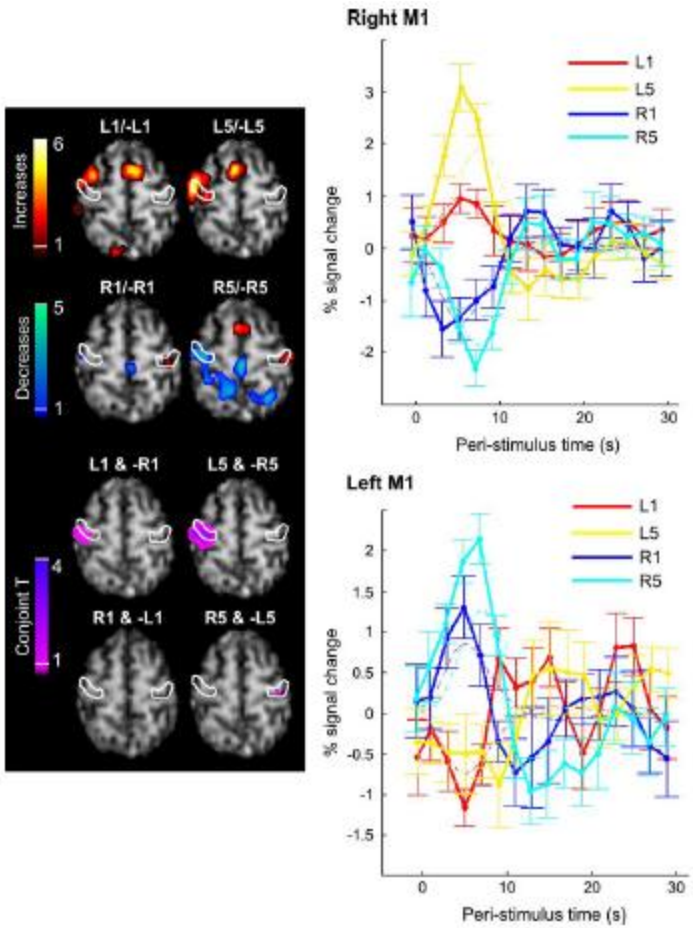
# Inhibition and Excitation in Functional Connectivity

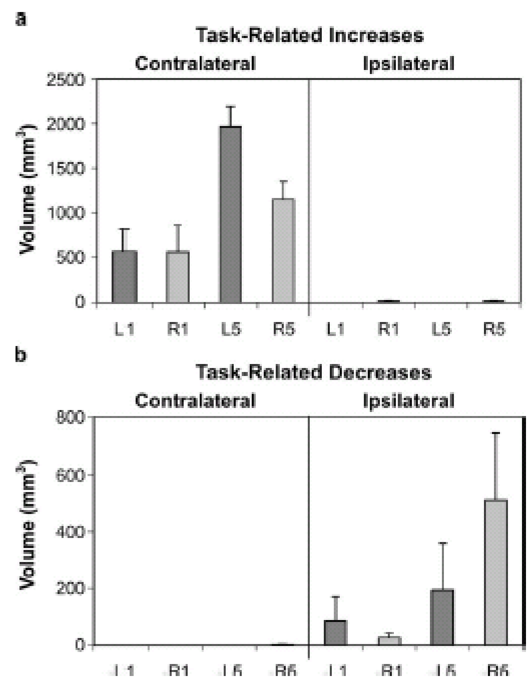
# Key Concepts

- "Downstream" effect of activation on behavior depends on excitatory and inhibitory connections
  - Inhibition/suppression occurs between areas that might compete for processing or output
  - Excitation between areas that co-operate in performing tasks ("selective engagement")
- Concept that activity in certain areas "modulates" activity in other areas
- Balance of excitatory and inhibitory inputs defines system output
- Lesion effects
  - Lack of excitation
  - Disinhibition (or release from inhibition)
  - Compensatory dedifferentiation



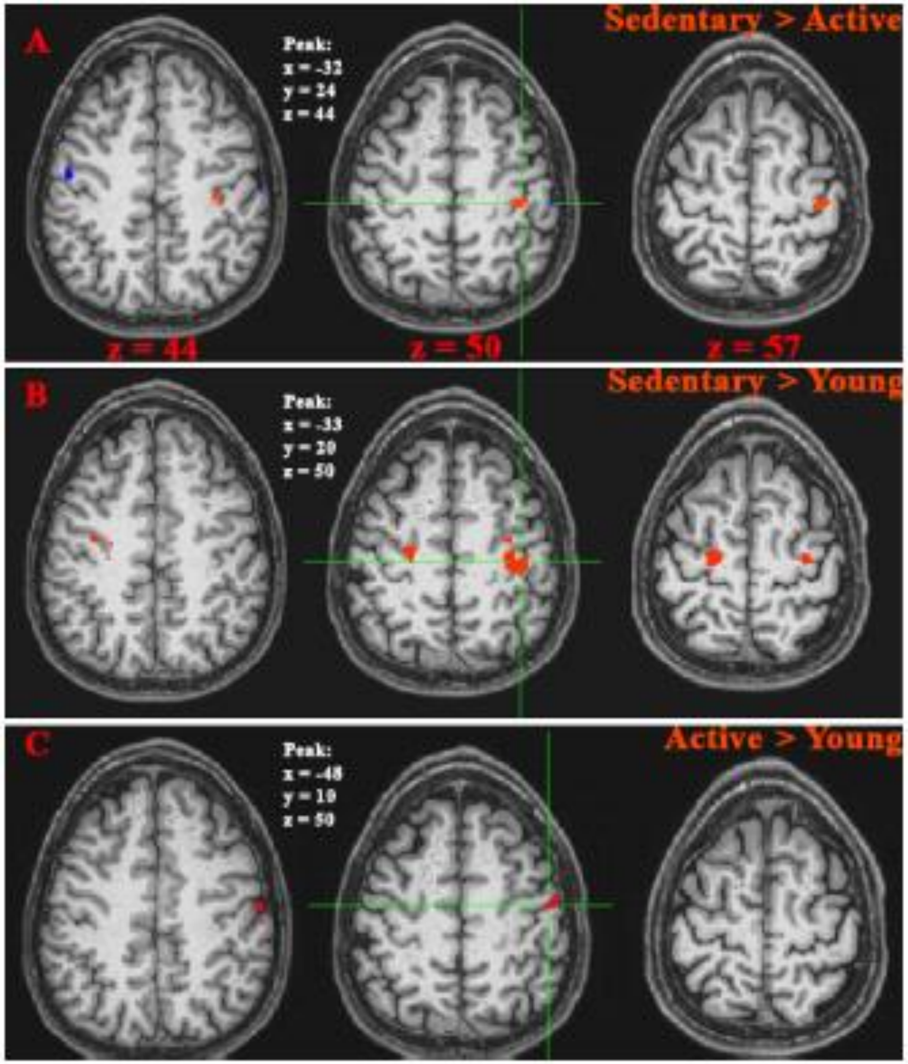
# Contralateral and Ipsilateral BOLD Changes with Unimanual Thumb Pressing



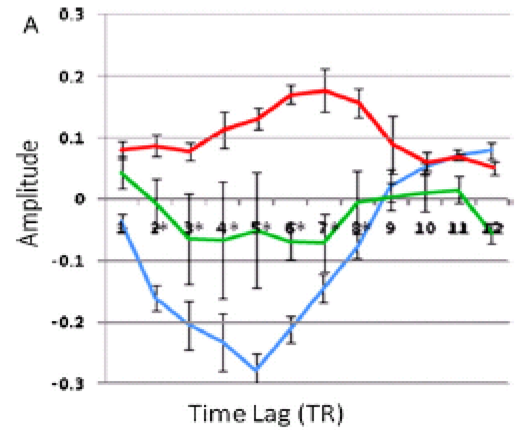



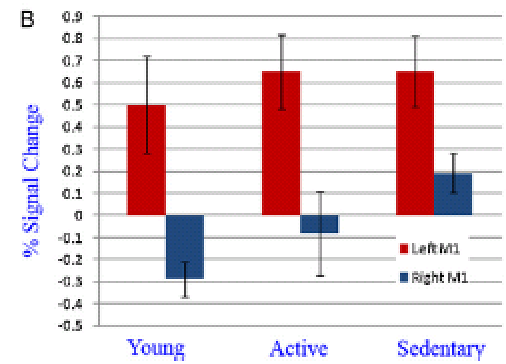

Newton et al, *Neuroimage*, 2005

# Loss of Inhibition of Ipsilateral Motor Cortex in Sedentary Older Adults




Right M1 hemodynamic response

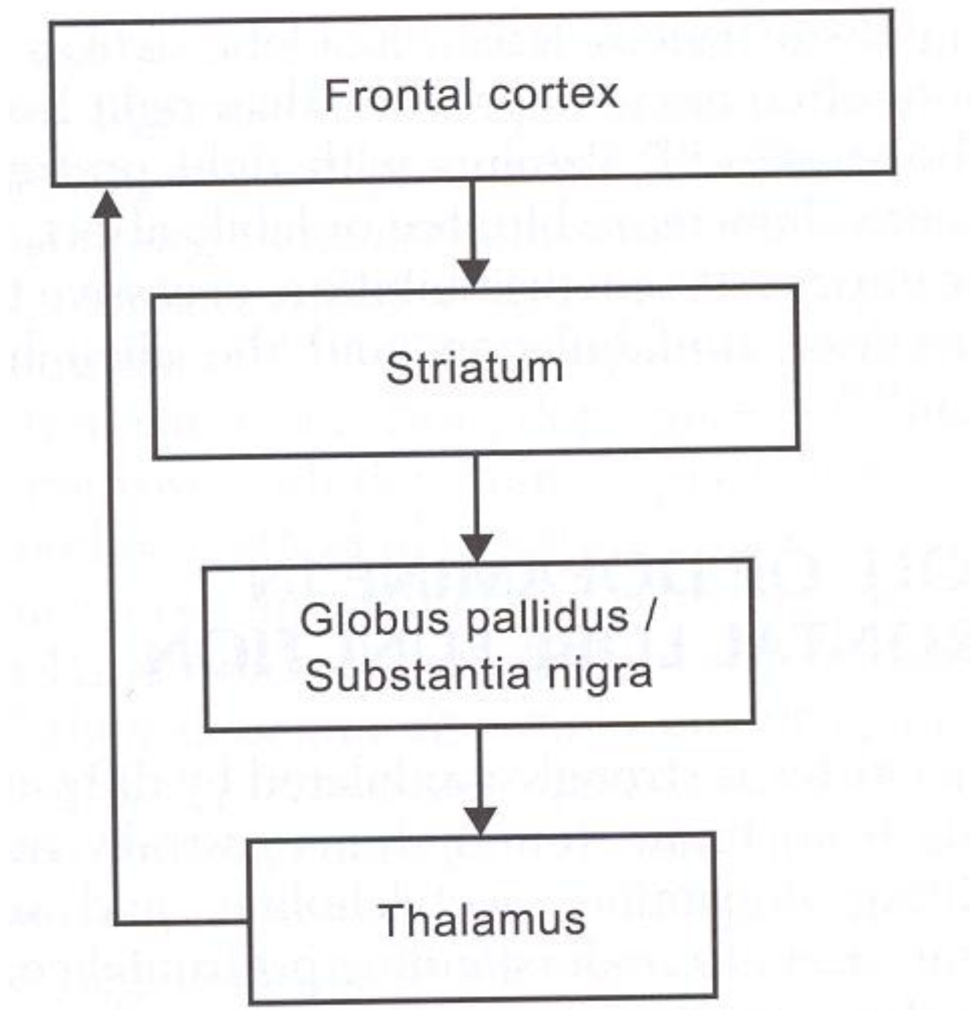


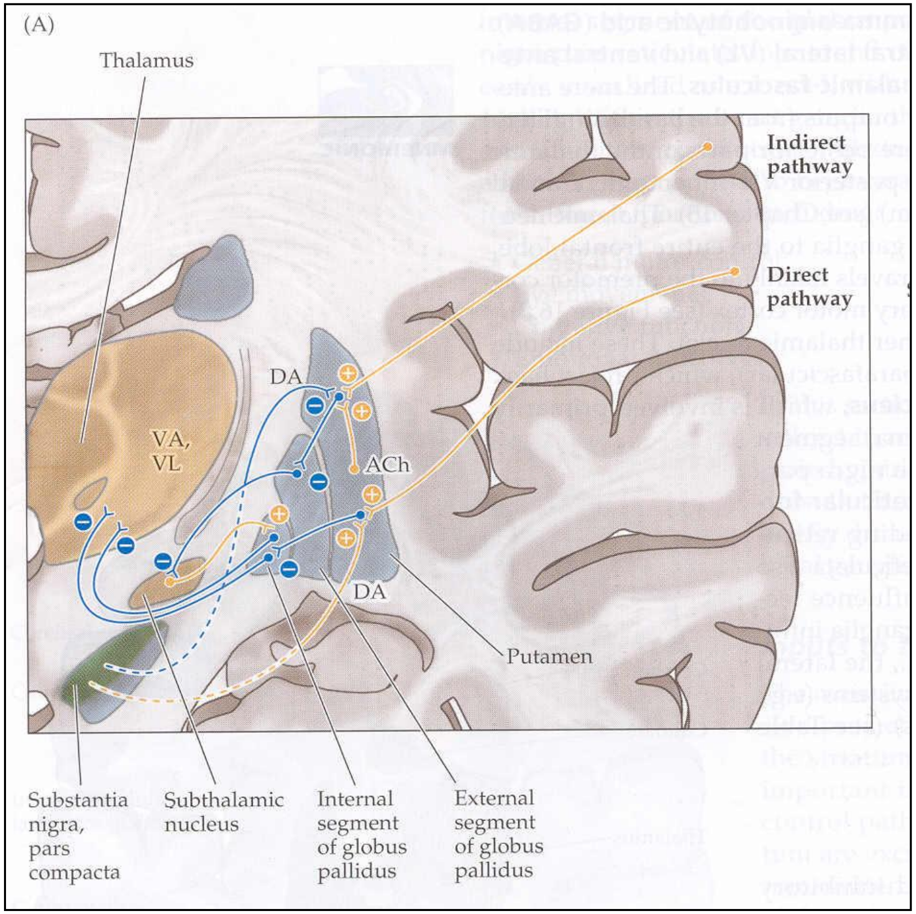

Percent signal change

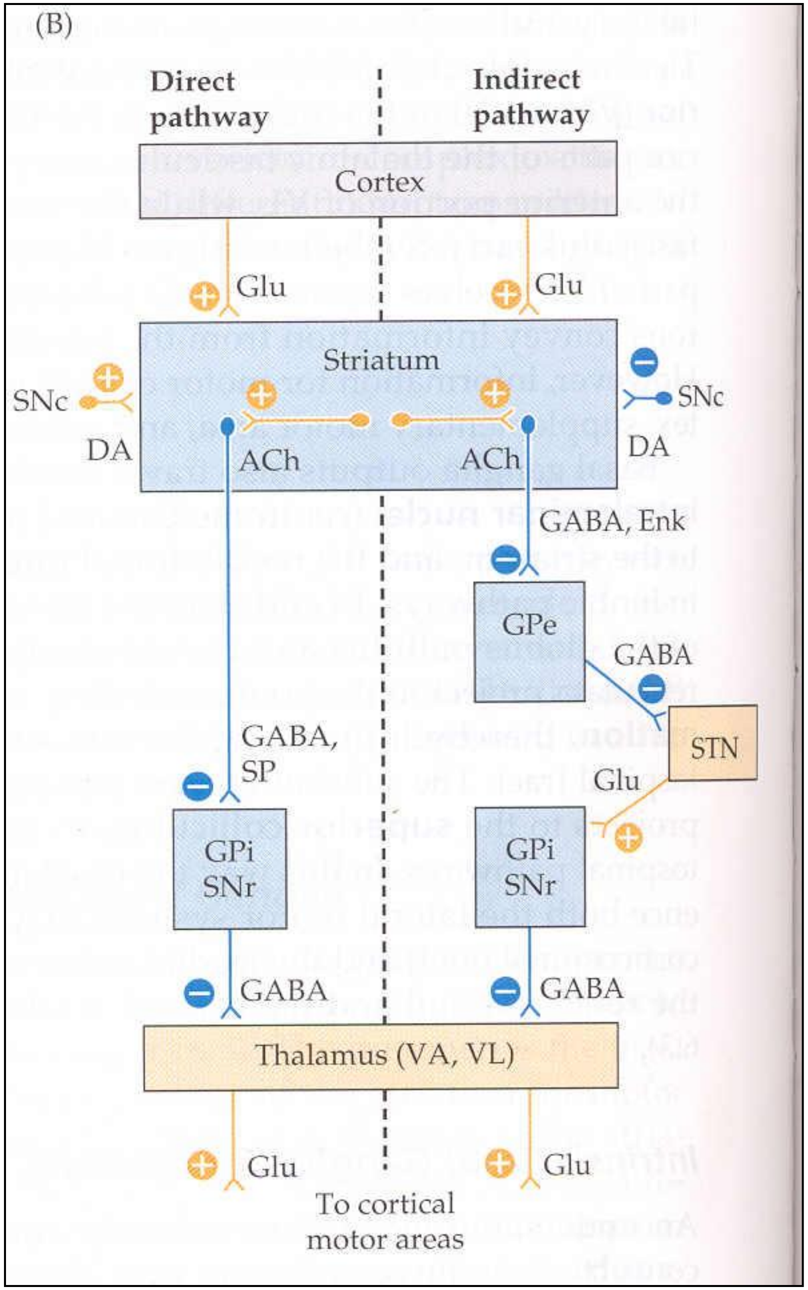
McGregor, Zlatar, Kleim, Sudhyahom, **Bauer**, Phan, Seeds, Ford, Manini, White, Kleim, & Crosson, *Behav Brain Res*, 2011

