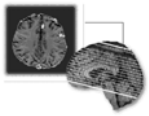
Neuroscience 2004
Functional Brain Imaging



Joy Hirsch, Ph.D., Professor
Director, fMRI Research Center
Columbia University Health Sciences
NI Basement

www.fmri.org

A Brief Outline

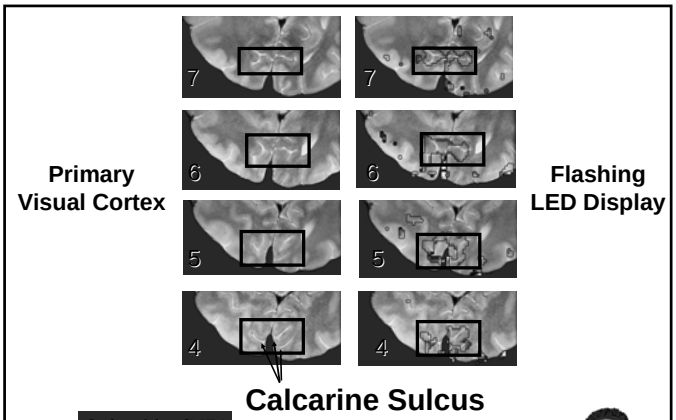
I. Hypothesis of functional specificity
- A. Single Areas
- B. Multiple Areas

II. Brain Mapping Techniques
- A. Lesion- Based Methods
  1. Positron Emission Tomography, PET
  2. Functional Magnetic Resonance Imaging, fMRI
- B. Cardiovascular Based Methods
  1. Positron Emission Tomography, PET
  2. Functional Magnetic Resonance Imaging, fMRI
- C. Electromagnetic-Based Methods
  1. SSEP Somatosensory Potentials
  2. Cortical Stimulation
  3. Magnetoencephalography, MEG
  4. Electroencephalography, EEG

III. Integration of Brain Mapping Techniques

I. Hypothesis of functional specificity

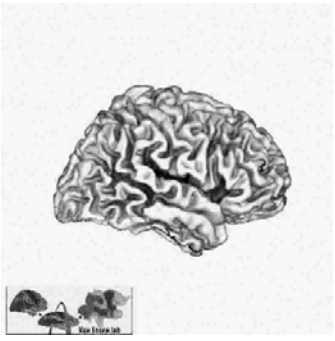
Specializations of single brain areas



I. Hypothesis of functional specificity

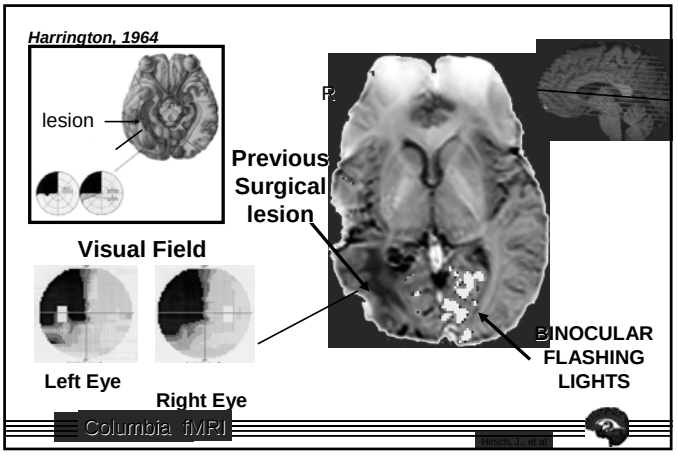
Specializations of single brain areas
Specializations of multiple brain areas

Functional Organization of Visual Cortex



II. Brain Mapping Techniques

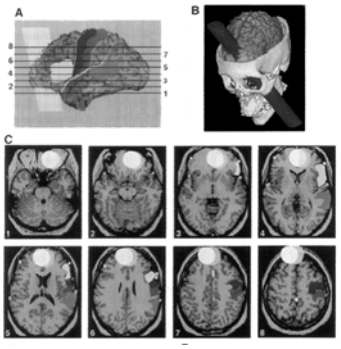
A. Lesion-Based Methods



HISTORICAL MILESTONES
FUNCTIONAL SPECIFICITY AND NEUROIMAGING

Neuroscience and Medicine		Physics and Engineering
BROCA Aphasia and lesions in GFi	1841	
	1845	FARADAY Magnetic properties of blood
HARLOW Phineas Gage	1861	
WERNICKE Aphasia and lesions in GTs	1874	
MOSSO Blood flow and cognitive events	1881	PAULING Change of magnetic state of hemoglobin with oxygenation
	1890	
ROY & SHERRINGTON Relationship between neural activity and vascular changes	1909	RABI
	1936	Discovery of Magnetic Resonance
BRODMANN Cytoarchitectonic regions of cortex	1945	PURCELL / BLOCK Demonstration of NMR in condensed matter
PENFIELD Intraoperative cortical maps	1949	HAHN
	1950	Discoverer of spin echo phenomenon

Phineas Gage



Damasio, H., et al; Science 264: 1102-1105, 20 May 1994

II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. Positron Emission Tomography, PET

HISTORICAL MILESTONES
FUNCTIONAL SPECIFICITY AND NEUROIMAGING

Neuroscience and Medicine		Physics and Engineering
	1971	DAMADIAN Discovery that biological tissues have different relaxation rates HOUNSFIELD CORMACK Invention of Computed Tomography
	1972	LAUTERBUR First MR image
TER-POGOSSOAN SOKOLOFF First PET studies of brain metabolism, blood flow, and correlates of human behavior	1976 1977	MANSFIELD First MRI of a body part invention of EPI (scans whole brain in secs.)
PETERSON/FOX POSNER/RAICHLE PET study of human language Radiolabeled blood flow and neural events	1981 1984	HILAL First clinical MRI scanner
OGAWA Blood Oxygen dependent signal EPIMRI and neural events	1990	
BELLIVEAU Cortical map of the human visual system: fMRI	1992	

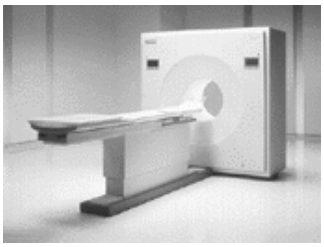
Columbia fMRI

a. Source of Signal
Positron Emission Tomography

Radionuclides that emit positrons such as ^{15}O and ^{18}F are introduced into the brain.

$H_2{}^{15}O$ behaves like $H_2{}^{16}O$ and indicates blood flow (rCBF) (half life = 123 seconds) integration time ≈ 60 seconds.

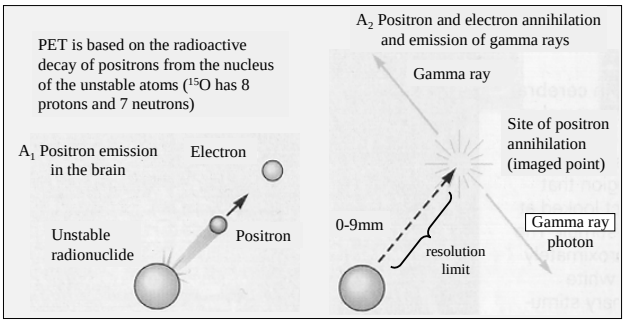
^{18}F – deoxyglucose behaves like deoxyglucose and indicates metabolic activity (half-life = 110 minutes) integration time ≈ 20 minutes



PET SCANNER

From: www.epub.org.br/cm/n011pet/pet.htm

Principle of PET



From: Principles of Neural Science (4th. Ed.) Kandel, Schwartz, & Jessell, p. 377.

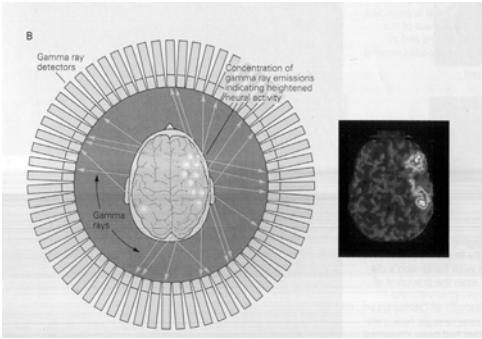
II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. Positron Emission Tomography, PET

a. Source of signal
b. Measurement techniques

Gamma Ray Detections to Location of Function



From: Principles of Neural Science (4th. Ed.) Kandel,Schwartz, & Jessell, p. 377.