# General Organization of Frontal cortical-striatal-pallidal-thalamic-cortical loops

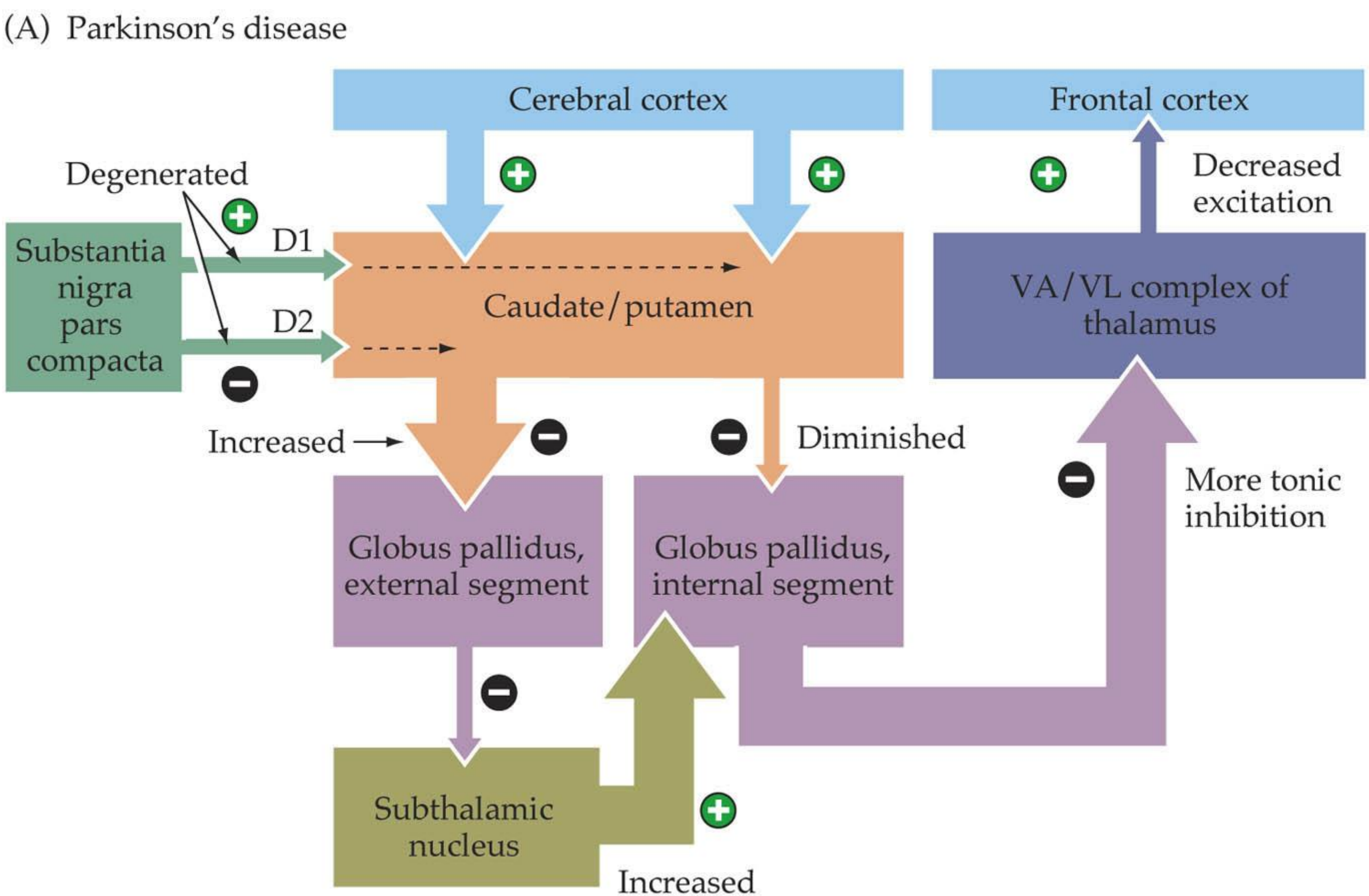


# Cortical-Striatal-Pallidal-Thalamic-Cortical Loop

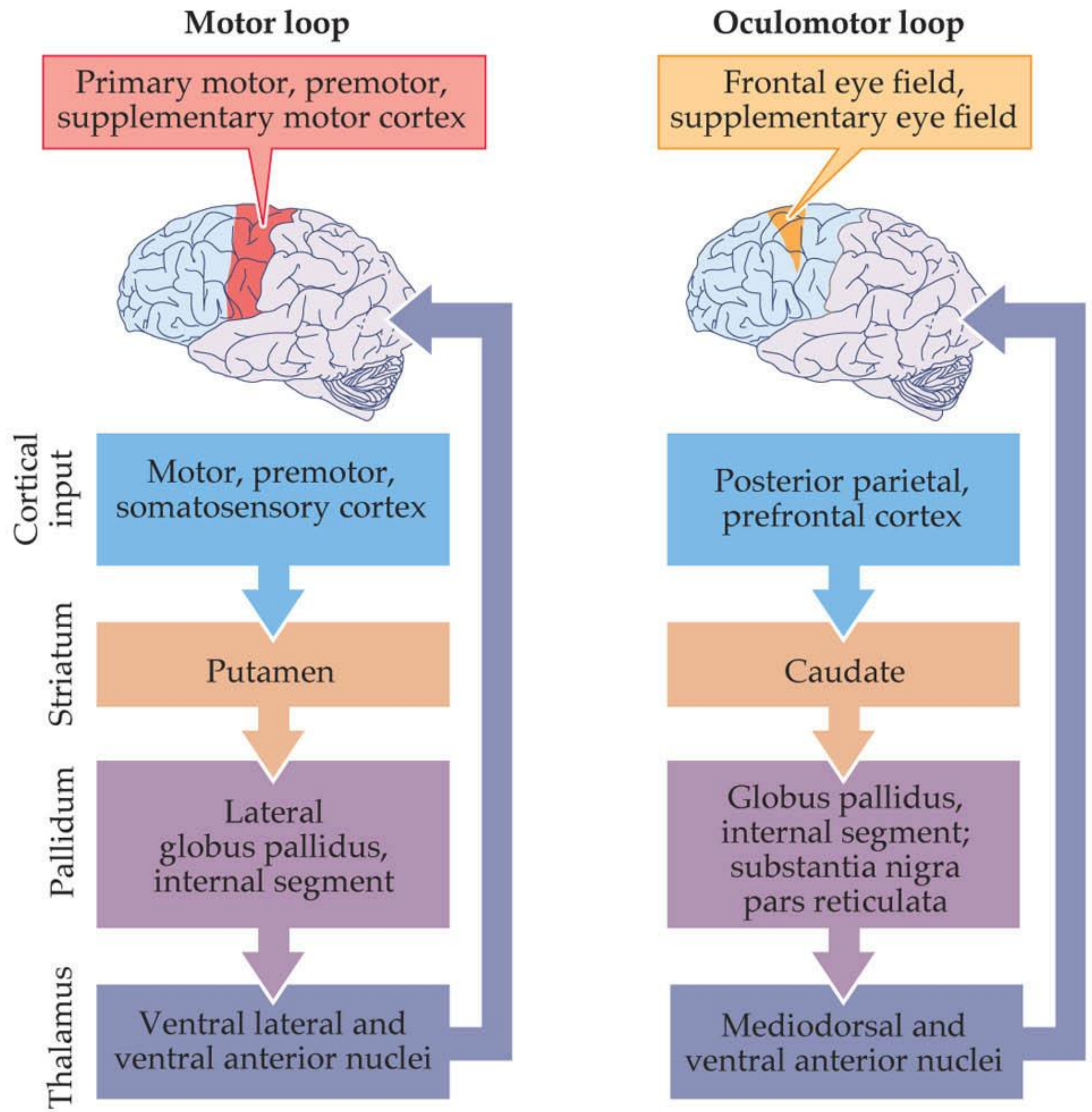


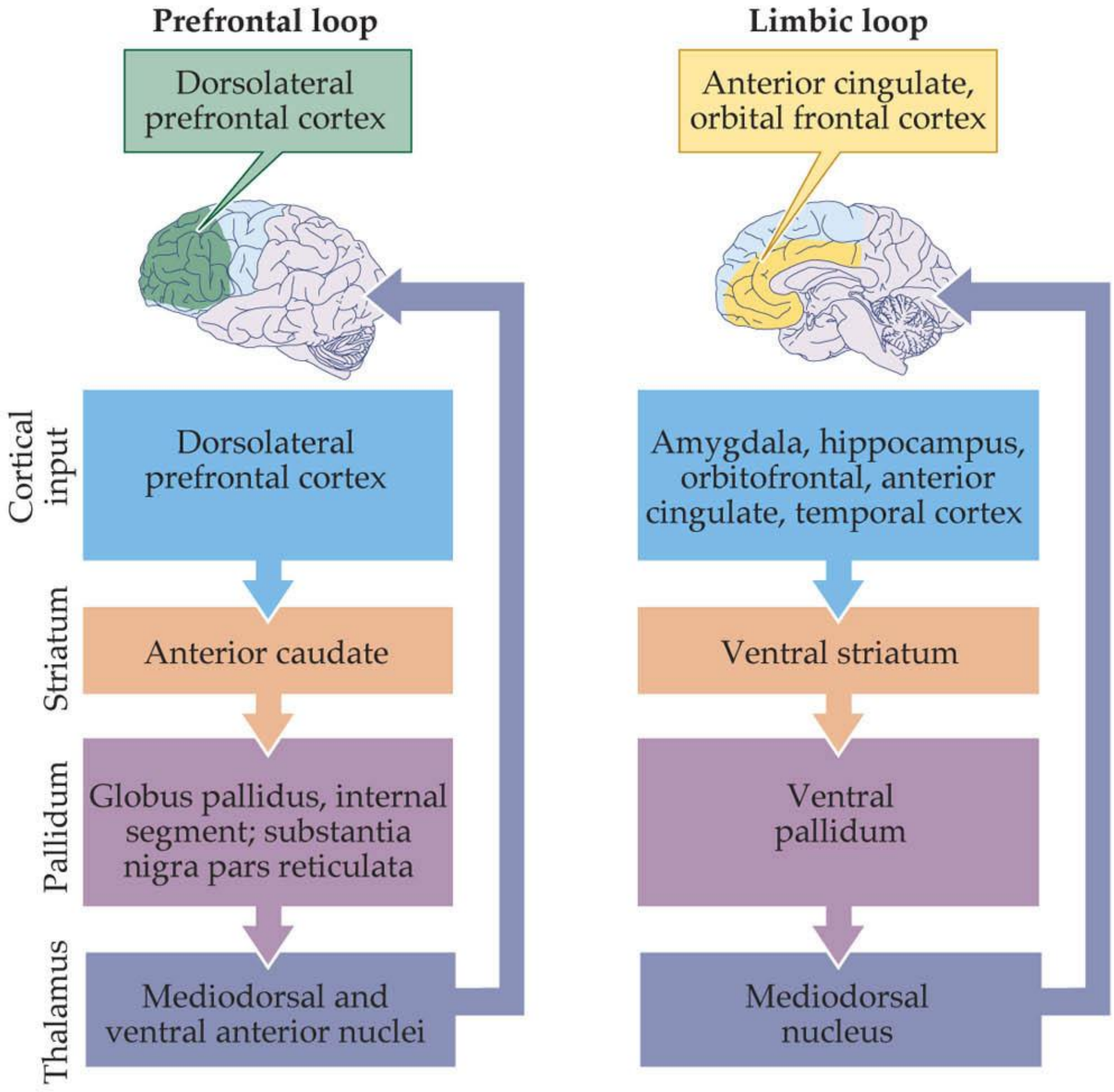

*Blumenfeld, 2002*




*NEUROSCIENCE, Third Edition*, Figure 17.10 (Part 1) © 2004 Sinauer Associates, Inc.



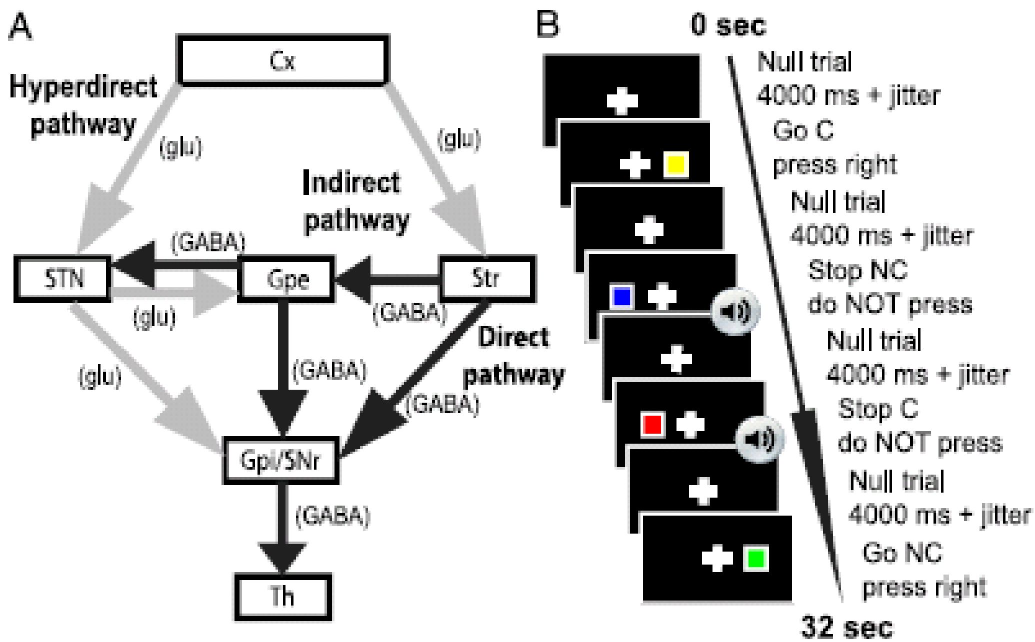

 © 2004 Sinauer Associates, Inc.




*NEUROSCIENCE, Third Edition*, Chapter 17, Box C (Part 2)

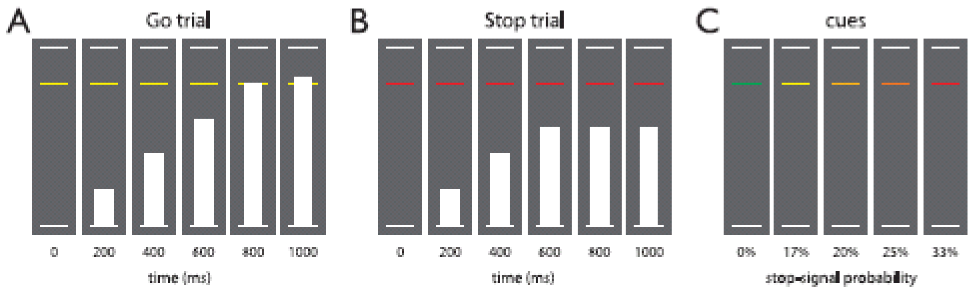
© 2004 Sinauer Associates, Inc.

# Connectivity Analysis of Simon/Stop Task



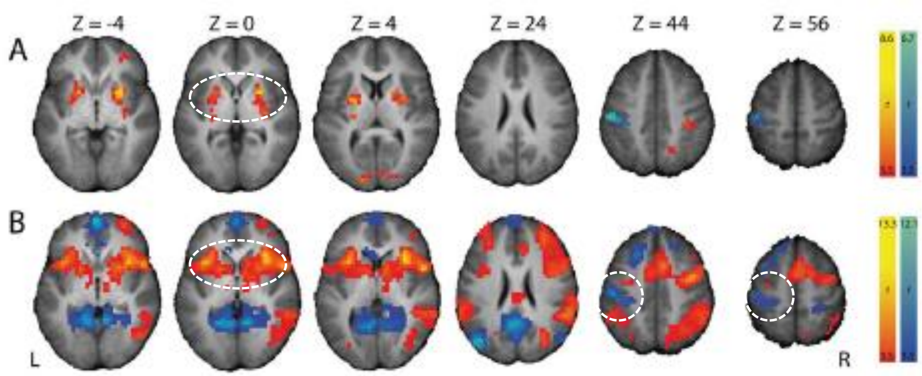

Jahfari, et al., *J Neurosci*, 2011

# Striatal Activation Predicts Contralateral Motor Deactivation in Stop Signal Task




Stop success v. stop failure

Stop success v. Go

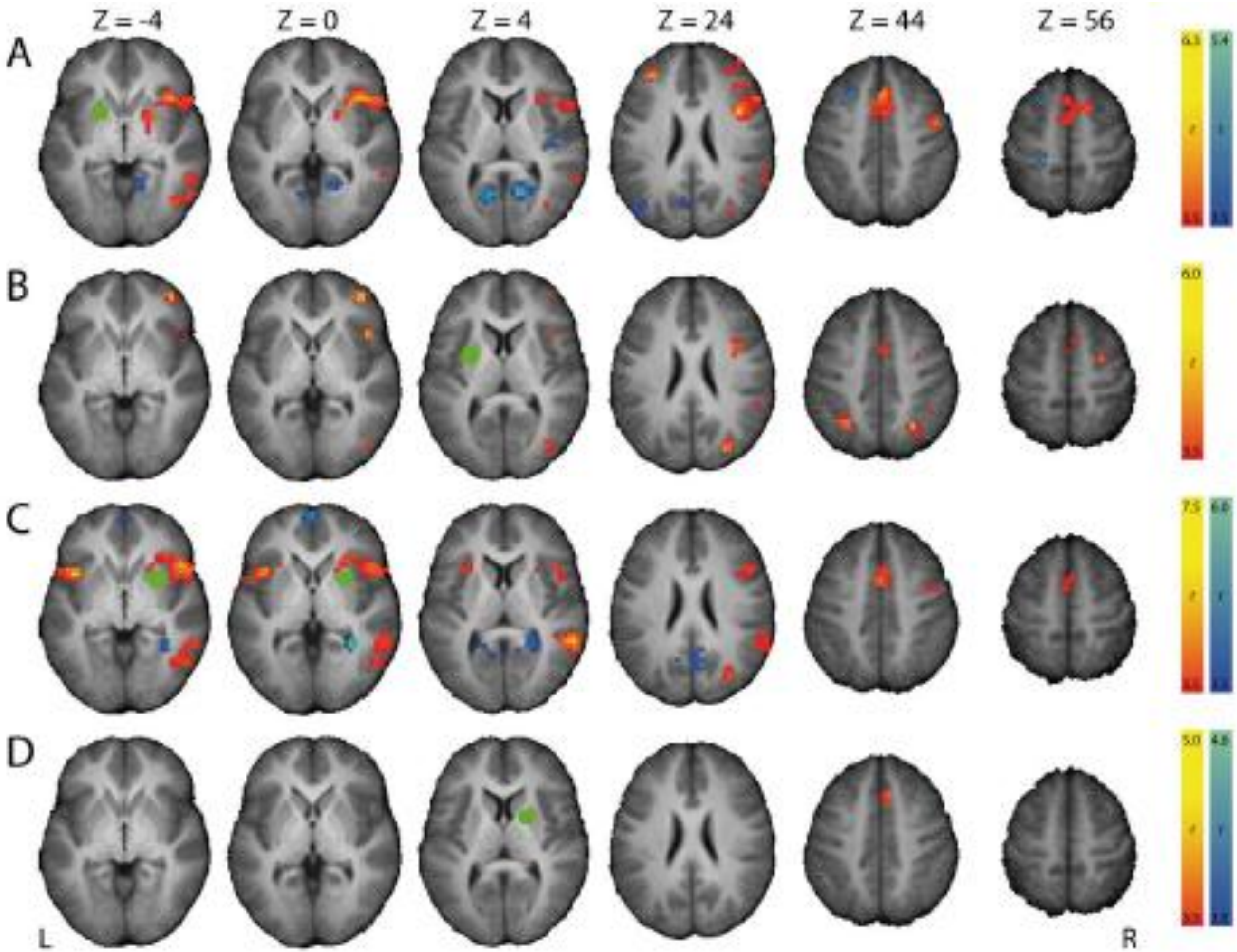



Left and right putaminal activation signal stop success; note also L M1 deactivation

Warm colors = activation during stop success; cool = deactivation

Main Findings: (1) striatal activation; left M1 deactivation during successful stop
(2) Striatal activation and left M1 deactivation were coupled during successful stopping
(3) Striatal activation linked to stop-signal probability, and linked to activation of SMA and rIFC

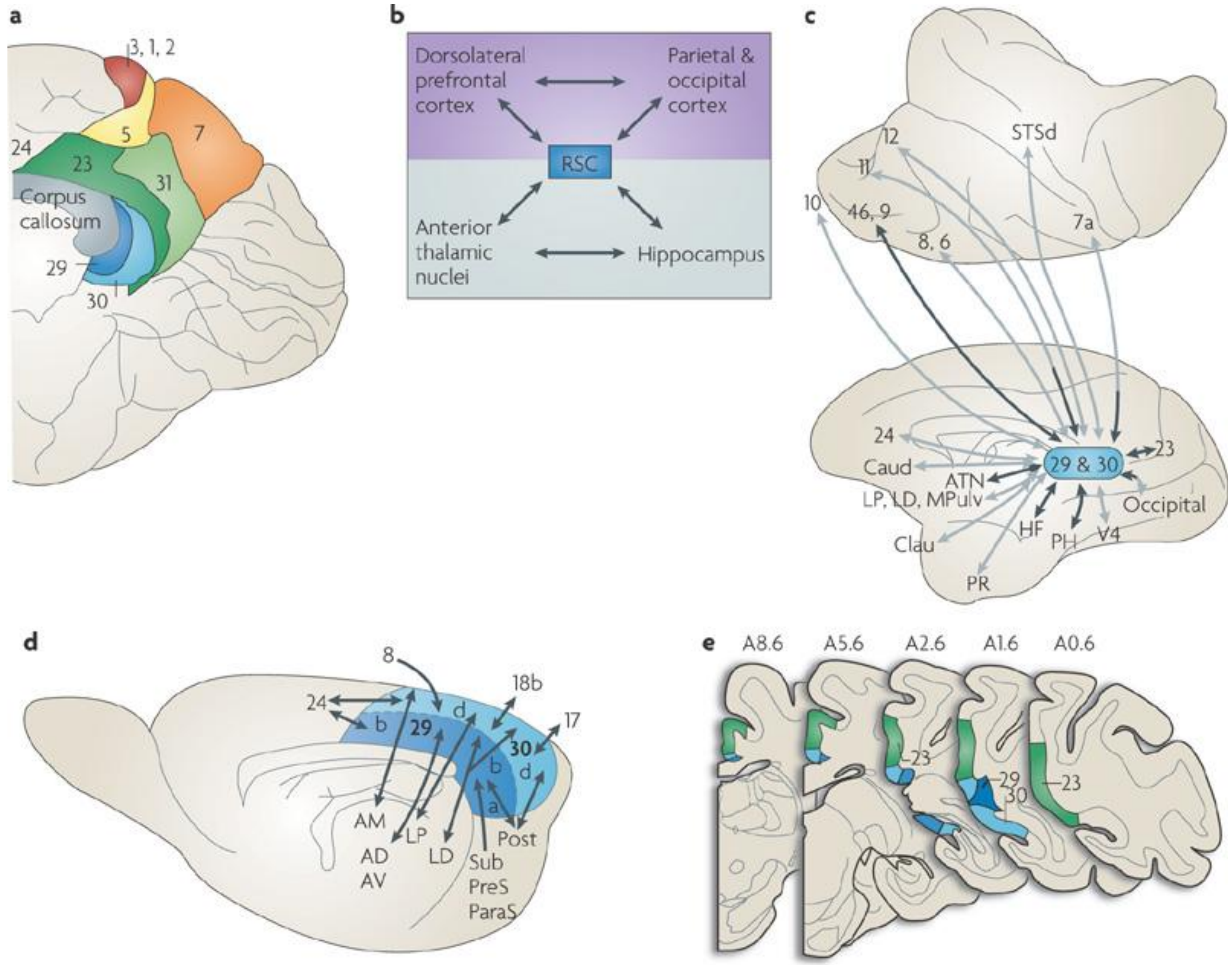
Brain regions with significant differences in coupling with the striatum as a function of Stop trial outcome (StopSuccess vs. Stop Failure)




Green dots indicate “seeds” evaluating proportionality between striatal activation and activation of other regions