Injection of radioactive-labeled water for PET scanning

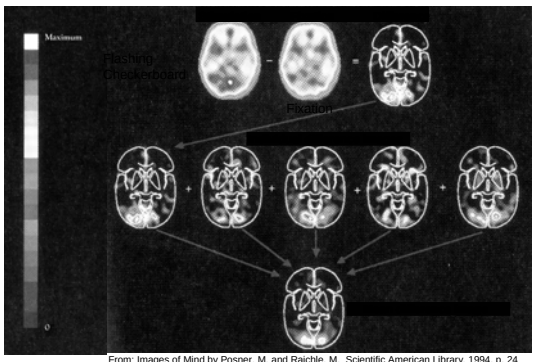
II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. Positron Emission Tomography, PET

a. Source of signal
b. Measurement techniques
c. Computation for analysis

Analysis of PET Results



From: Images of Mind by Posner, M. and Raichle, M. Scientific American Library, 1994, p. 24

II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. **Positron Emission Tomography, PET**
2. **Functional Magnetic Resonance Imaging, fMRI**

HISTORICAL MILESTONES

1971 — **DAMADIAN**: Discovered that biological tissues have different relaxation rates

1972 — **LAUTERBUR**: First MR image

1976 — **MANSFIELD**: First MRI of a body part; Invented EPI (scans whole brain in secs.)

1977 — **TER-POGOSSIAN SOKOLOFF**: First PET studies of brain metabolism, blood flow, and correlates of human behavior

1990 — **OGAWA**: **fMRI** Blood Oxygen dependent signal EPI / MRI Behavior

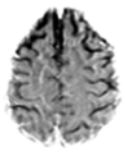
1992 — **BELLIVEAU**: Cortical Map: human visual system

II. Brain Mapping Techniques

1. **Functional Magnetic Resonance Imaging, fMRI**
   a. **Source of signal**

a. Source of Signal — Principles of fMRI

The MR Signal and 4 Magnetic Fields



MAGNETIC FIELD 1:

- Scanner Environment [1.5] T
- Protons align along an axis

MAGNETIC FIELD 2:

- Created when a radio frequency pulse (63.3 mgHz) is applied
- Protons precess around the axis and create a small current (MRI signal)
- Protons return to aligned state when radio frequency pulse is turned off

MAGNETIC FIELD 3:

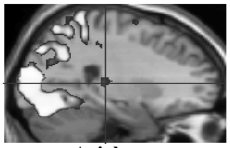
- Location of the MR signal
- A detectable radio frequency is emitted by the protons as they relax into their aligned state
- The frequency is dependent upon field strength
- Application of magnetic field gradient (mT) is sufficient to convert detected frequencies to location

MAGNETIC FIELD 4:

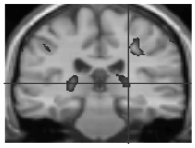
- Local signal change at a single voxel is due to change in proportions of oxyhemoglobin/deoxyhemoglobin
- Deoxyhemoglobin is paramagentic and reduces the uniformity of the precessing and therefore the signal intensity
- This change is called BOLD

Vision-related cortical effects

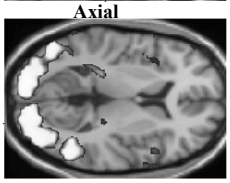
Sagittal



Coronal

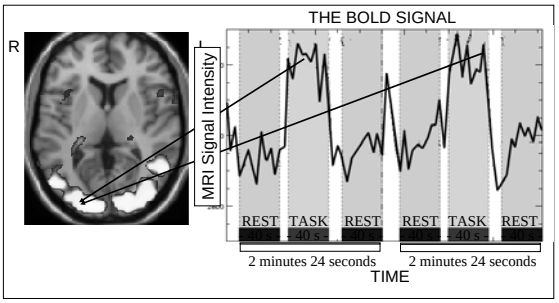


Axial



QuickTime™ and a Video decompressor are needed to see this picture.

Current Developments in MR are focused on the structure/function problem



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PHYSIOLOGY

NEURAL ACTIVATION
IS ASSOCIATED WITH AN INCREASE IN BLOOD FLOW

O2 EXTRACTION IS RELATIVELY UNCHANGED

RESULT:
REDUCTION IN THE PROPORTION OF DEOXY HGB IN THE LOCAL VASCULATURE

PHYSICS

DEOXY HGB
IS PARAMAGNETIC

AND DISTORTS THE LOCAL MAGNETIC FIELD CAUSING SIGNAL LOSS

RESULT:
LESS DISTORTION OF THE MAGNETIC FIELD RESULTS IN LOCAL SIGNAL INCREASE

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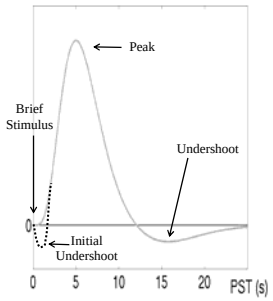
BOLD Impulse Response Model

- Function of blood oxygenation, flow, volume (Buxton et al, 1998)
- Peak (max. oxygenation) 4-6s poststimulus; baseline after 20-30s
- Initial undershoot can be observed (Malonek & Grinvald, 1996)
- Similar across V1, A1, S1…
- … but differences across: other regions (Schacter et al 1997) individuals (Aguirre et al, 1998)



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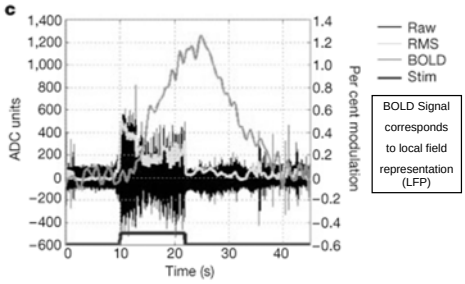
BOLD ORIGIN



Logothetis, N.K., Pauls, , Augath, M, Torsten, T, Oeltermann, A, (2001) Neurophysiological investigation of the basis of the fMRI signal. Nature 412 150-157

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II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. **Positron Emission Tomography, PET**
2. **Functional Magnetic Resonance Imaging, fMRI**
   a. **Source of signal**
   b. **Measuremnet techniques**

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Imaging While Naming Objects

QuickTime™ and a Video decompressor are needed to see this picture.

QuickTime™ and a
Radius SoftDV™ - NTSC decompressor
are needed to see this picture.

Scanner acquires the whole brain every [4] secs:

[26] axial slices

Resolution [1.5 x 1.5 x 4.5] mm

Each voxel is analyzed seperately

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COMPUTATIONS FOR *f*UNCTIONAL IMAGE PROCESSING

Acquisition

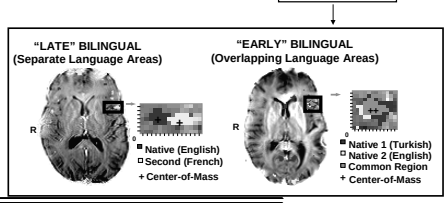
RECONSTRUCTION

ALIGNMENT

VOXEL BY VOXEL ANALYSIS

GRAPHICAL REPRESENTATION

Functional Brain Map



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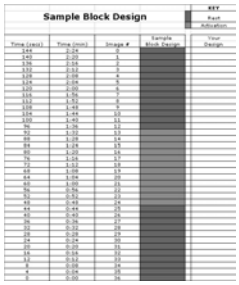
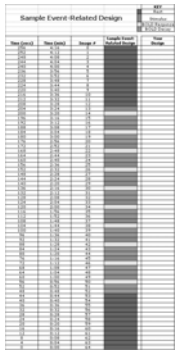
from *Nature* **388**, 171-174 (1997)
Kim, Relkin, Lee, & Hirsch

Block Design



Event-Related Design



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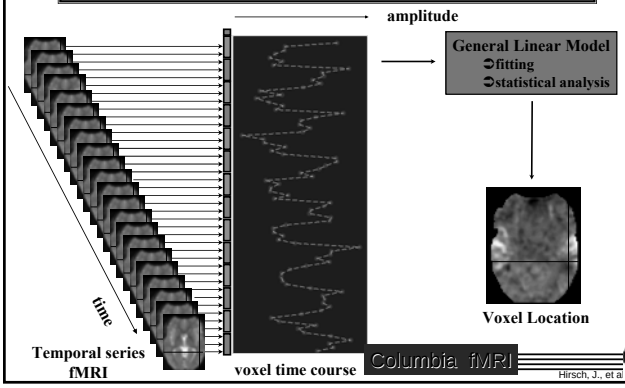
One voxel = One test (t, F, ...)