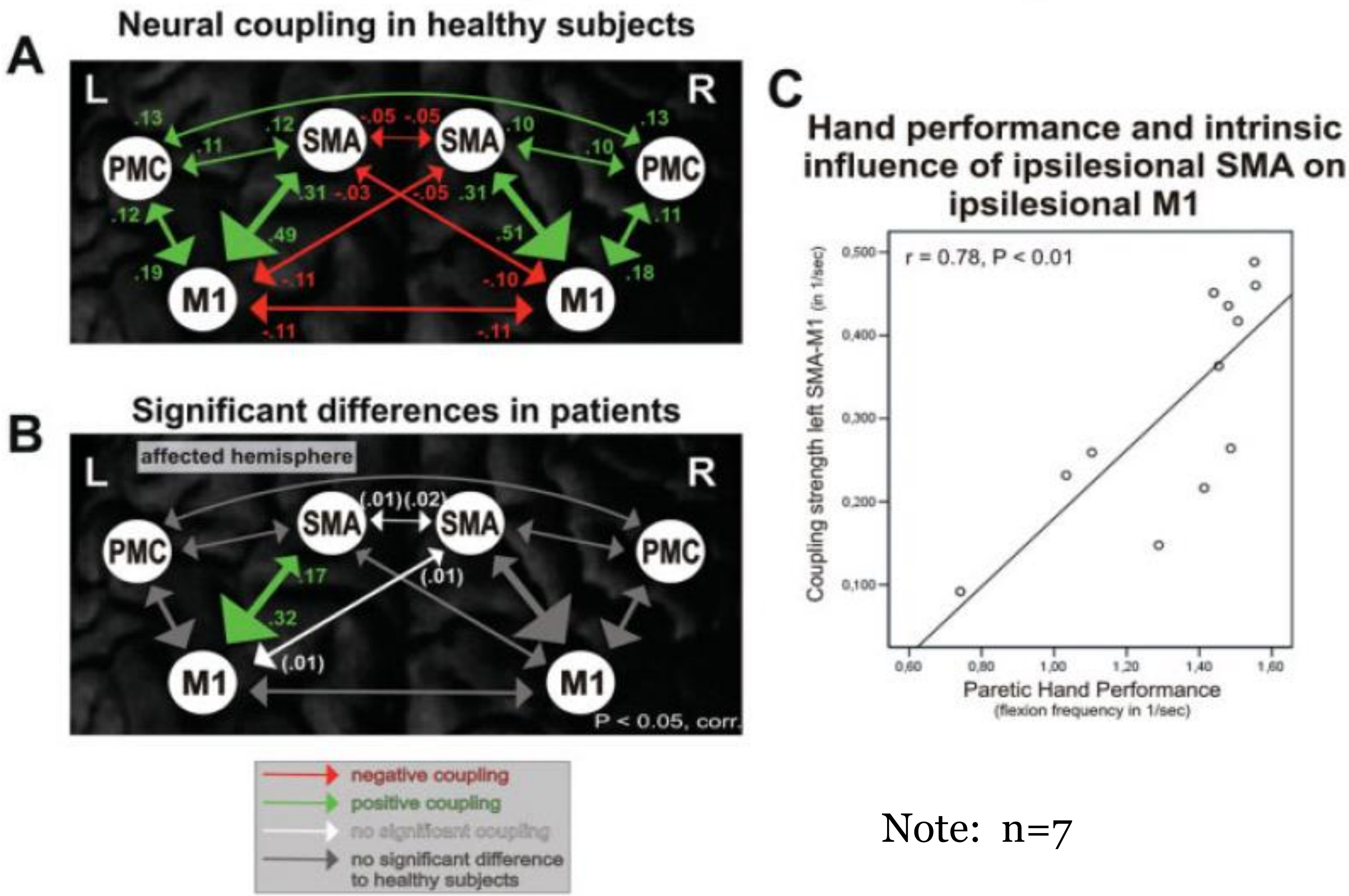
Zandbelt & Fink, PLoS One, 2010

# Retrosplenial Area Connectivity




Nature Reviews | Neuroscience

## Functional Connectivity in Healthy Subjects and Patients with Hemiparesis after Subcortical Stroke

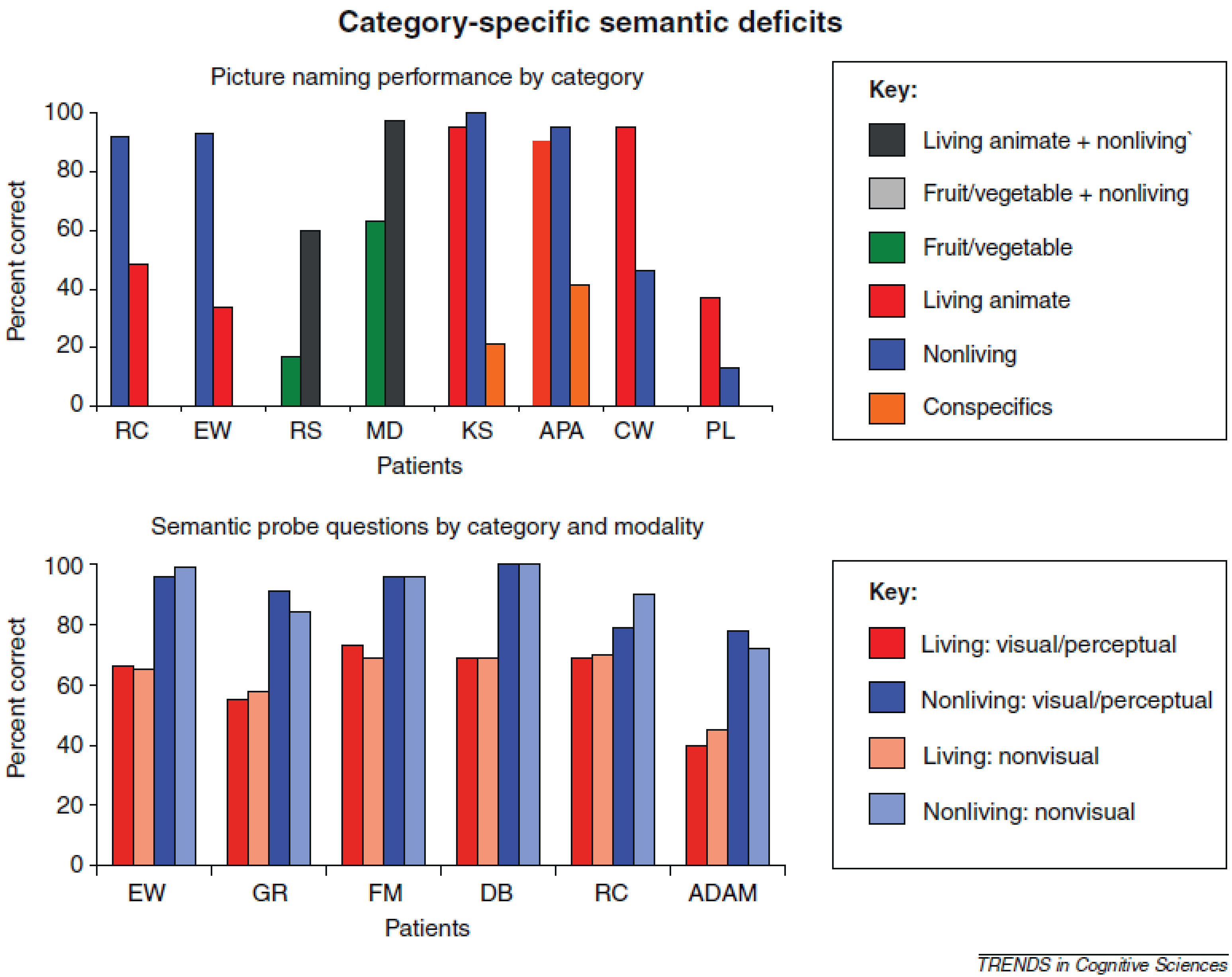



Note: n=7

# Domain-Specificity vs. Domain-Generality

# Key Concepts

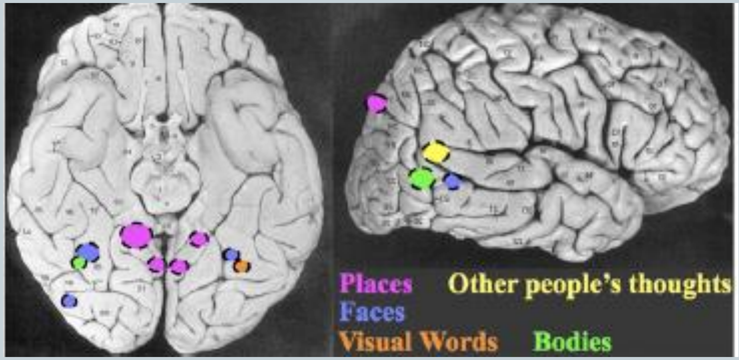
- Idea of "domain specificity" comes from fractionated neuropsychological deficits
  - Category-specific semantic deficits
    - Living v. nonliving things
    - Tools (action naming vs. object naming)
    - Medical implements
  - Optic aphasia (can name when feel but not when see)
- Implications for semantic memory organization
  - Modality-specific organization
  - Category-specific organization
  - Modality-nonspecific "hub" in temporal lobe




Mahon & Caramazza, 2011

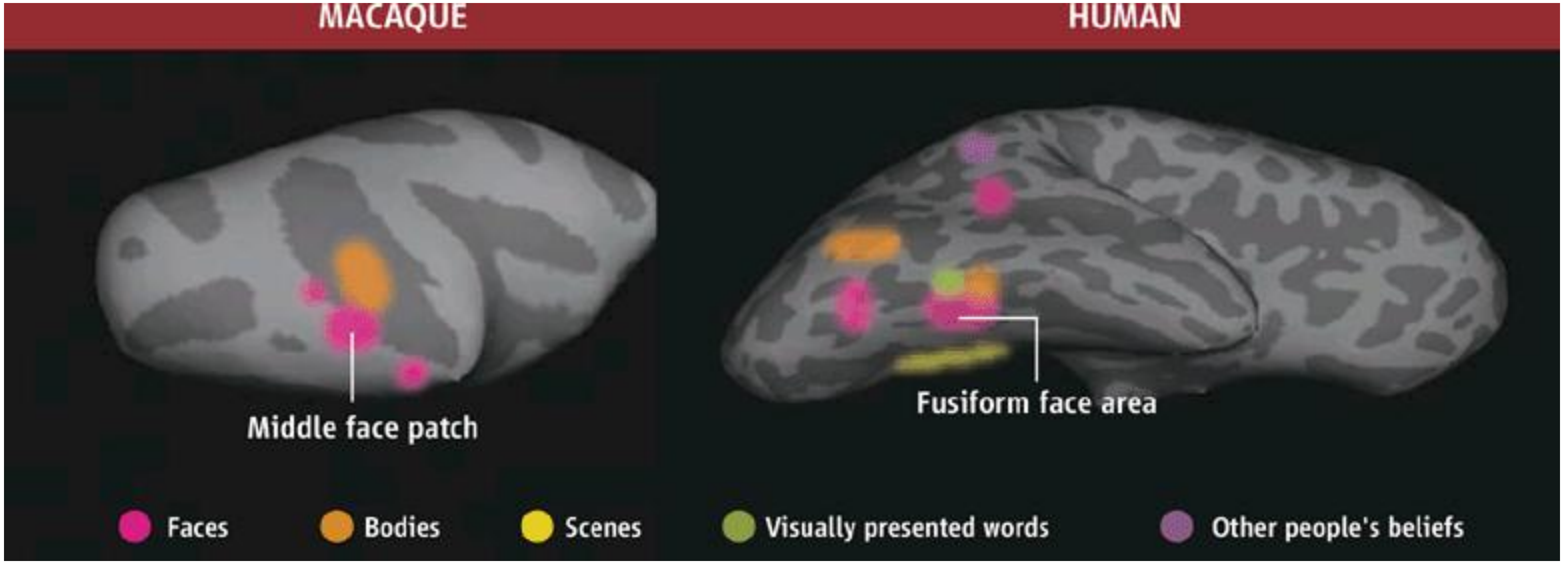
# Domain/Category-Specific "Modules"

- Identified Areas
  - Faces (FFA)
  - Places (PPA)
  - Body Parts (EBA)
  - Tools
  - Animals
  - Visual Word Forms (VWFA)
  - Other People's Thoughts (POJ)
- Unresolved Question: Are these areas sensitive to "higher-order" properties, or can their selectivity be explained by "lower-order" selectivity?

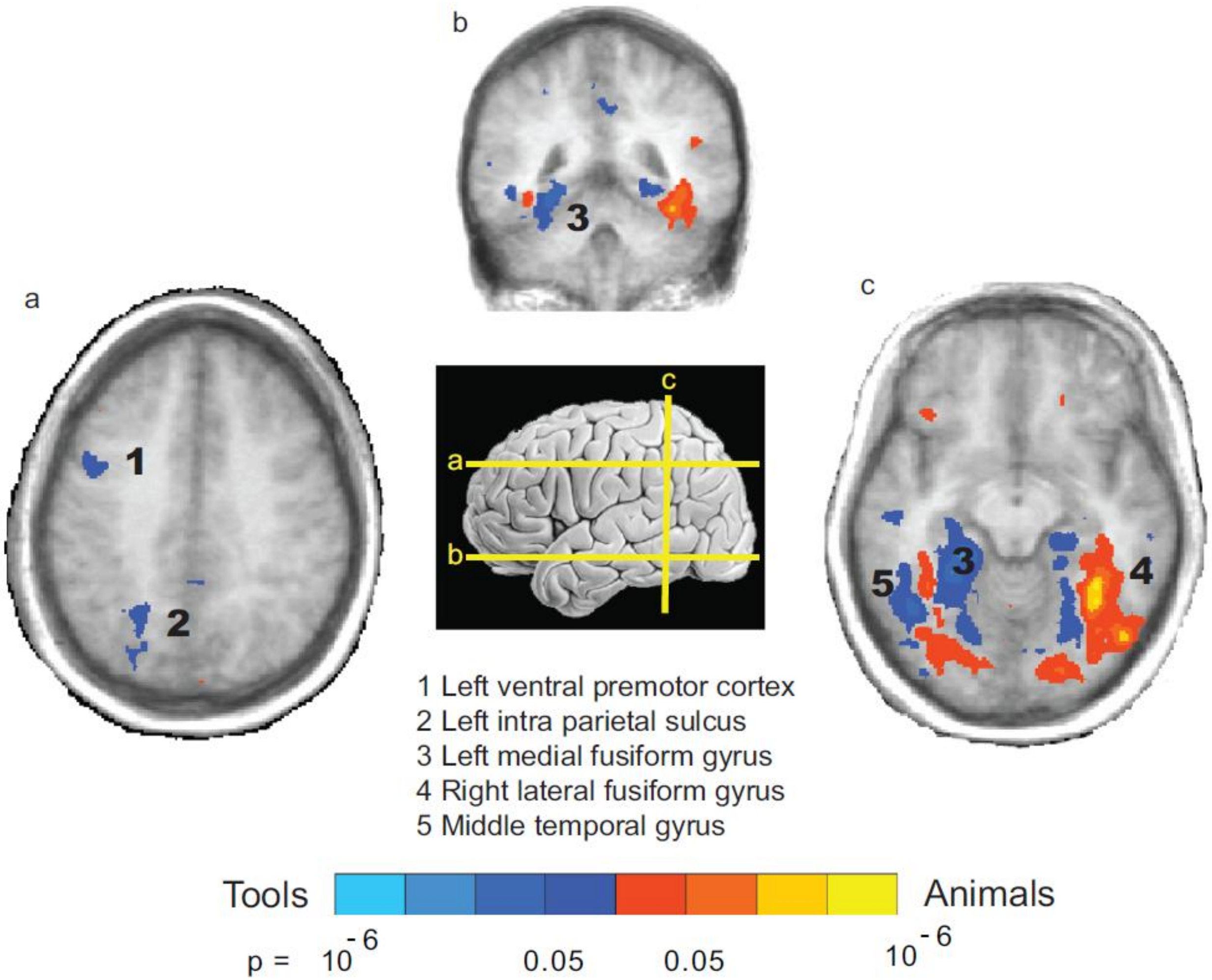



Kanwisher, 2010

# Kanwisher's Domain Specific Processing Areas

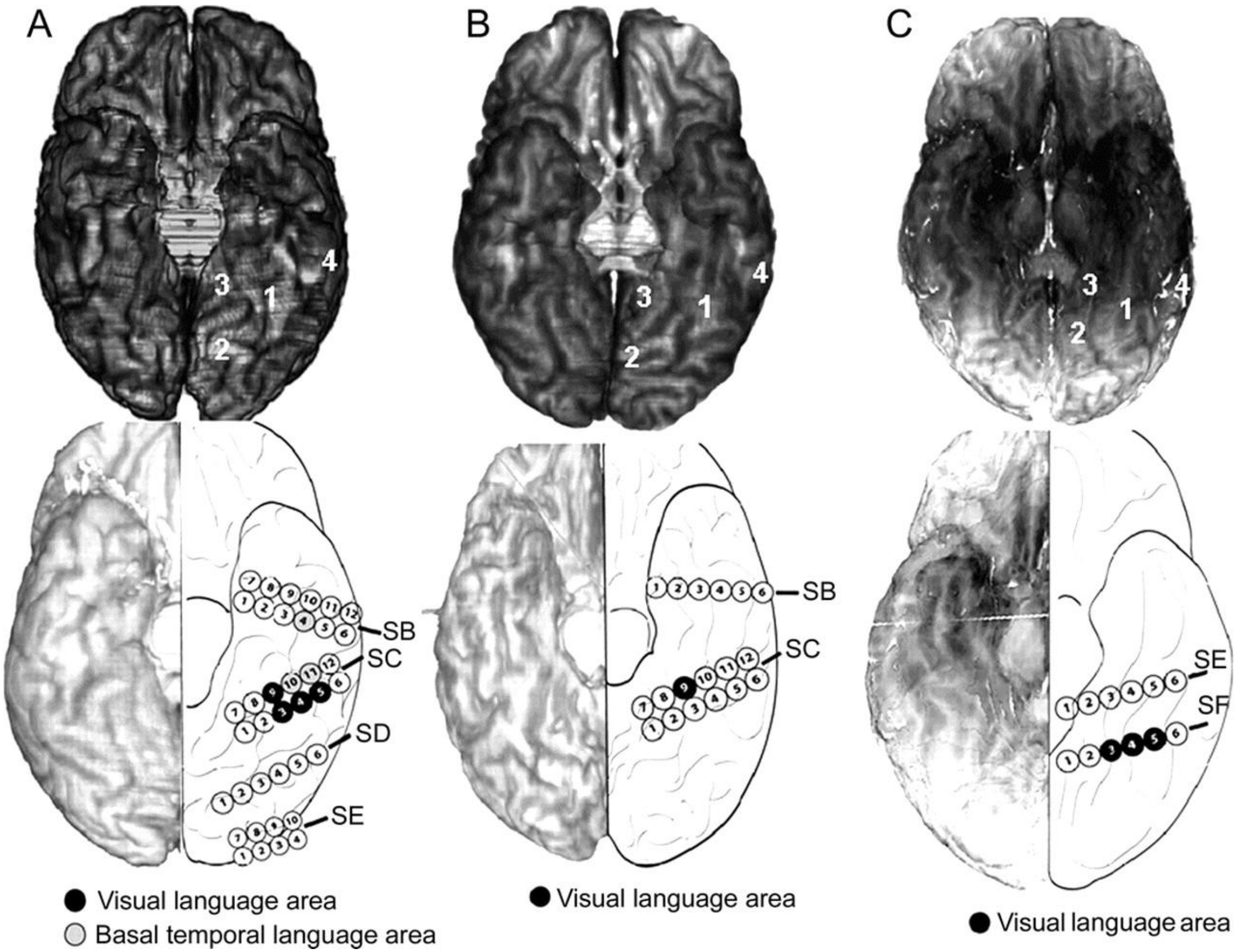


# Category-Specific BOLD Responses in Healthy Brain




Mahon & Caramazza, *Ann Rev Neurosci*, 2009

# Evidence for a Visual Language Center in basal temporal cortex



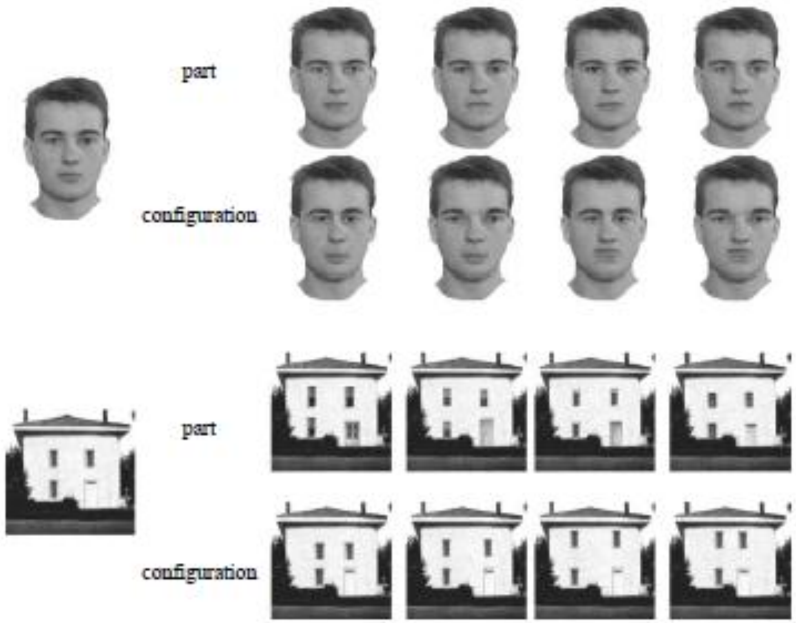

**Mani J et al. Neurology 2008;71:1621-1627**

©2008 by Lippincott Williams & Wilkins

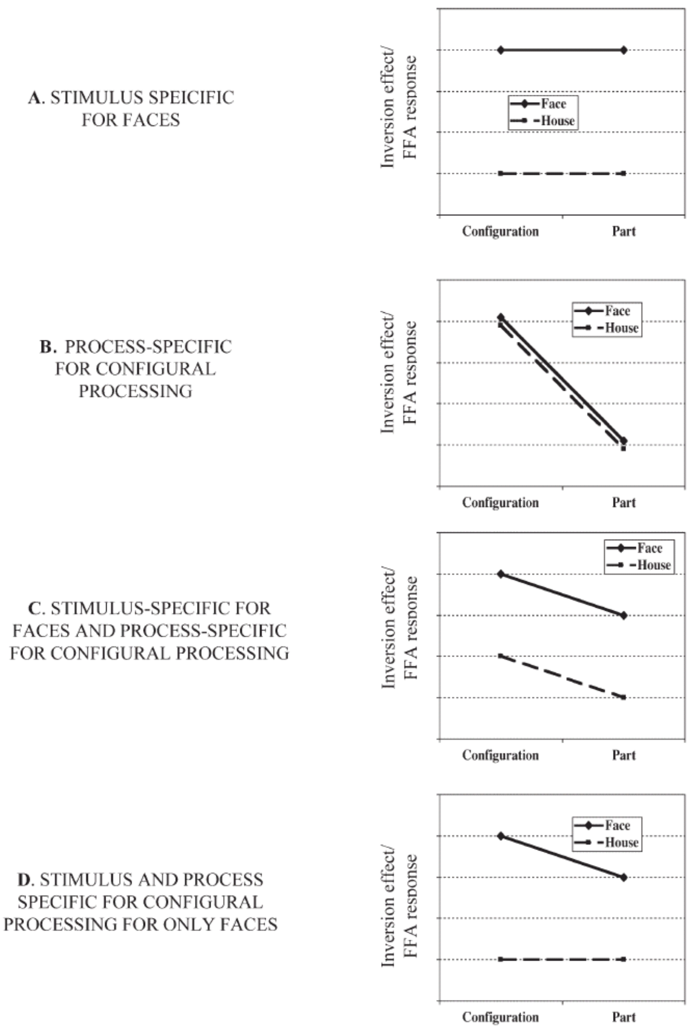
# Functional Implications of Domain-Specificity