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1. **Positron Emission Tomography, PET**
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   c. **Computation for analysis**

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Voxel statistics…

- parametric
  - one sample *t*-test
  - two sample *t*-test
  - paired *t*-test
  - Anova
  - AnCova
  - correlation
  - linear regression
  - multiple regression
  - *F*-tests
  - etc…

all cases of the
General Linear Model

assume normality
to account for serial correlations:

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two-sample *t*-test

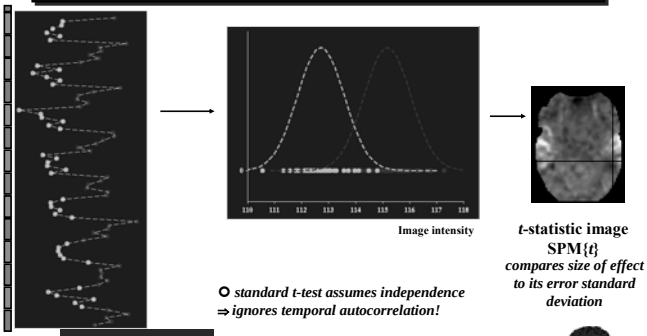

Image intensity

***t*-statistic image**
SPM{*t*}
compares size of effect to its error standard deviation

- ***standard t-test assumes independence***
  ⇒ ***ignores temporal autocorrelation!***

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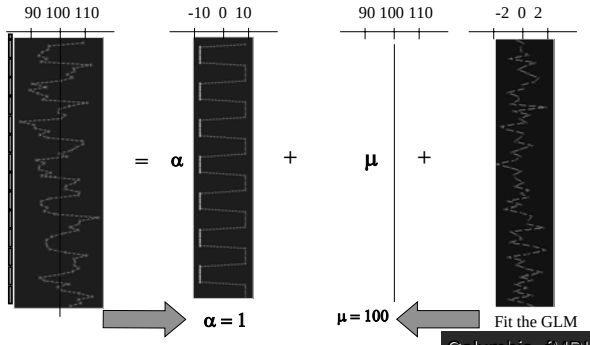
Regression



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II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. Positron Emission Tomography, PET
2. Functional Magnetic Resonance Imaging, fMRI
   a. Source of signal
   b. Measuremnet techniques
   c. Computation for analysis
   d. Individual brain maps

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Mapping Specific Functions to Locate Specific Areas

Brain Mapping and Neurosurgery:
[Fixed Effects]

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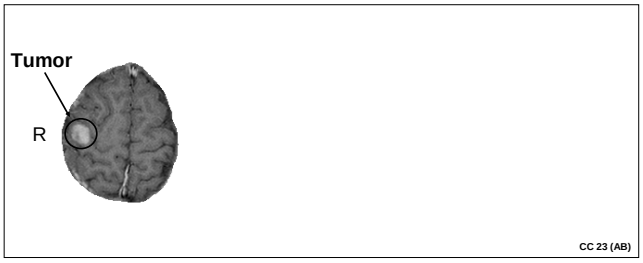
Conventional Imaging



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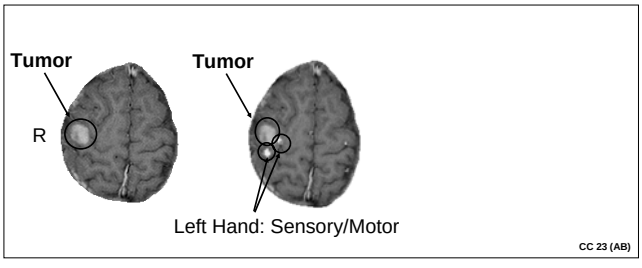
Conventional Imaging | Functional Imaging

Before Surgery



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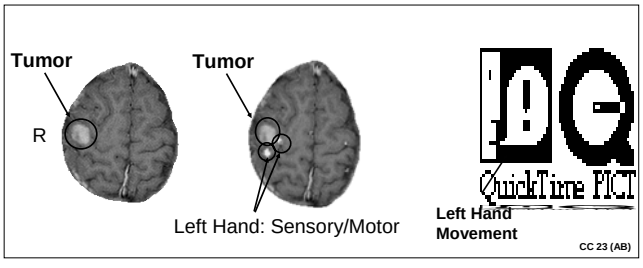
Conventional Imaging | Functional Imaging

Before Surgery **After Surgery**



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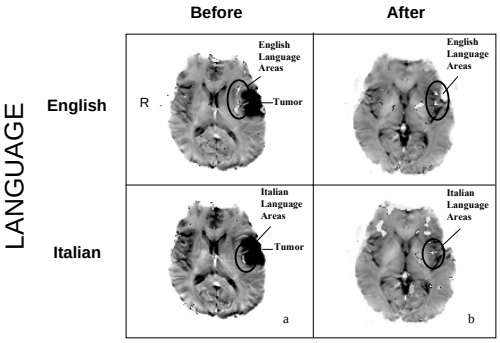
Surgery