- Origins
  - Evolution (survival value)
  - Expertise (becomes more specialized with experience)
- Advantages
  - Efficiency – small neuronal population dedicated to specific function – Simon's "near decomposition"
  - Dynamics – minimize "wiring length" in cortex
  - Fidelity – provide consistent ability to perform function
- Disadvantages
  - Graceful degradation not possible

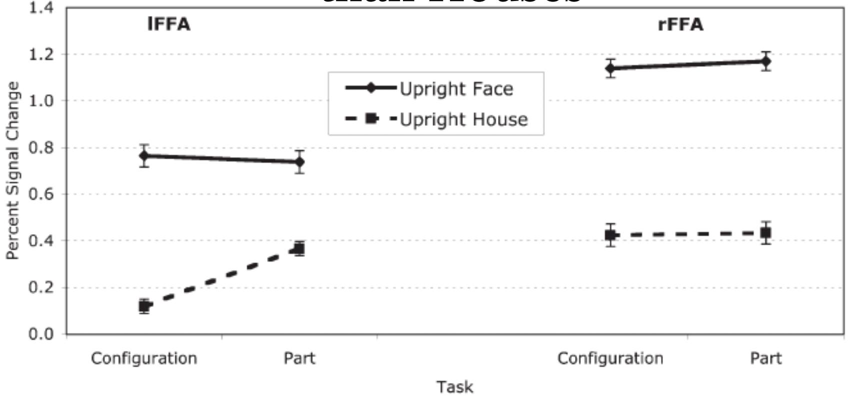
# Evidence for Face-Specificity in FFA

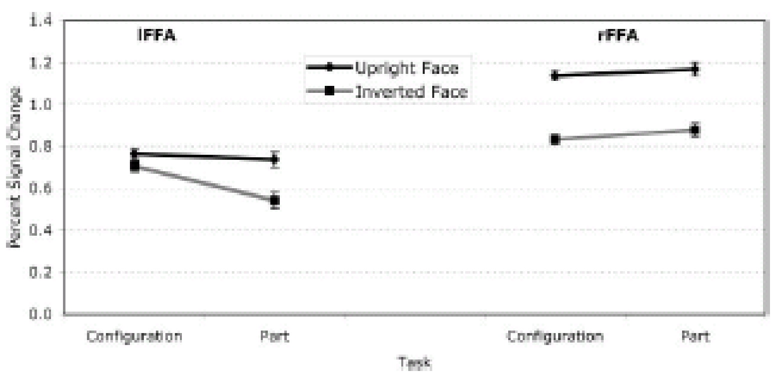



predictions

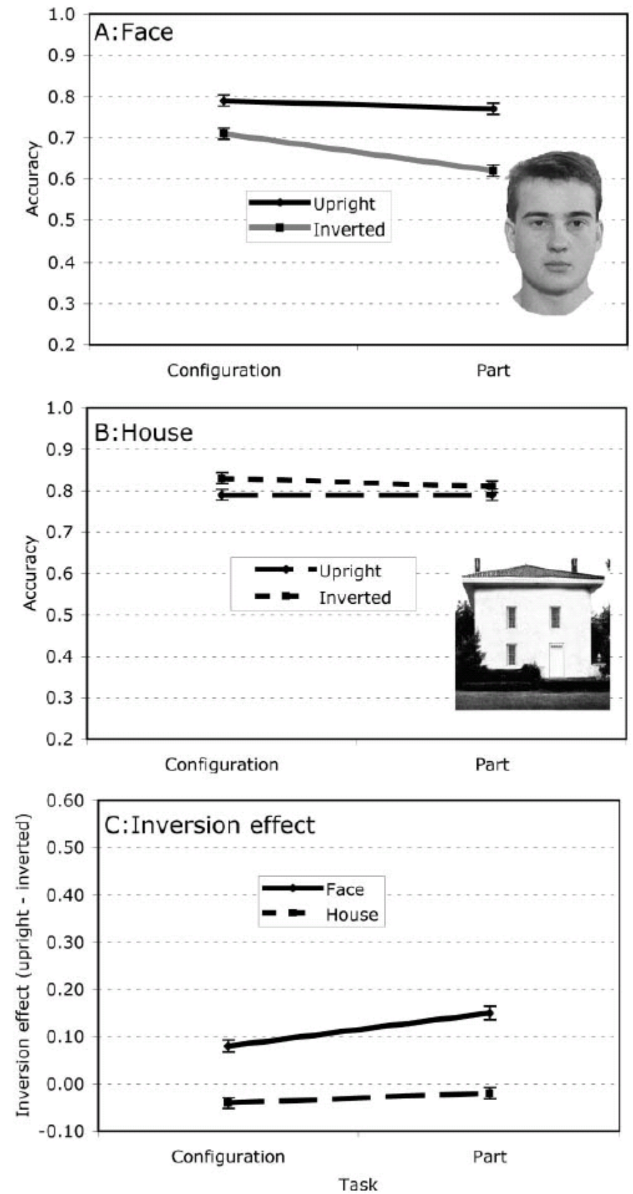


1. Higher Signal Change to Faces than Houses




2. Inversion Effect seen in both Part and Configuration Condition for faces




3. No Inversion Effect for Houses

# Specificity

- How specific, or exclusive, is the neural response to in-category items?
- Two “extreme” outcomes
  - Neural response of module ONLY to target category
  - Neural response of module driven by some physical or semantic dimension on which multiple categories differ in a “continuous” fashion

# Stimuli Used in Category-Specificity Experiments

Downing, et al., *Cerebral Cortex*, 2006

# Differential Response of FFA for Faces

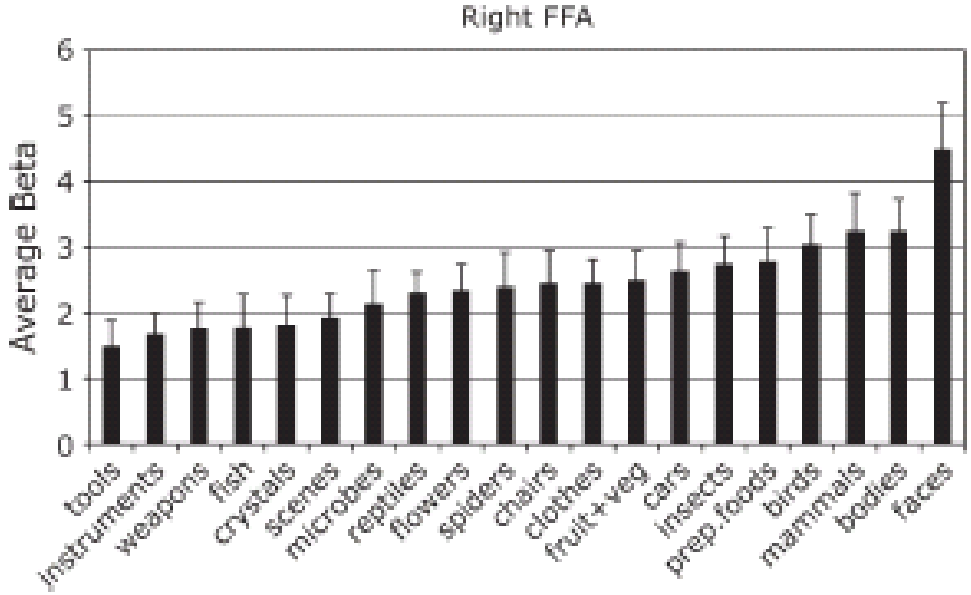



**Figure 2.** Mean parameter estimate of the response to each category in the FFA. Each ROI was identified individually in each subject. The data sets used to define the ROIs were independent from those used to produce the values in this figure and in Figures 3–7. Error bars reflect the standard error of the mean.

Downing, Chan, Peelen, Dodds, & Kanwisher, *Cerebral Cortex*, 2006

PPA and Scenes

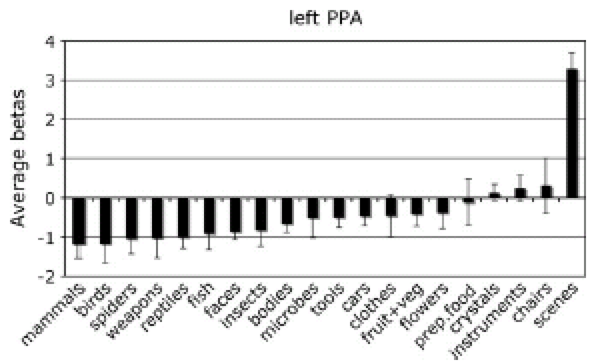



**Figure 3.** Mean parameter estimate of the response to each category in the left hemisphere PPA. Conventions as in Figure 2.

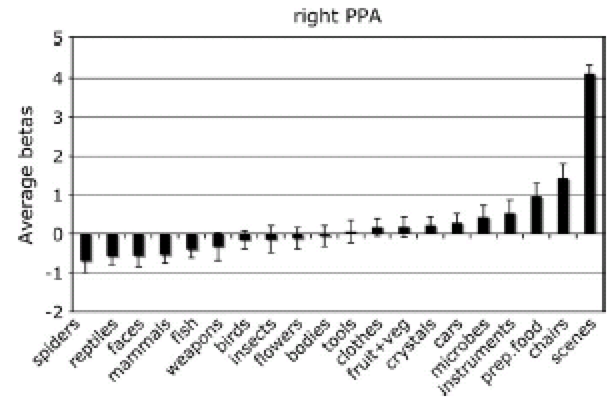



**Figure 4.** Mean parameter estimate of the response to each category in the right hemisphere PPA. Conventions as in Figure 2.

EBA and Bodies

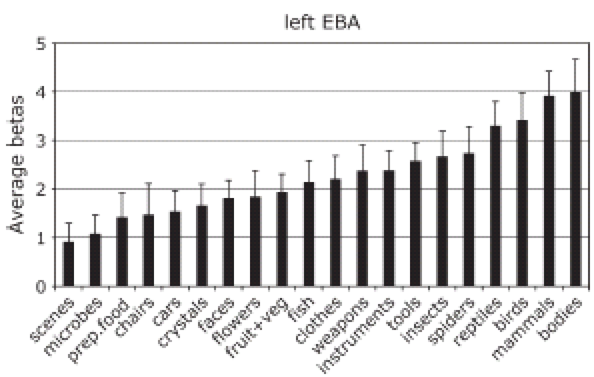



**Figure 5.** Mean parameter estimate of the response to each category in the left hemisphere EBA. Conventions as in Figure 2.

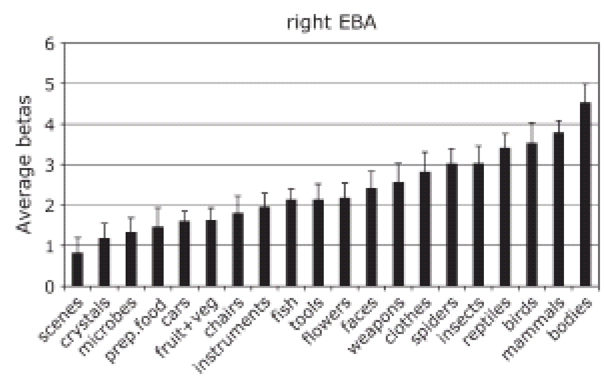
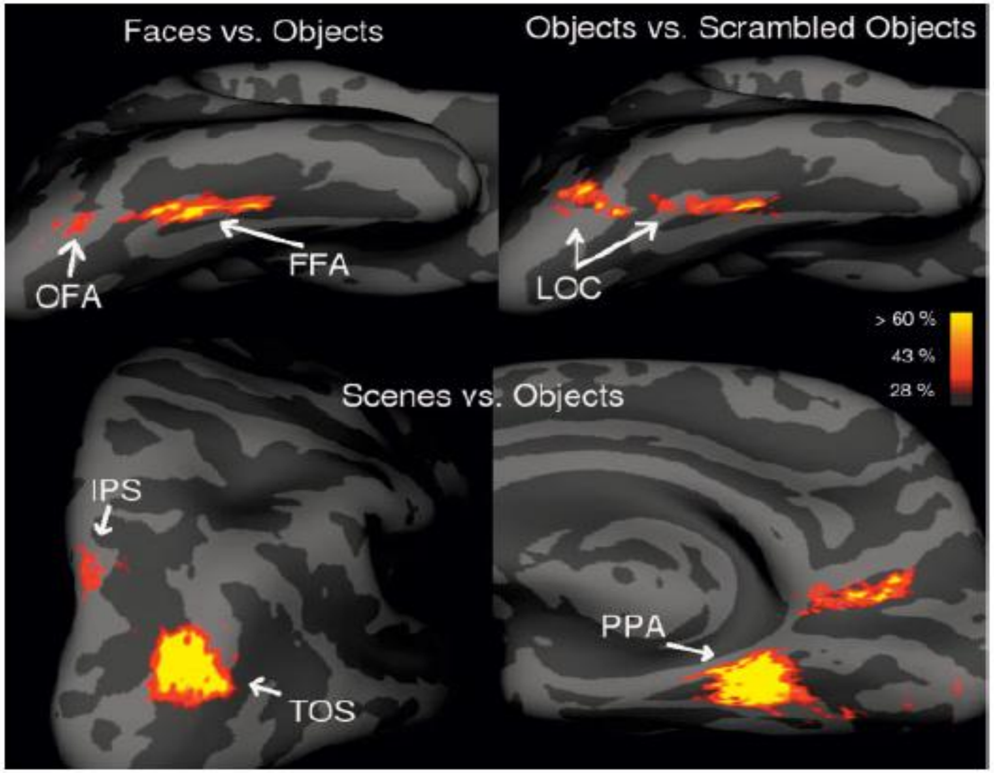
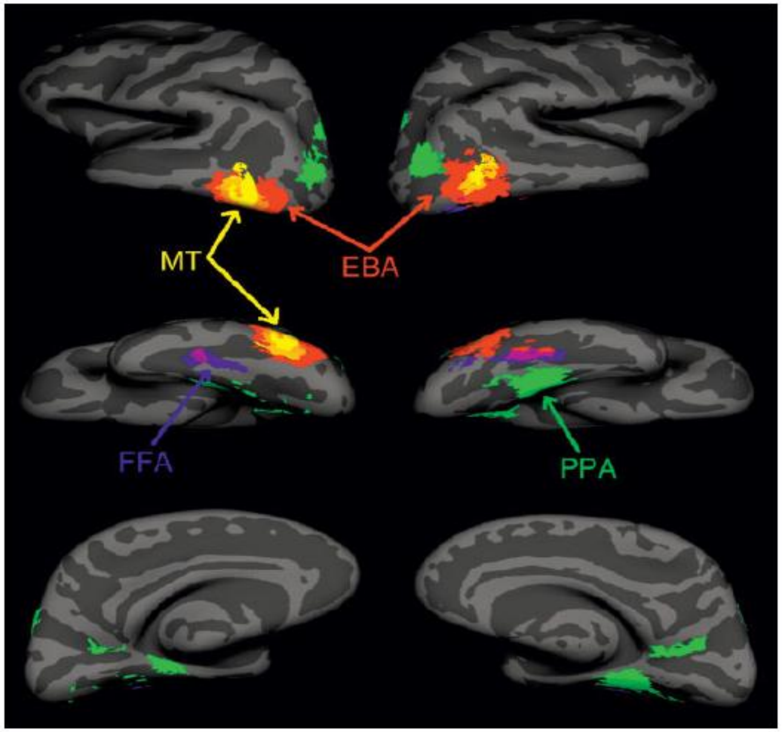



**Figure 6.** Mean parameter estimate of the response to each category in the right hemisphere EBA. Conventions as in Figure 2.

Downing, Chan, Peelen, Dodds, & Kanwisher, *Cerebral Cortex*, 2006

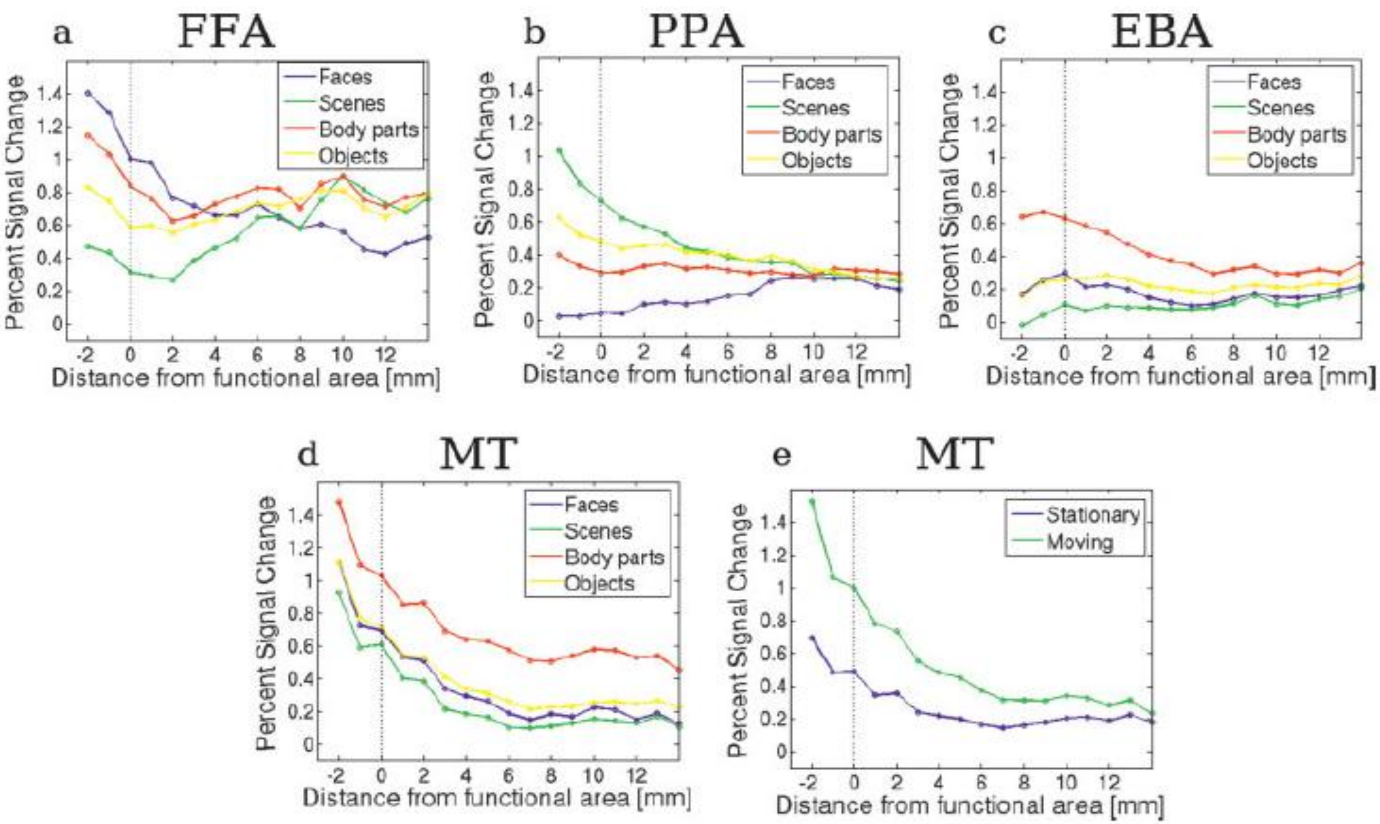



Are Visual “Modules” really selective?



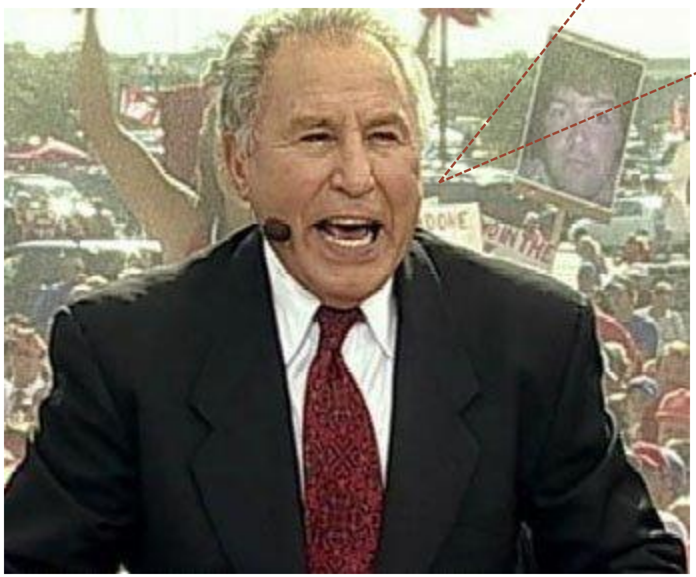

Spiridon, Fischl, & Kanwisher, <u>Hum Brain Mapping</u>, 2006

# Activation Patterns in "Visual Modules": Specialization is not 'pure'

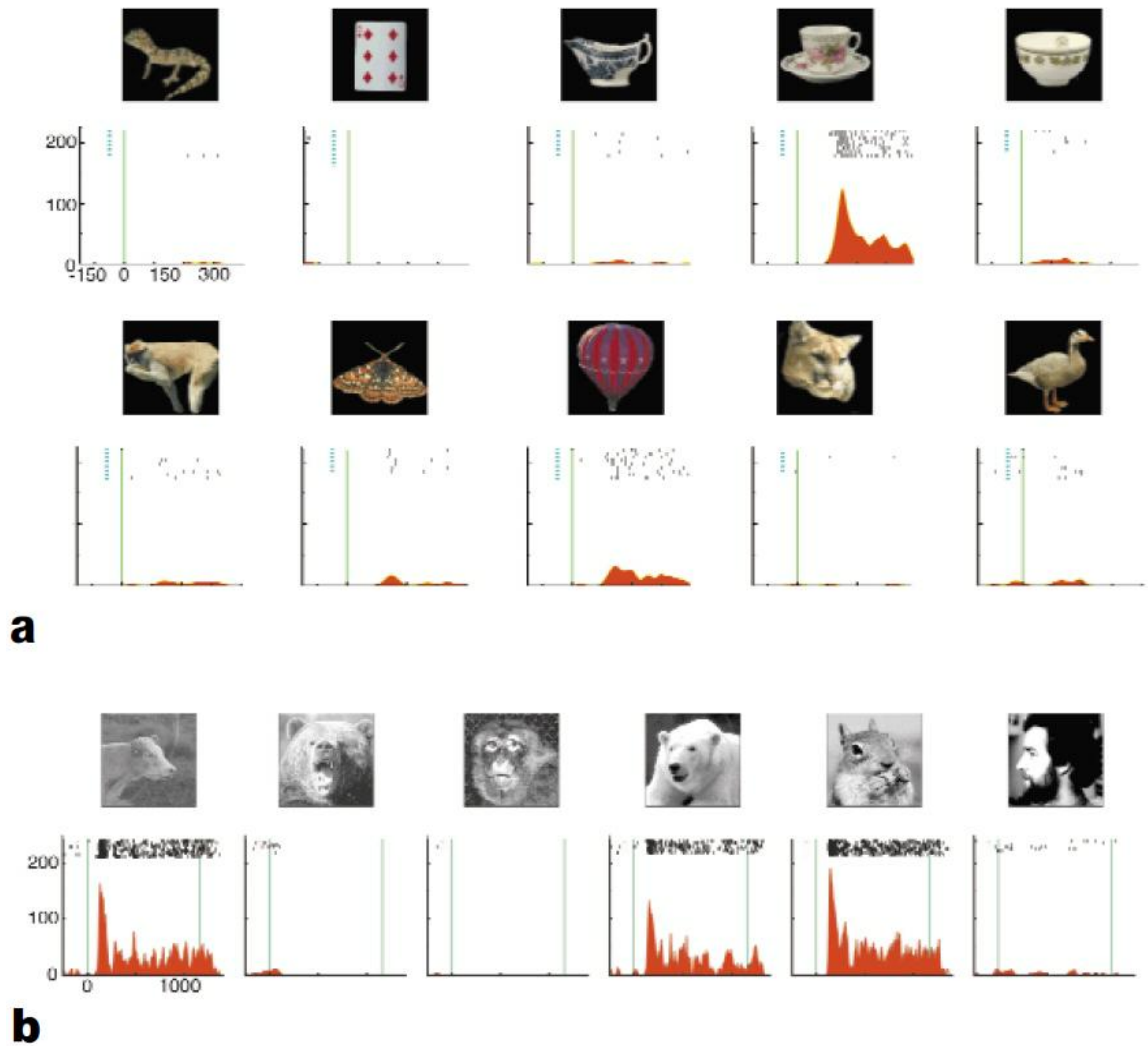



Spiridon, Fischl, & Kanwisher, Hum Brain Mapping, 2006

Not so fast,
my
friend!!!!



# Complex Selectivity of Inferotemporal Neurons to Specific Stimuli




Tarr & Gauthier, 2000

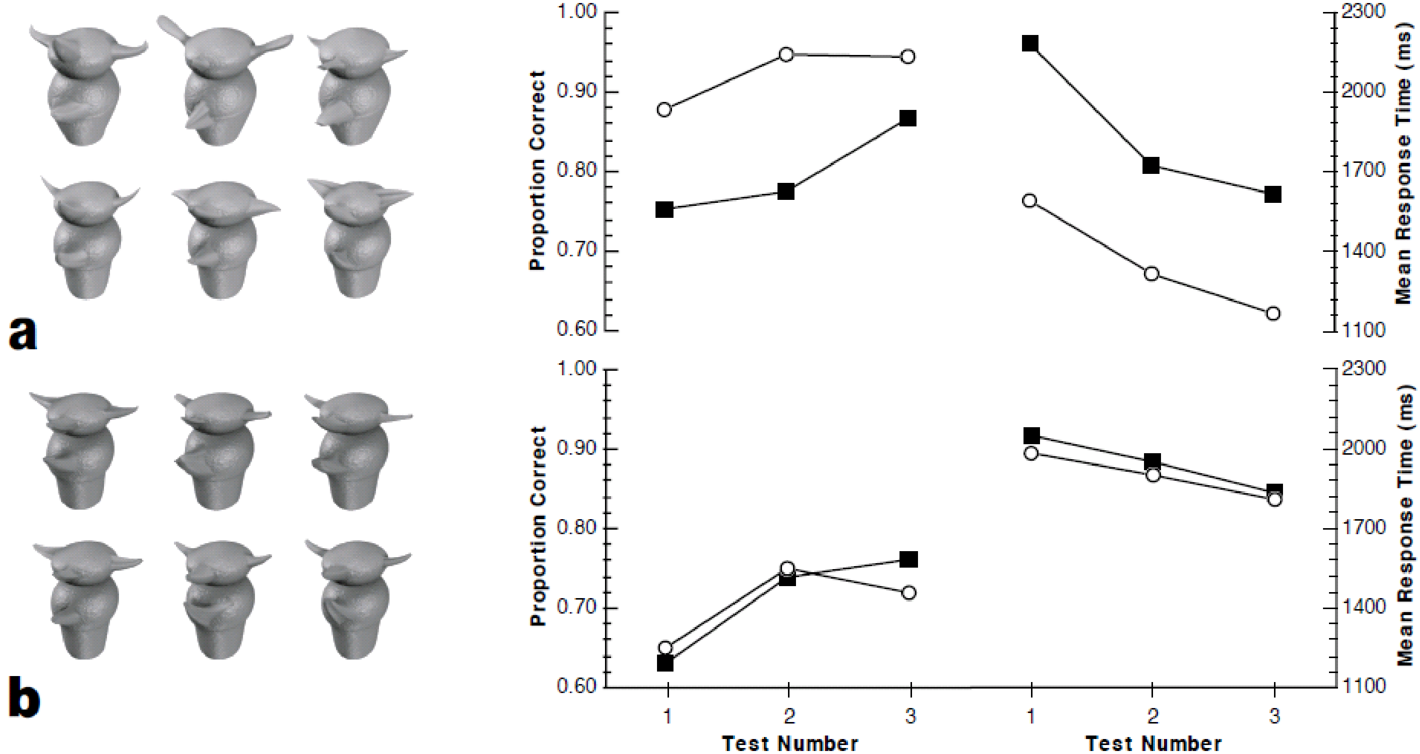
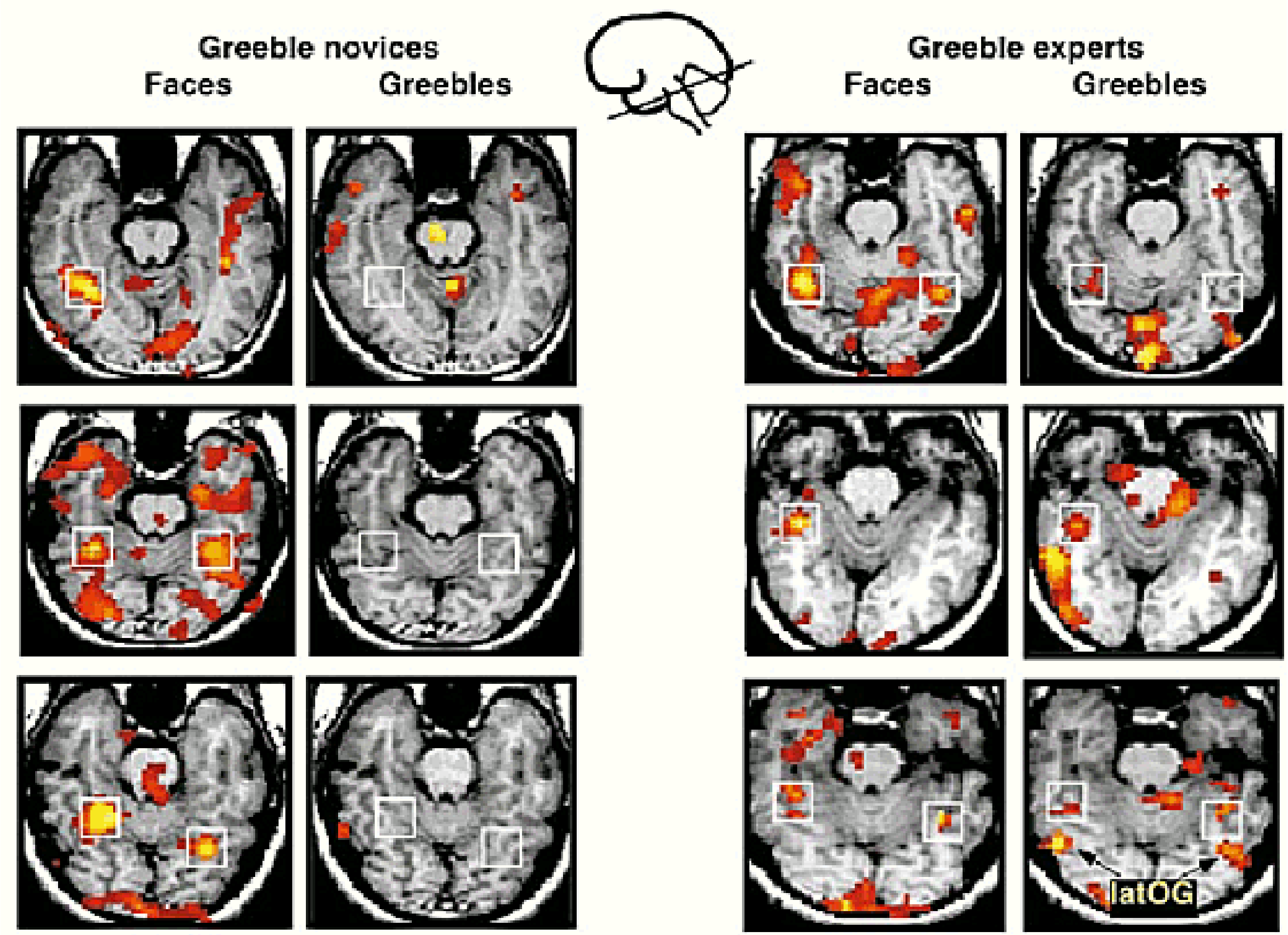
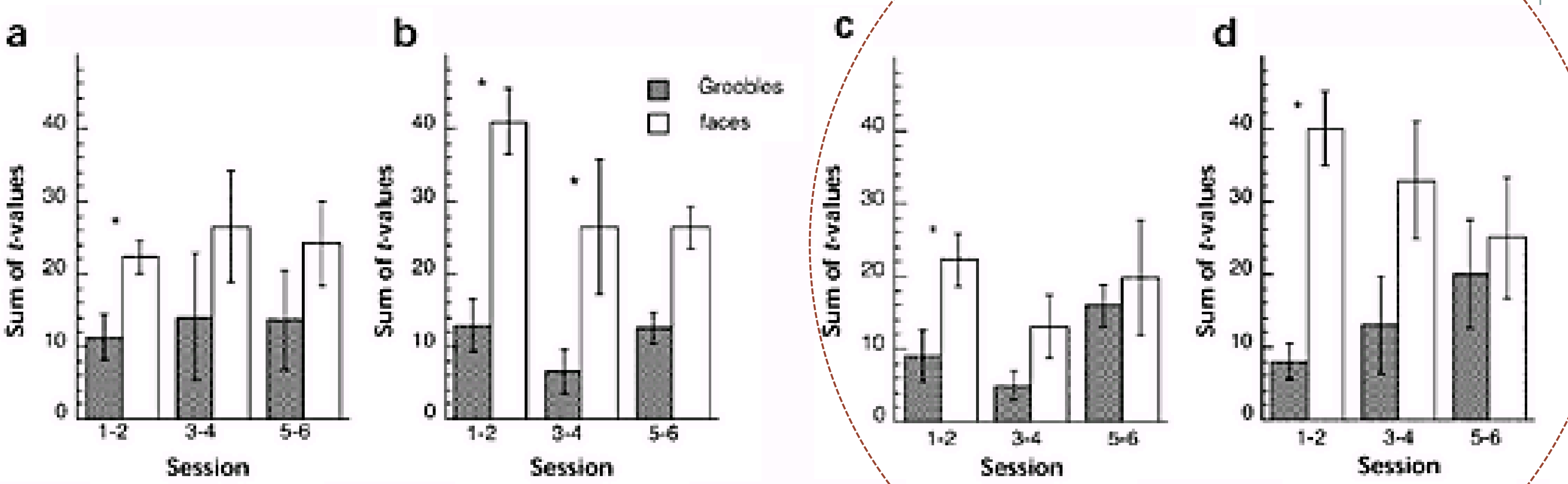



**Fig. 1.** Examples of Greebles. (**a**) Greebles from a set that Greeble experts could learn to recognize faster than novices. (**b**) Another set of Greebles, which the same experts could not learn faster than novices, presumably because they are more visually homogeneous than Greebles in the training set. Filled squares denote data from novices, and open circles denote data from experts[43].




Gauthier, et al., *Nature Neurosci*, 1999

Posterior (L and R) FFA activation increases with expertise




L anterior

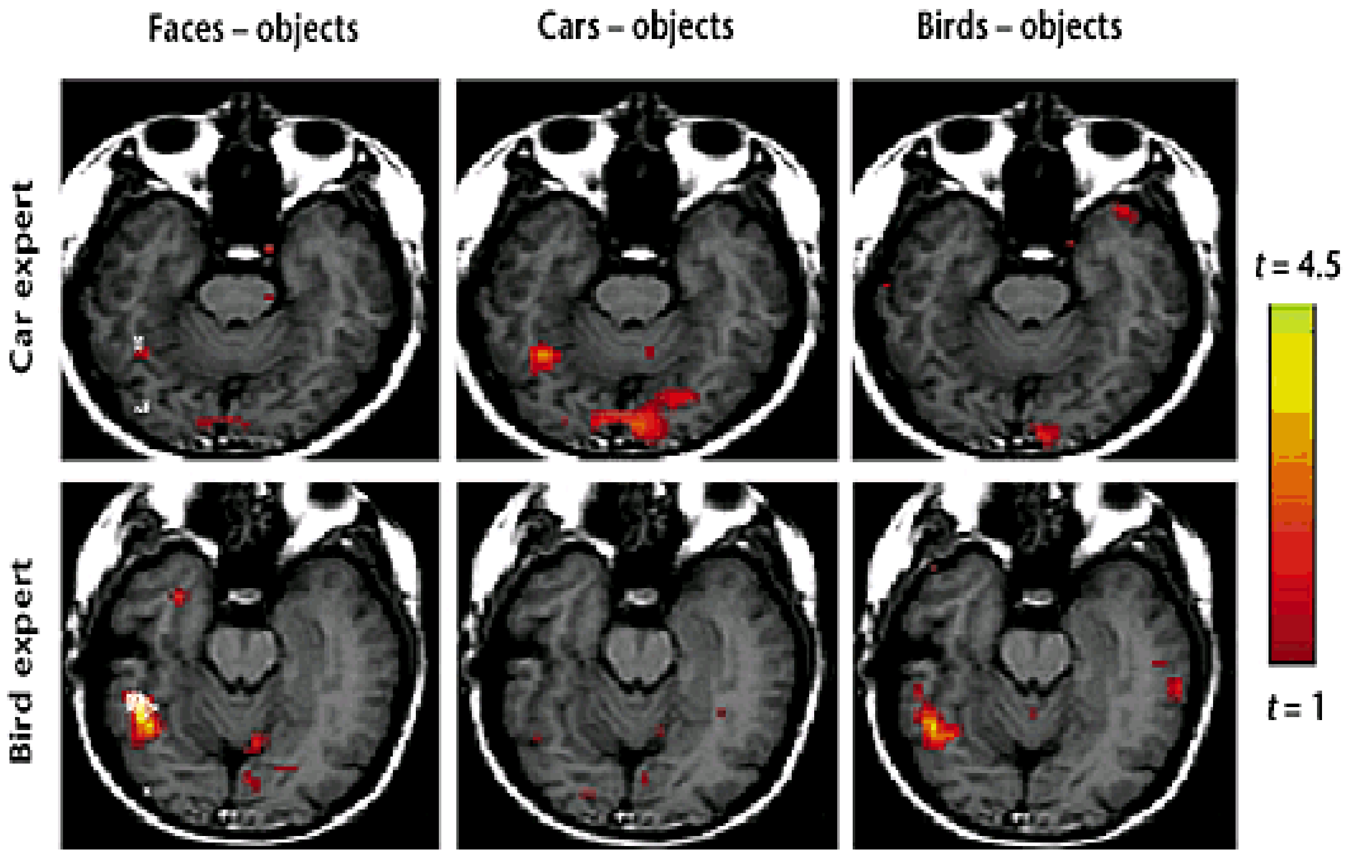
R anterior

L posterior

R posterior

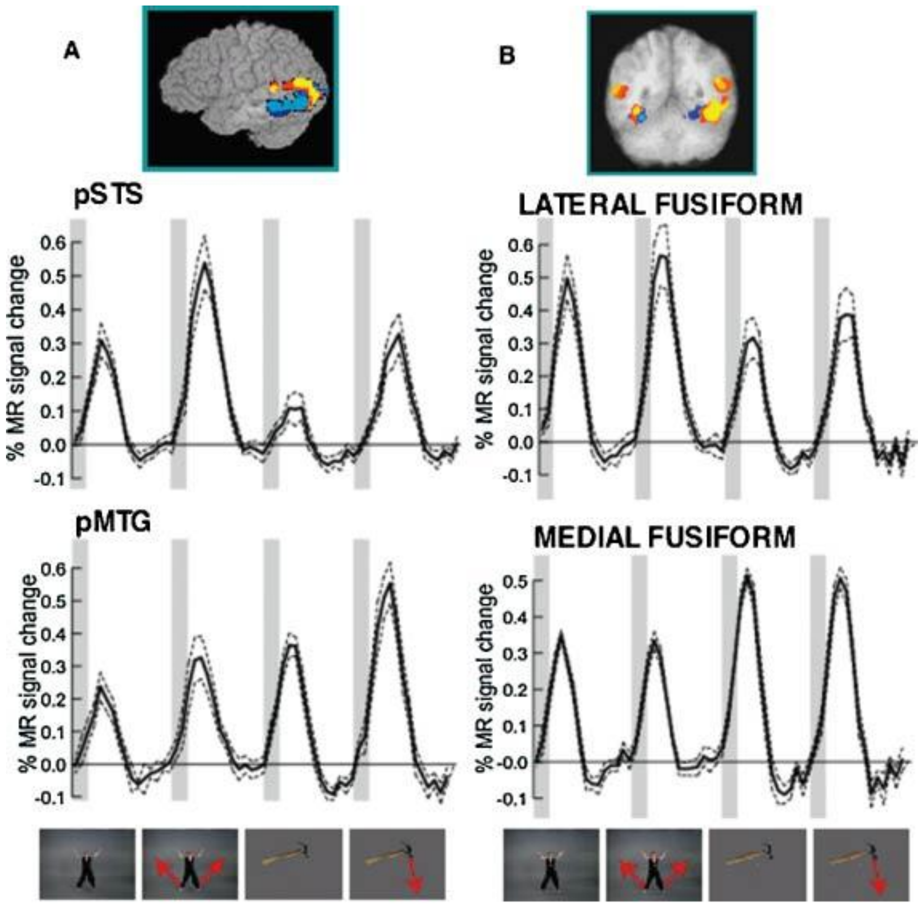
Gauthier, et al., *Nature Neurosci*, 1999

Right FFA shows expertise effect for cars and birds




Gauthier et al., *Nature Neurosci*, 2000

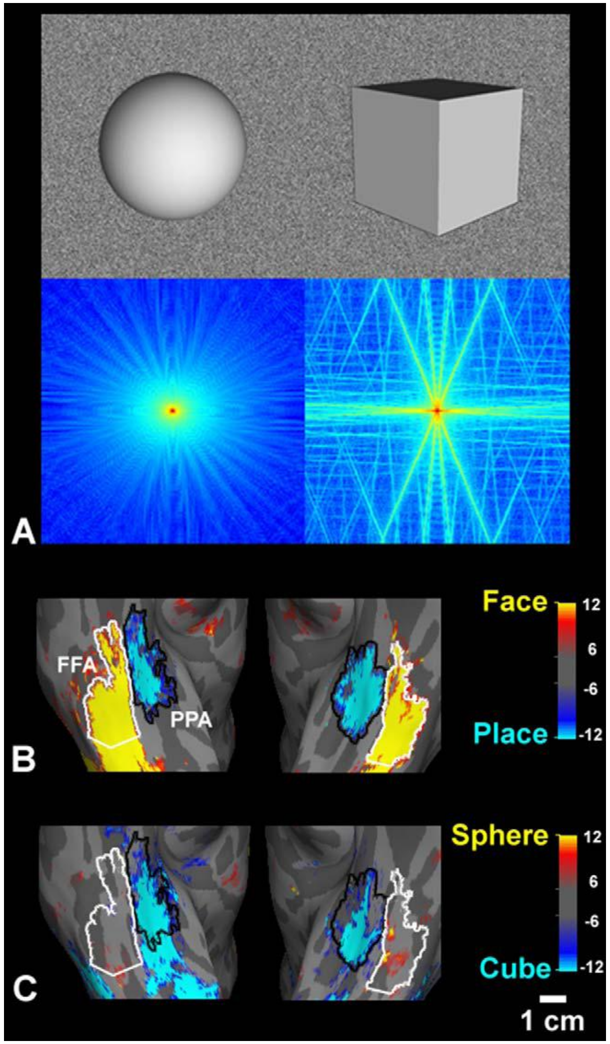
Lateral Cortical Areas: Category + motion
Ventral Areas: Category Only

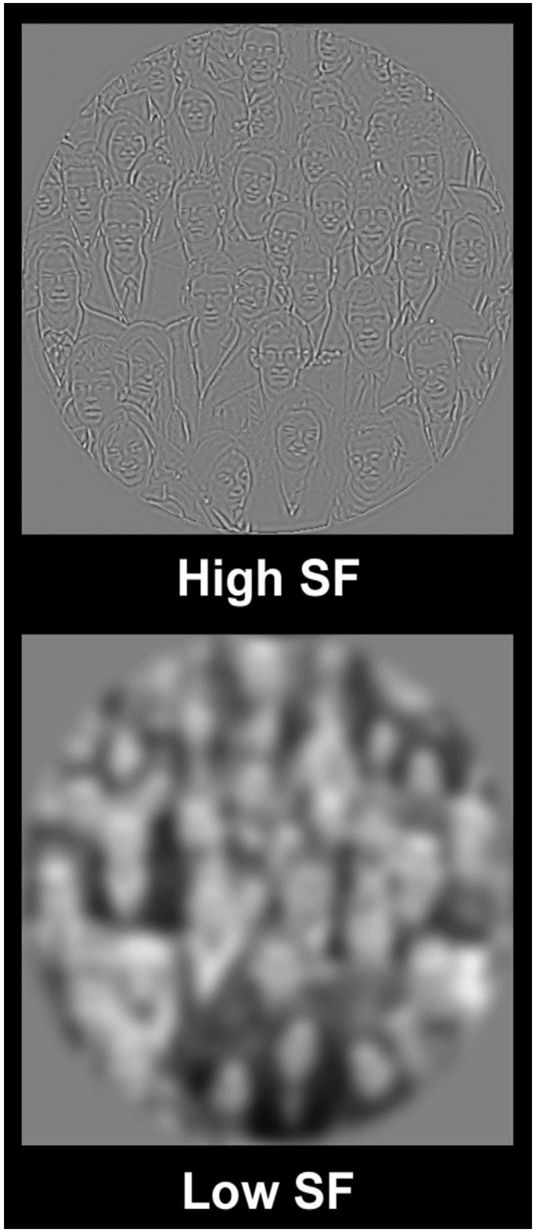



Martin A. 2007.
Annu. Rev. Psychol. 58:25–45

Property-based (motion vs. not) vs. Category-based (people v. tools) activation

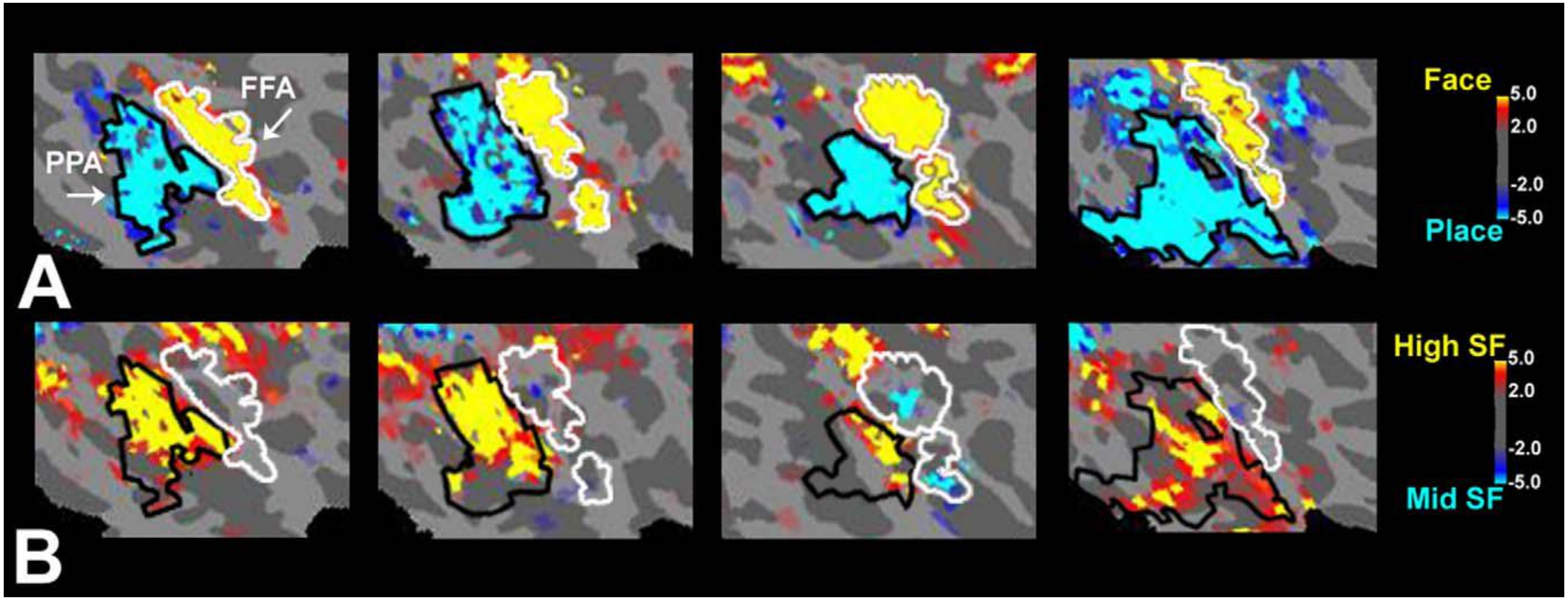
“Domain-Specificity” of PPA?




Rajimehr, et al, *PLoS Biology*, 2011

PPA response is not place-specific, per se, but specific to high SF




Rajimehr, et al, *PLoS Biology*, 2011

# Summary

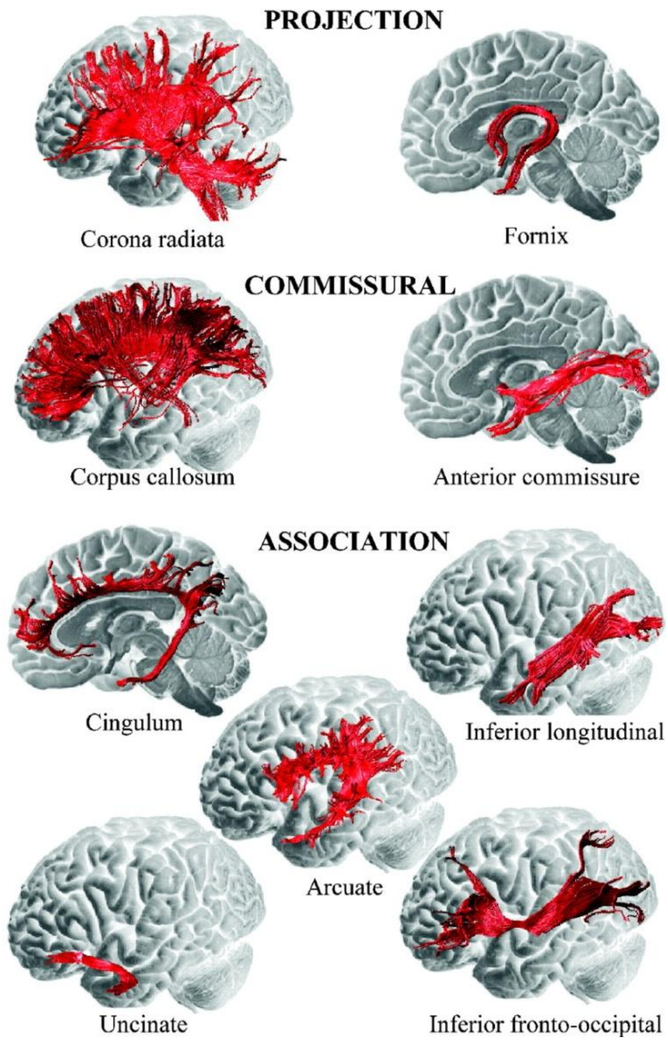
- Areas do exist that seem ‘preferentially involved’ in the neural network that processes specific object categories
- Effective stimuli that elicit single-unit activity can vary nonintuitively
- Specific characteristics of neuronal sensitivities in these regions are controversial

# Disconnection vs. Processor Impairment

# Key Questions

- To what extent can deficit syndromes be conceptualized as network disconnections vs. the result of impaired processors?
- What are the key differences between the two possibilities?
- What classic syndromes are likely the result of disconnection?
- What does contemporary brain science have to say about disconnection syndromes?

**Meynert's classification of white matter tracts visualized with diffusion tensor tractography and superimposed on medial and lateral views of the brain surface.**




Cortical to subcortical

Hemisphere to hemisphere

Ipsilateral cortical to cortical

**Catani M , ffytche D H Brain 2005;128:2224-2239**

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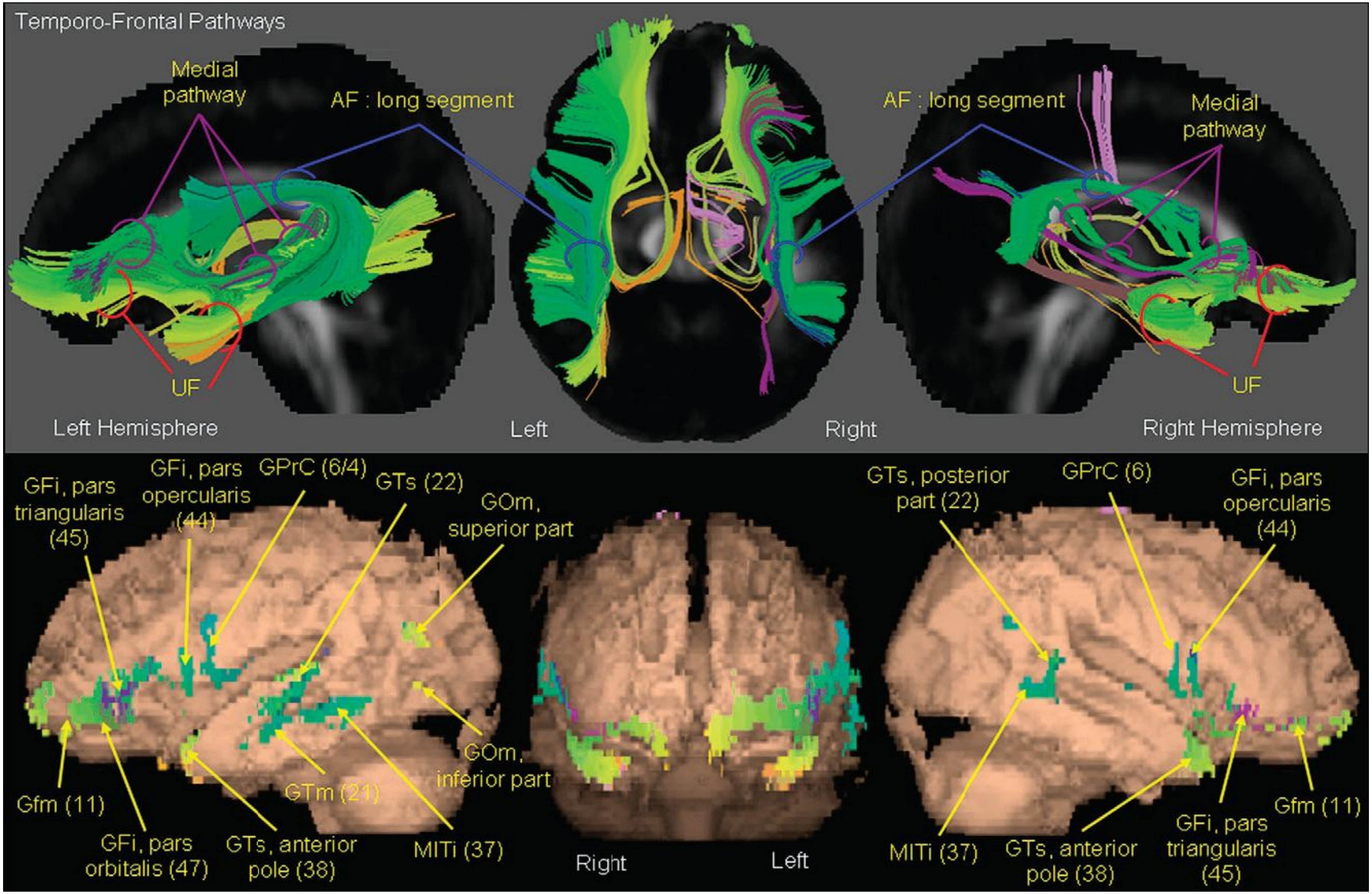
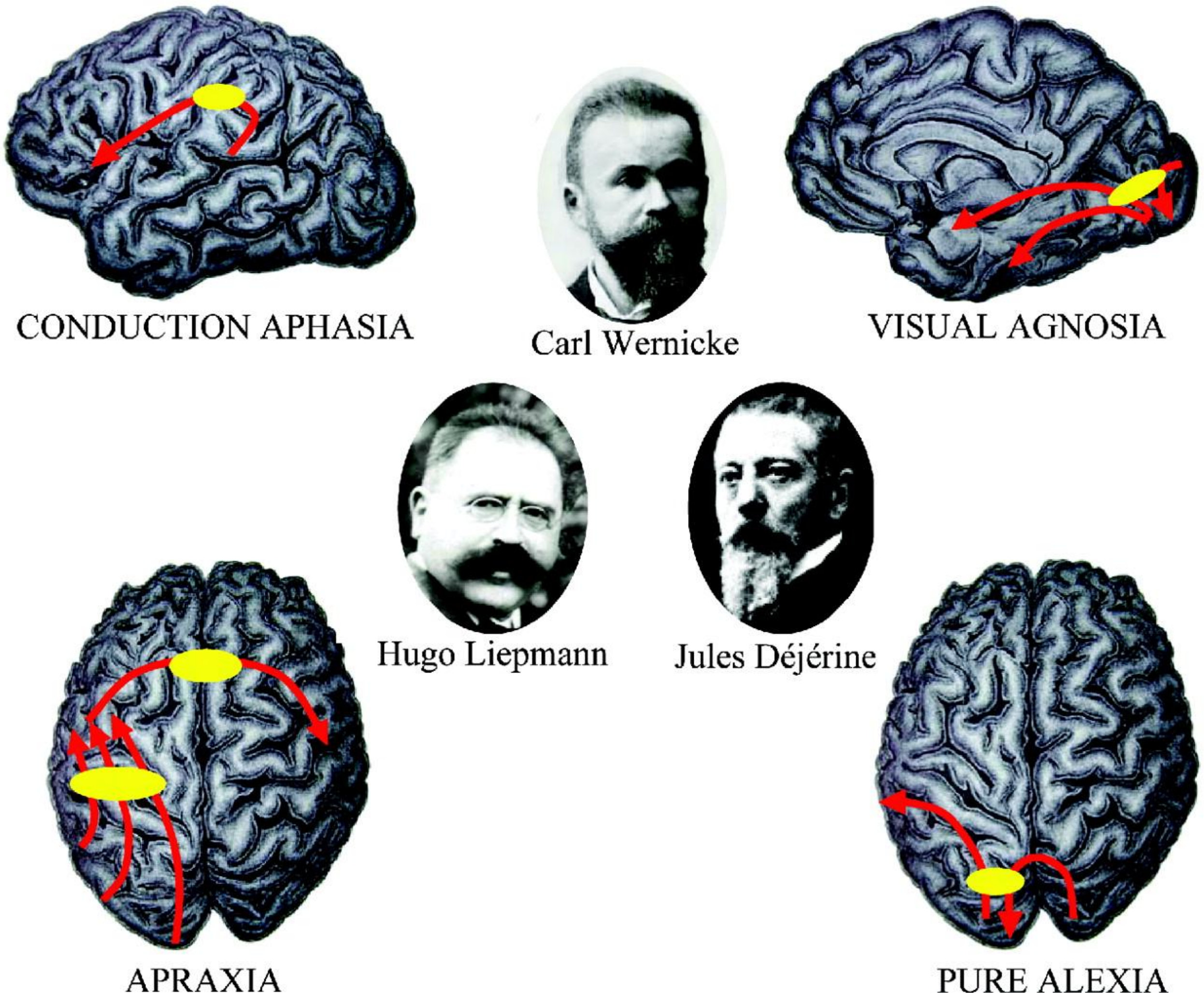



Barrick, et al., Cerebral Cortex, 2006

# The classical disconnection syndromes.

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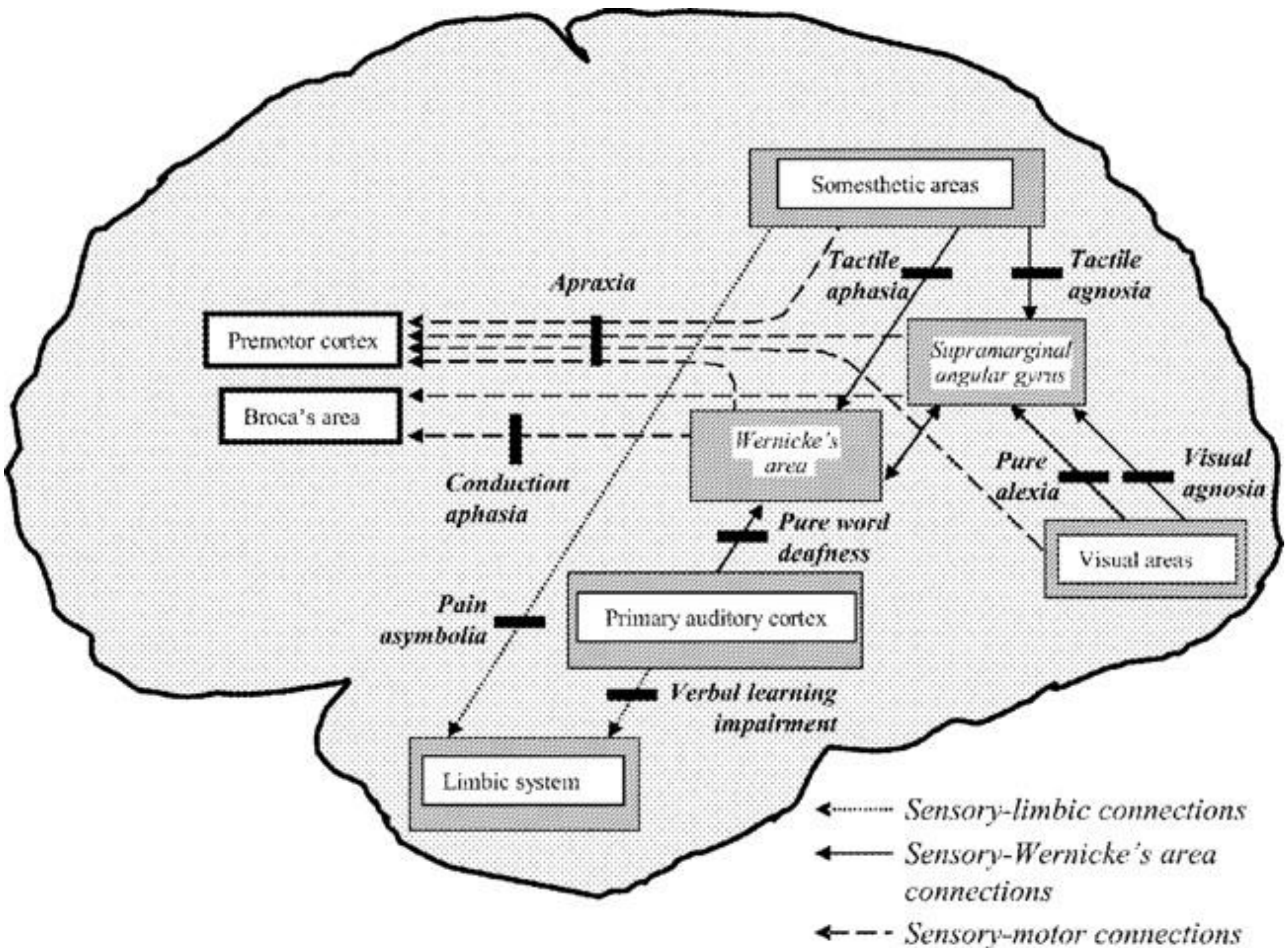
## Geschwind's disconnection syndromes.

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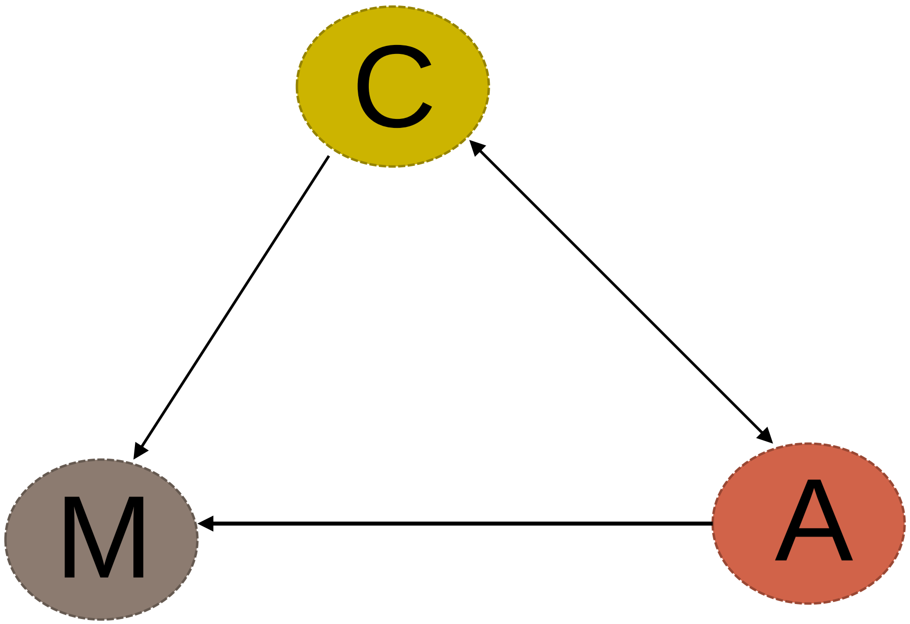



Lichtheim's Model

# A human cerebral deconnection syndrome

## A preliminary report

Norman Geschwind, M.D., and Edith Kaplan, M.A.

We propose in this paper to present a patient whose clinical picture appears to us to be most simply explainable by a partial deconnection of the two cerebral hemispheres. He appears to behave as if there were 2 nearly isolated half-brains, functioning almost independently.

In the early years of this century several cases were described which showed some of the phenomena that are present in our patient. Sittig[1] reviews these cases in his monograph on apraxia. The earlier workers generally described these cases as showing apraxia and apractic agraphia of the left side and left-sided astereognosis and attributed these findings to lesions of the corpus callosum.

In the 1940's considerable doubt was cast on the role of the corpus callosum by the extensive studies of Akelaitis[2] and his co-workers on humans whose corpora callosa had been sectioned surgically (to prevent the interhemispheric spread of seizures) and who subsequently presented virtually no abnormalities. Earlier physiological work in animals also failed to show convincing disturbances. Bremer, Brihaye, and André-Balisaux[3] have reviewed this literature. By contrast, in the last five years, the work of Sperry[4] and his co-workers has convincingly proved that in animals, section of the callosum produces behavior which is most simply explained as resulting from deconnection of the 2 hemispheres. It was Sperry's work which alerted us to the possibility of deconnection syndromes in man.

Our patient shows behavior similar to that described by the earlier workers. In addition we have observed several manifestations not previously mentioned. Detailed anatomical confirmation of the localization of the lesion is not yet available. The patient continues to be studied actively at this time. However, in view of the unusual character of these findings, we are presenting this brief clinical description as a preliminary report in the hope of stimulating other workers to look for similar cases and to investigate their anatomical substratum. A more detailed report of this patient will be published at a later date.

### CASE REPORT

P.J.K., (BVAH U-53490), a 41-year-old white, married police officer, was admitted to the Boston V.A. Hospital, Neurology Section, on March 2, 1961. One month before admission the patient had begun to develop dull headaches, primarily over the left orbit, lasting several hours, recurring 3 to 4 times a week, and frequently associated with nausea and vomiting. The members of the family had over the previous few months noticed increasing behavioral changes manifested by indifference; apathy; forgetfulness; diminished alertness; confusion for dates, events, and people; diminution in personal neatness; and increased friction in interpersonal relations, particularly at work.

The patient had no significant history of birth or childhood illness. He had been graduated from high school at 18, had served in the Navy from 1941 to 1945, and since 1949 had been a policeman. Past history and family history were otherwise not relevant.

General physical examination revealed a well-developed, well-nourished man. The temperature was 98.6° F., blood pressure was 110/90, and pulse, 80. There were no significant abnormalities in the remainder of the general examination.

---

From the Aphasia Unit, Section of Neurology, and the Section of Psychology, Boston Veterans Administration Hospital; Section of Psychology, Massachusetts Institute of Technology, and Department of Neurology, Boston University School of Medicine.

Supported in part by research grants from the National Institutes of Health to the Section of Psychology, Massachusetts Institute of Technology (M-1802) and to the Department of Psychology, Clark University (M-4187), Worcester, Massachusetts.

Portions of the results were presented at the Boston Society of Psychiatry and Neurology on December 14, 1961.

# Brief History

- EFK saw 41-year old, right-handed policeman grasping doorknobs; had translated a German paper indicating PMA was a form of grasp reflex
- Headache, apathy, forgetfulness, confusion
- Resection of left frontal lobe and <u>frontal polar artery</u>
- Mild tremor, marked grasp, in R hand; dense weakness of R leg
- Sensory grossly normal on R, normal on L, but obscured by problems reporting L-sided sensory experiences
- <u>EFK discovered on 5/22/61 that the patient could not write with his left hand.</u>

# Spared and Impaired Abilities

| Patient could… | Patient could not… |
|---|---|
| Write spontaneously and to dictation with right hand, though there were grasp-related writing deficits | Write with left hand (aphasic) |
| Type with right hand | Type with left hand |
| Name objects placed in right hand | Name objects placed in left hand |
| Draw objects placed in right hand | Select, write the name, or draw with one hand an object placed in the other hand |
| Appropriately handle objects in both hands | Recreate with left foot an object drawn in his left hand |
| Perform matching-to-sample with both hands | Perform actions with his left hand |
| Perform actions with right hand | |
| Imitate examiner's movements with either hand | |
| Perform bilateral movements involving both hands | |

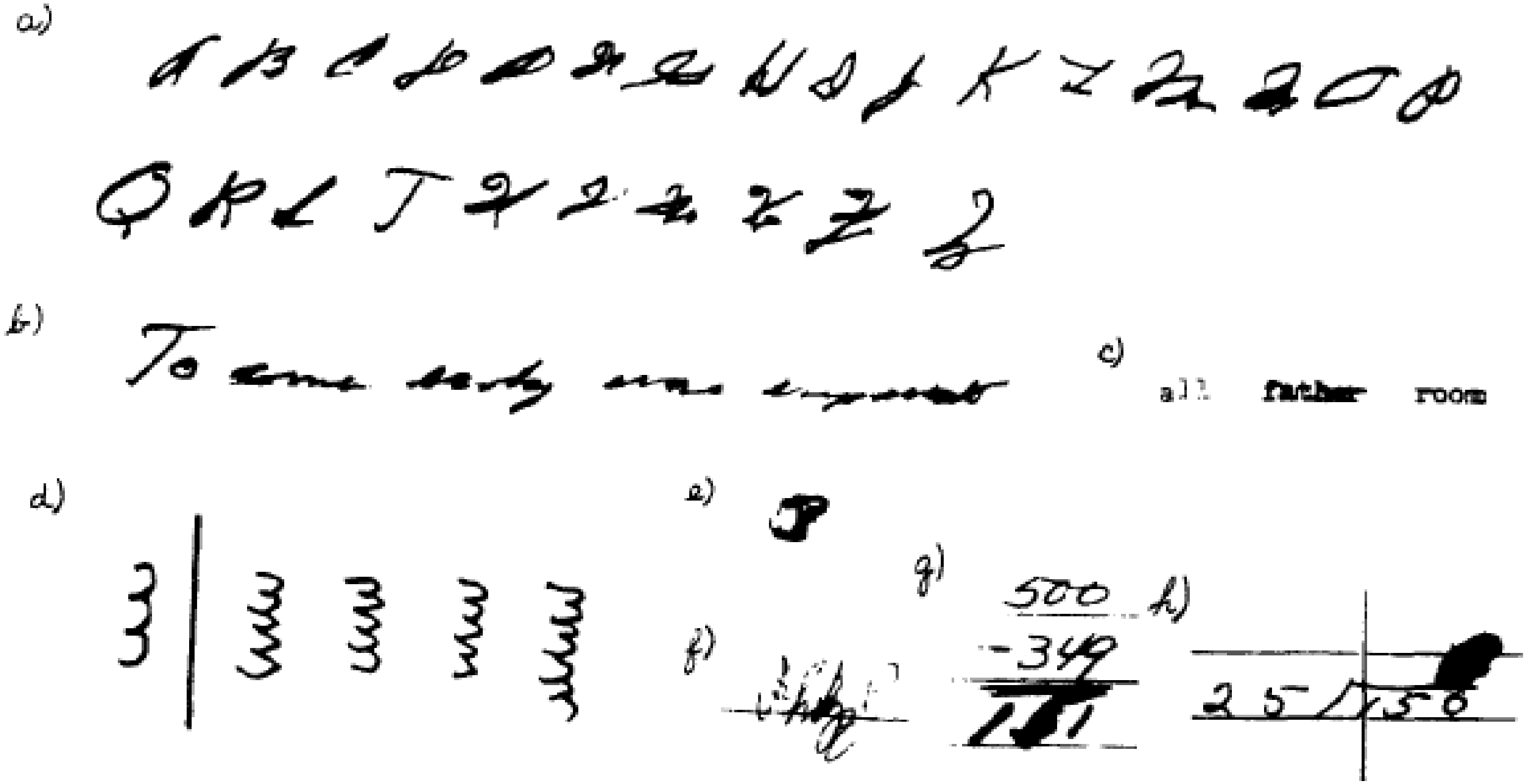


Fig. 1. Samples of performances with the right hand, demonstrating the effect of the grasp reflex: (a) the alphabet; (b) the sentence, "To come early was impossible" written to dictation; (c) the words, "all," "father," and "room" typed with the right index finger; (d) to the left of the vertical line examiner's model three-looped figure, to the right of the line patient's successive attempts to copy the model; (e) the number "3" written to dictation; (f) the patient's preoperative writing of his first name; (g) and (h) the heavily written numbers are the patient's solutions to the problems written by the examiner (preoperative).

# Right Hand

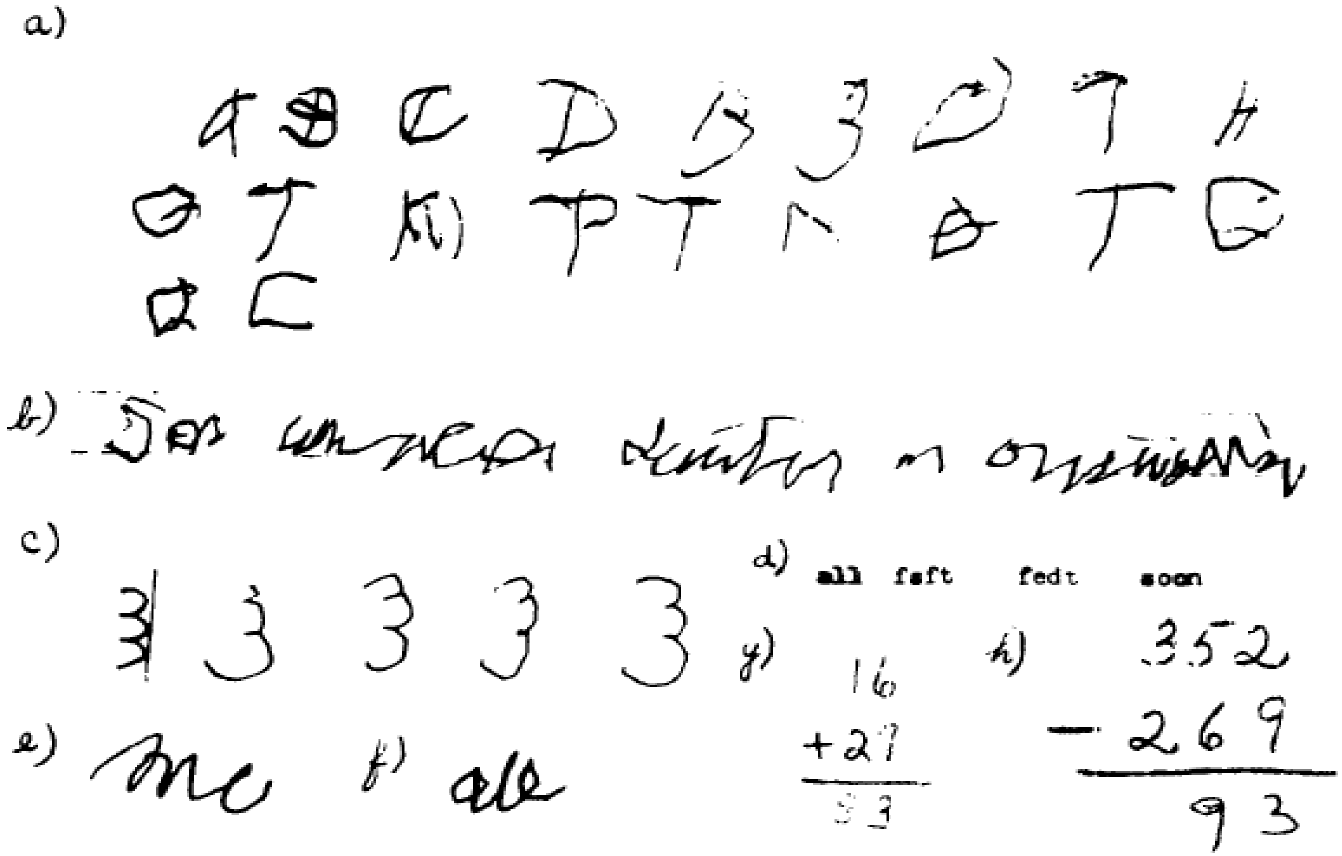
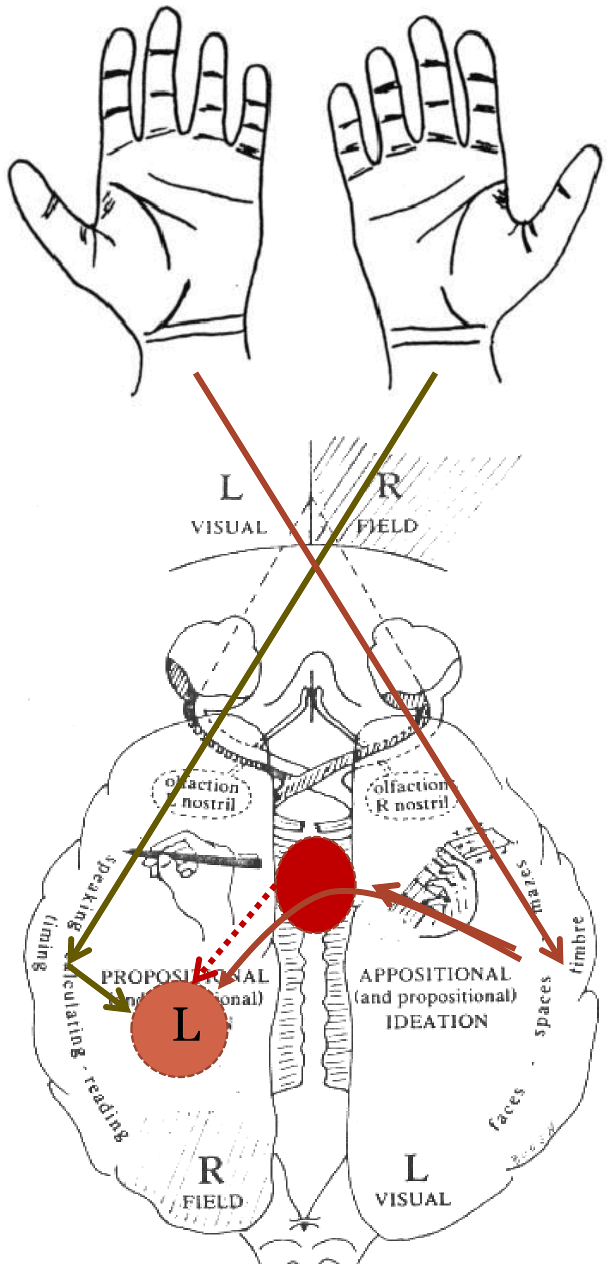



Fig. 2. Samples of performances with the left hand, demonstrating errors in language and calculation along with the absence of disturbances due to grasp reflex: (a) the alphabet; (b) the sentence, "To come early was impossible" written to dictation; (c) to the left of the vertical line examiner's model three-looped figure, to the right of the line patient's successive copies of the model; (d) attempts with left index finger to type the words, "all," "father," "father" (the second being a spontaneous attempt to correct the first error), and "room;" (e) attempt to write "run" to dictation; (f) attempt to write "go" to dictation; (g) and (h) the patient's solutions to the problems set by the examiner.

# Left Hand - aphasic



L
VISUAL
R
FIELD
olfaction
L nostril
olfaction
R nostril
speaking
timing
calculating · reading
PROPOSITIONAL
L
APPOSITIONAL
(and propositional)
IDEATION
mazes
timbre
spaces
faces
R
FIELD
L
VISUAL

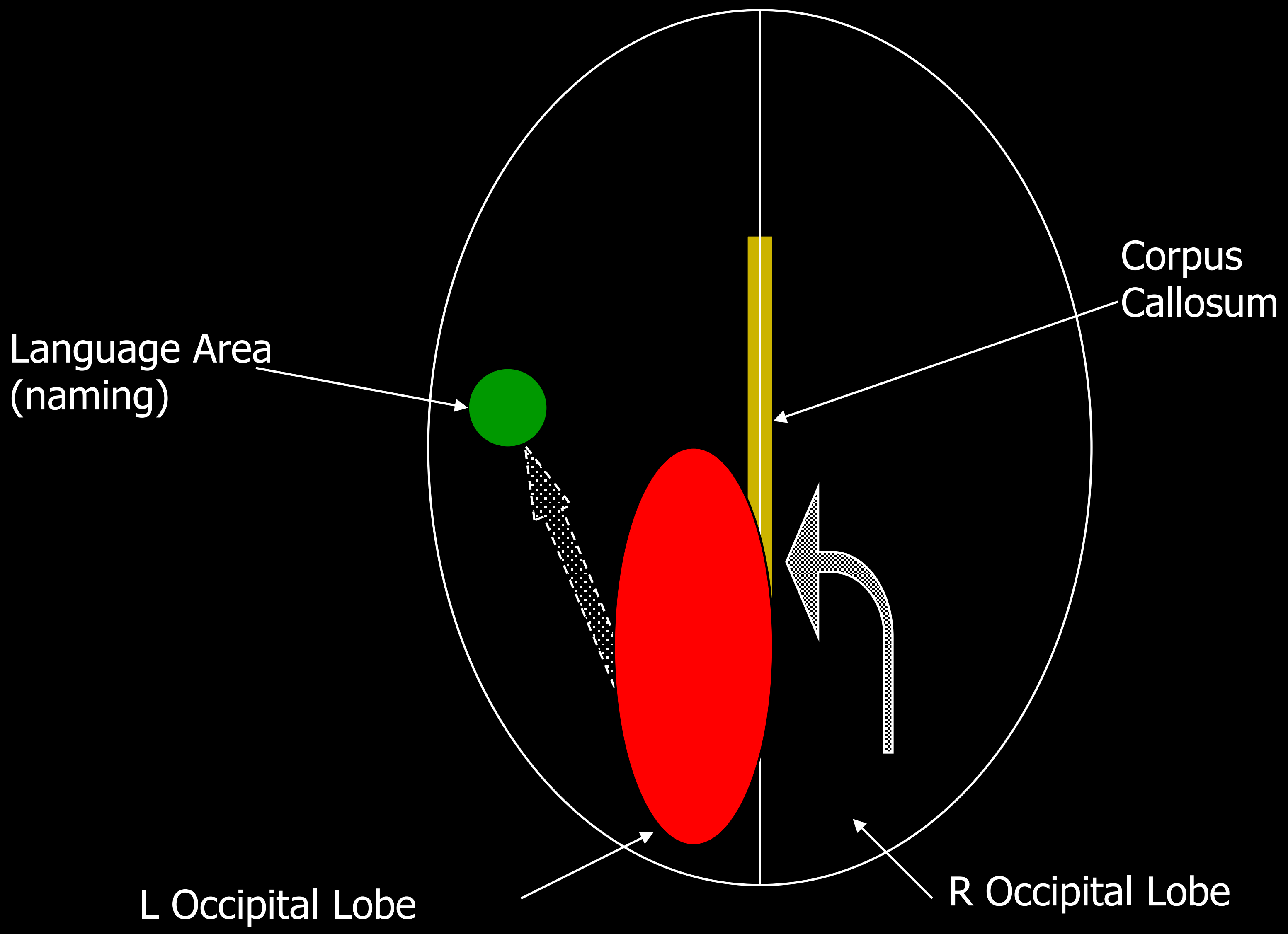
# Key Lessons

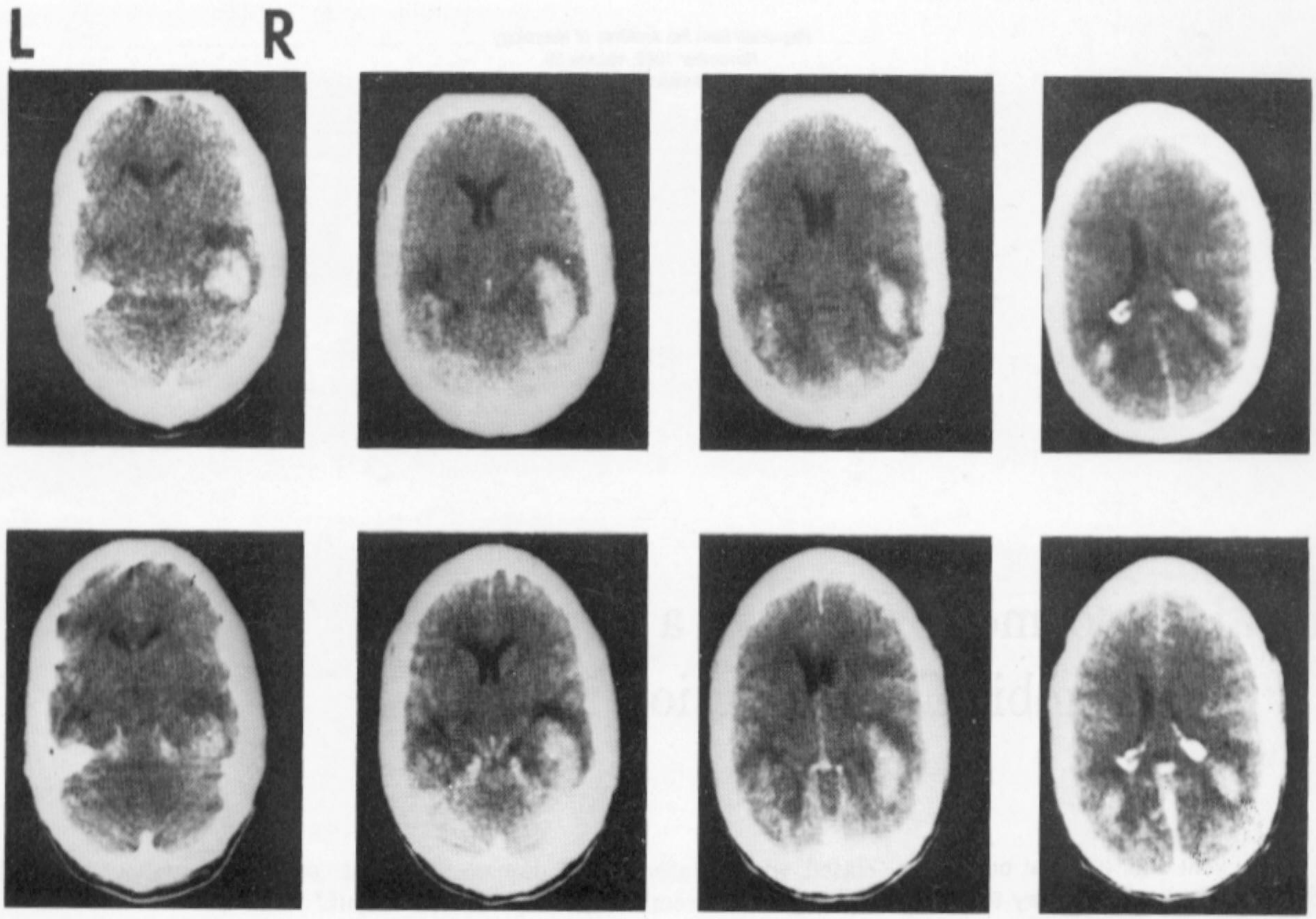
- Unit of analysis is not “the patient” but the set of inputs, processes and outputs in a given task
- Test protocol should manipulate these factors
- Task performance is possible if processor is accessed appropriately
- Task performance is the product of processors and their connections (functional system)
- Disconnection and processor impairment may have different performance signatures
- Analysis requires knowledge of functional anatomy of disordered system

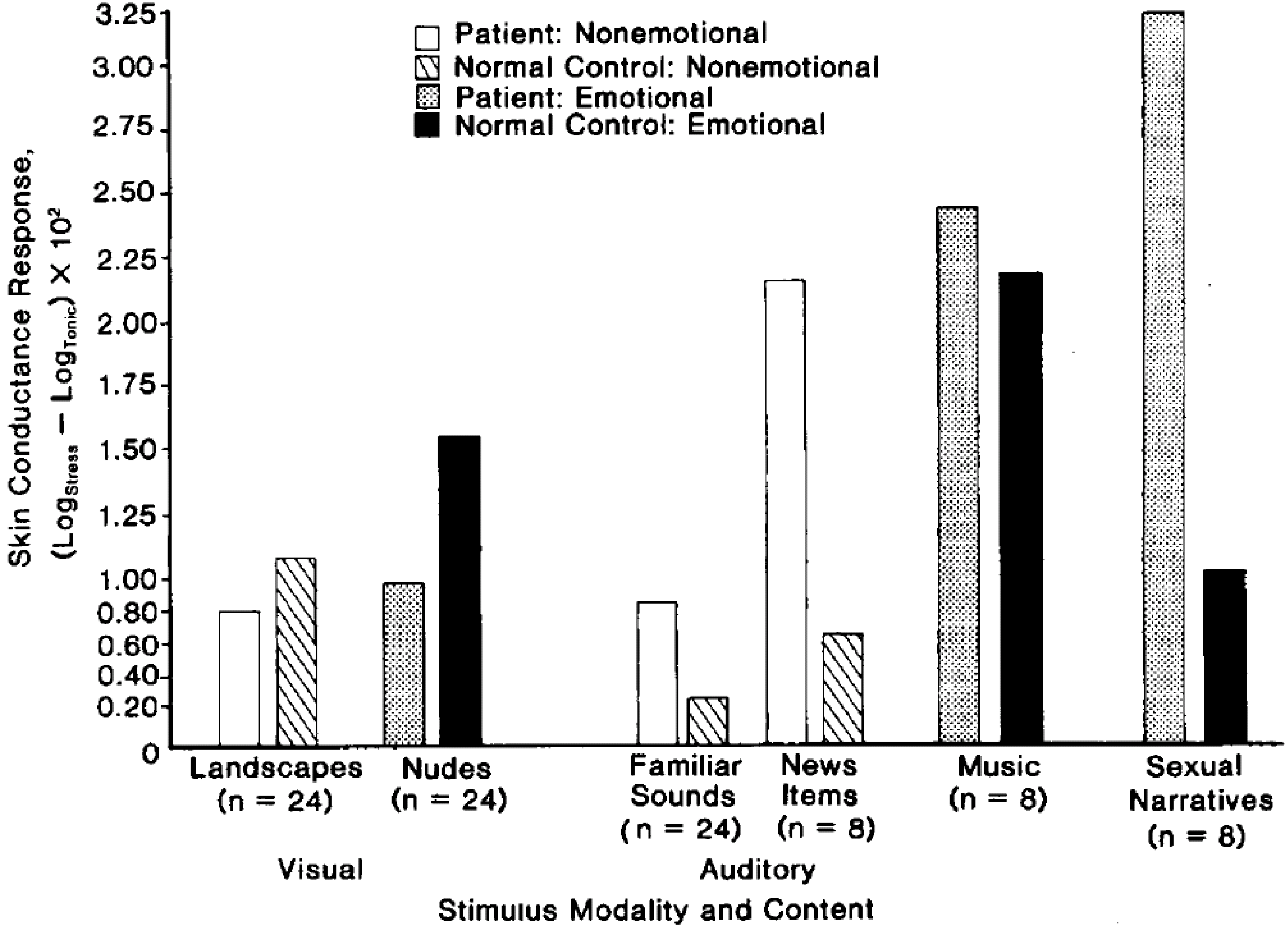
# Disconnection v. Processor Impairment

- Processor Impairment
  - Task cannot be completed under any circumstances
  - Deficit is "cognitively impenetrable"
  - Manipulation of response alternatives has no effect
- Disconnection
  - Task can be completed under certain circumstances
  - Manipulation of input (e.g., modality) and output (e.g., response alternatives) has significant effect
  - Deficit is often "fractional" (material-specific, modality-specific, lateralized, response-specific)

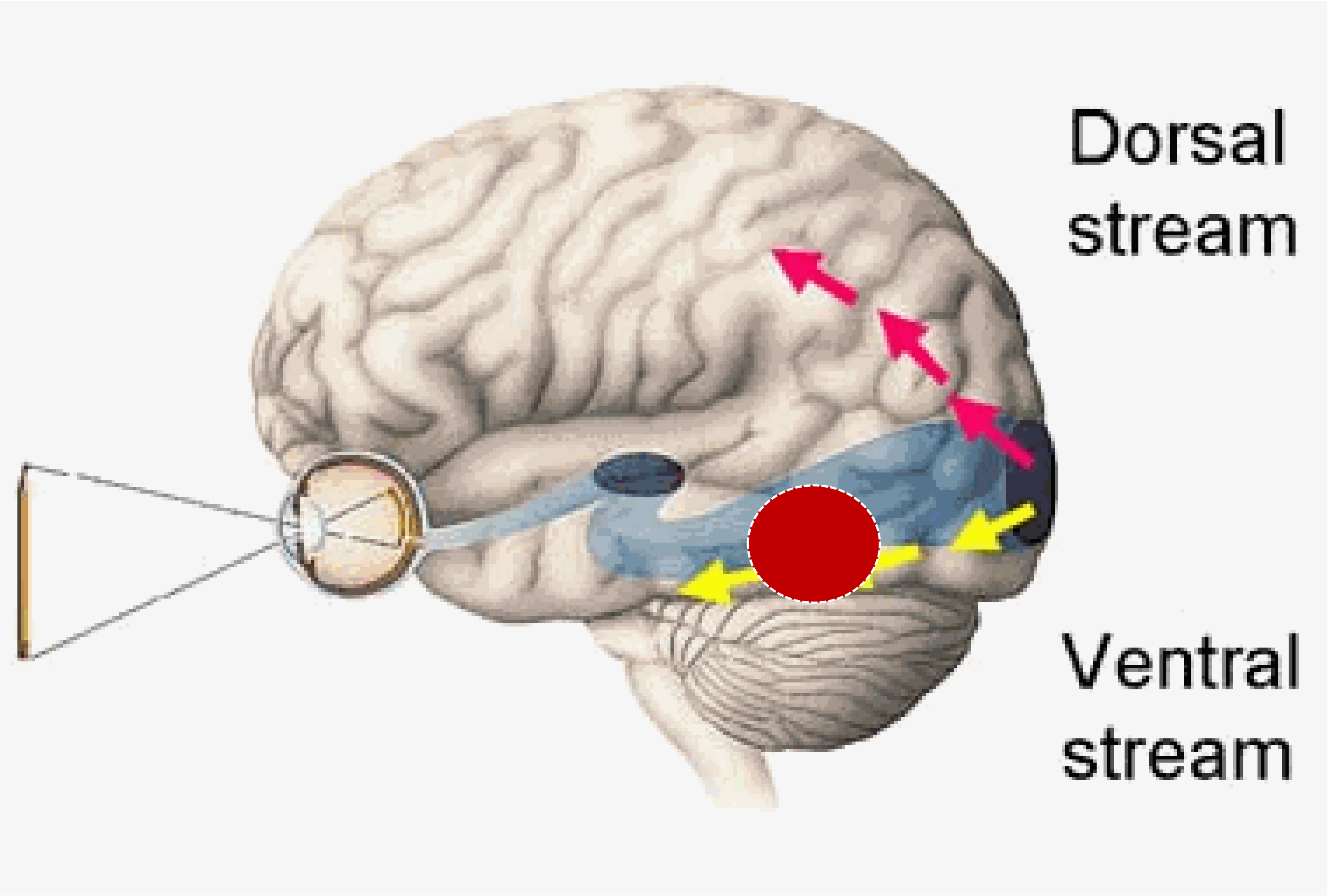
# Visual-Verbal Disconnection: Alexia without Agraphia, Color Anomia



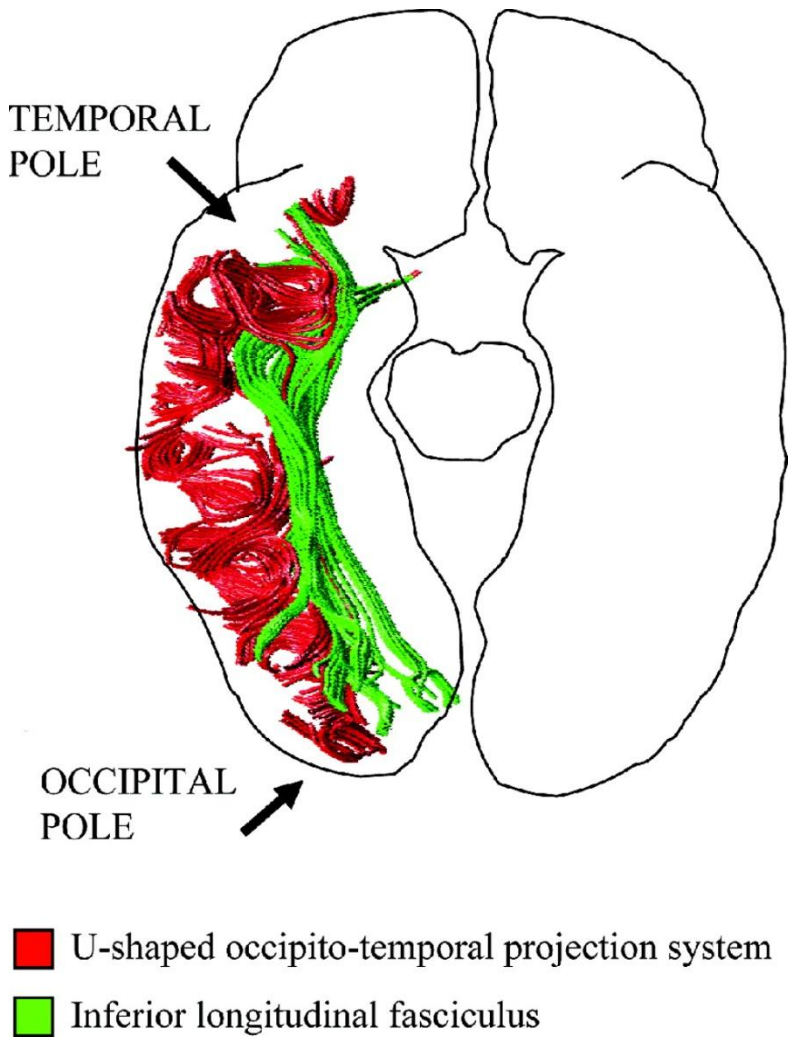

L
R



Patient: Nonemotional
Normal Control: Nonemotional
Patient: Emotional
Normal Control: Emotional
Skin Conductance Response, $(\mathrm{Log}_{\mathrm{Stress}} - \mathrm{Log}_{\mathrm{Tonic}}) \times 10^2$
3.25
3.00
2.75
2.50
2.25
2.00
1.75
1.50
1.25
1.00
0.80
0.60
0.40
0.20
0
Landscapes (n = 24)
Nudes (n = 24)
Familiar Sounds (n = 24)
News Items (n = 8)
Music (n = 8)
Sexual Narratives (n = 8)
Visual
Auditory
Stimulus Modality and Content


Dorsal
stream
Ventral
stream

## Occipitotemporal pathways.

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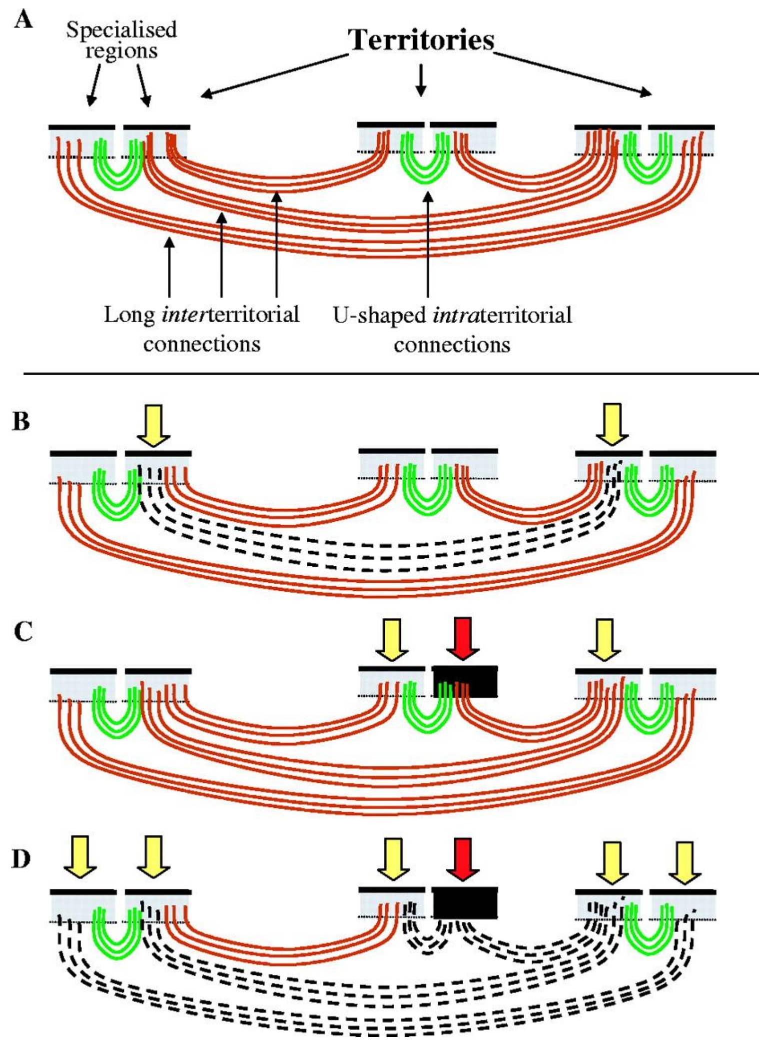
## A hodotopic framework for clinicopathological correlations.




White Matter Damage

Cortical Damage

Combined Damage

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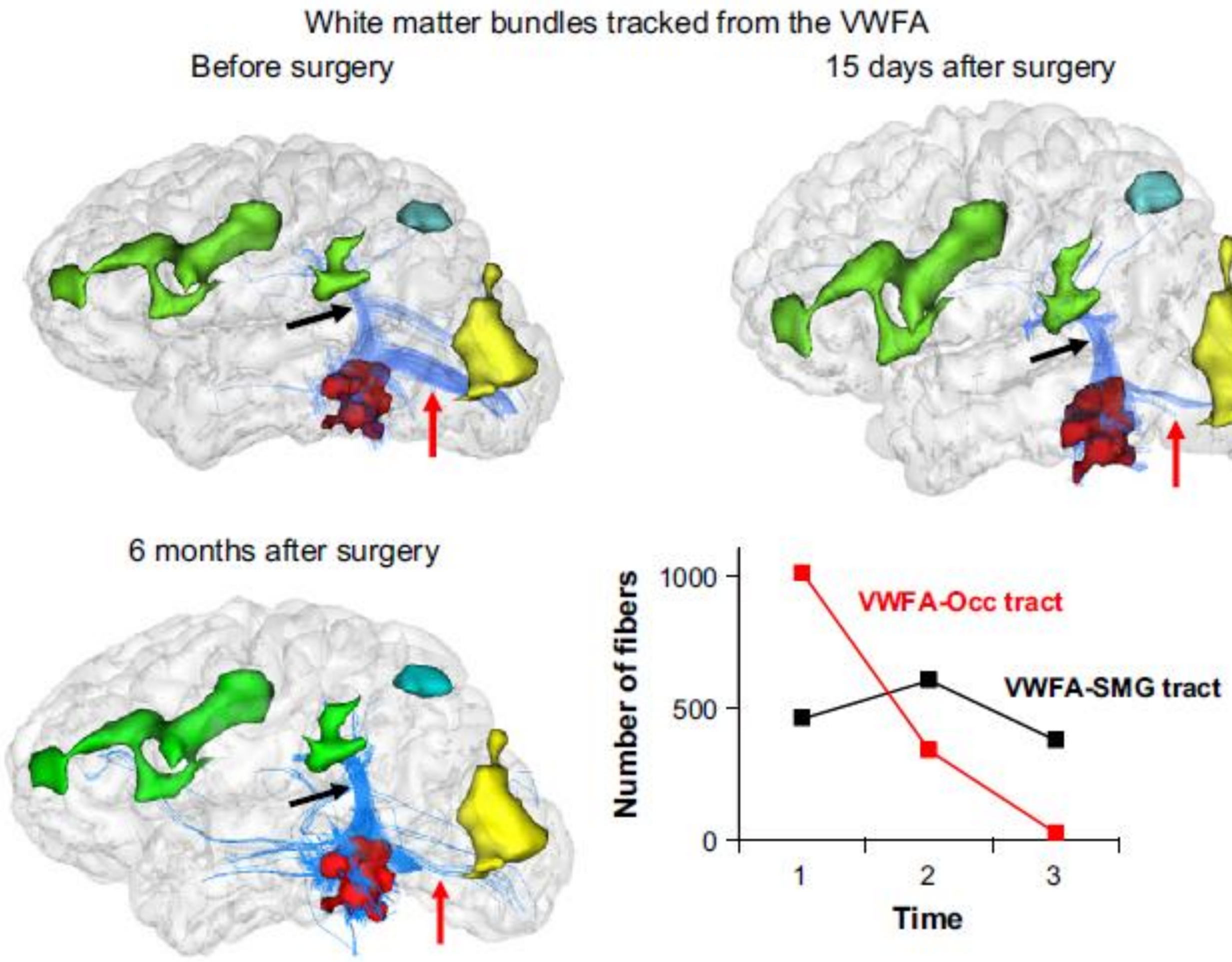
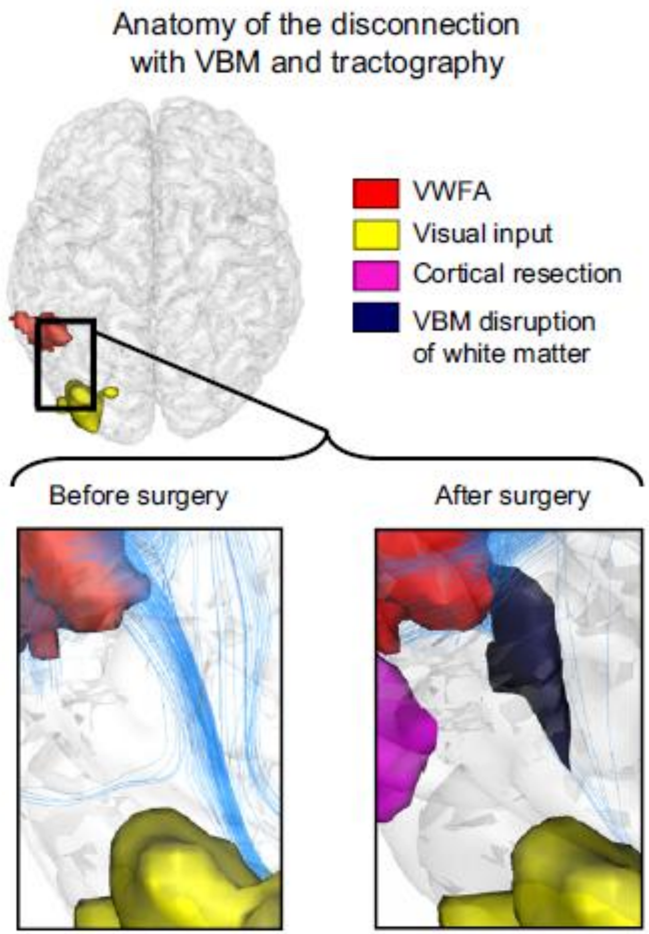
# Pure Alexia and White Matter Tractography




Epelbaum, et al., 2008

# Pure Alexia and White Matter Tractography




Epelbaum, et al., *Cortex*, 2008

# Summary

- New structural imaging techniques validating aspects of disconnection theory
- However, cortico-cortical connection is more complex than originally thought
- Hodologic models and concepts useful for further understanding syndromes


AP