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Standard Brain Mapping Tasks

SENSORY	MOTOR	LANGUAGE		VISION
Touch	Finger Thumb Tapping	Picture Naming	Listening to Words	Reversing Checkerboard
(passive)	(active)	(active)	(passive)	(passive)
GPoC	GPrC	GOi	GTT GFi GTs	CaS

From Hirsch, J., et al; Neurosurgery 47: 711-722, 2000

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II. Brain Mapping Techniques

C. Electromagnetic - Based Methods

- **Somatasensory Evoked Potential, SSEP**
- **Direct Cortical Stimulation**

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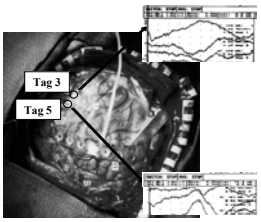
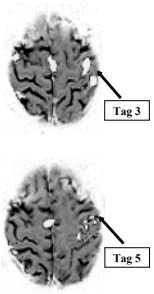
Sensory Motor Mapping

Craniotomy	SSEP	Direct Cortical Stimulation	Localization fMRI



"Twitching of hand, focal seizure involving arm "

"Twitching in 1st three digits"



From Hirsch, J., et al; An Integrated Functional Magnetic Resonance Imaging Procedure for Preoperative Mapping of Cortical Areas Associated with Tactile, Motor, Language, and Visual Functions, Neurosurgery 47: 711- 722, 2000.

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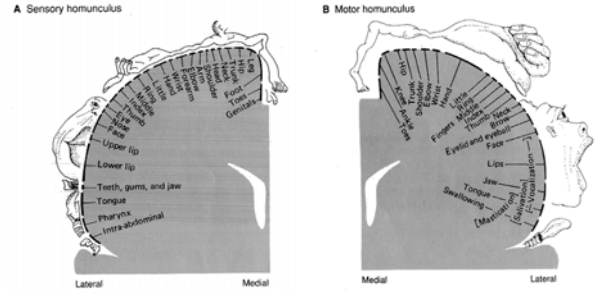
Homonculus



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Language Mapping

fMRI	Intraoperative Stimulation	Response
Broca's Area		Speech Arrest During Counting
Wernicke's Area		Literal paraphasic speech error during picture naming

From Hirsch, J., et al; An Integrated Functional Magnetic Resonance Imaging Procedure for Preoperative Mapping of Cortical Areas Associated with Tactile, Motor, Language, and Visual Functions, Neurosurgery 47: 711 722, 2000.

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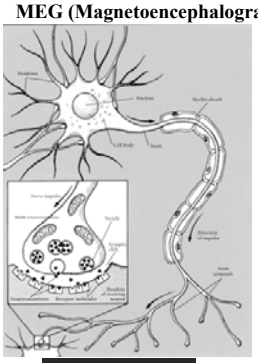
II. Brain Mapping Techniques

C. Electromagnetic - Based Methods

- Somatasensory Evoked Potential, SSEP
- Direct Cortical Stimulation
- Magnetoencephalography, MEG
  a. Source of signal

Methods to Measure Electromagnetic Activity:

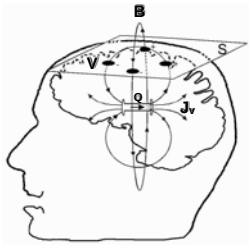
MEG (Magnetoencephalography) - EEC (Electroencephalography)



- Signal Source: Electrical Activity of nerve cells.
- What is measured on the surface of the head is the result of mostly postsynaptic potentials (excitatory or inhibitory)
- Many nerve cells are aligned in palisades (e.g. pyramidal cells) and post-synaptic electrical fields sum with increasing area.
- Typically it is thought that 100,000 adjacent neurons acting in temporal synchrony are required to produce a measurable change in the magnetic field

Relationship between currents in the brain and the magnetic field outside the head.

- Based on the discovery that electrical currents generate magnetic fields: Hans Christian Oersted, a Danish physicist (early 19th. century)
- A current source with strength Q causes a current flow Jv within the brain.



- The current flow produces a potential difference V on the scalp: (measured by EEG)
- And a magnetic field B outside of the head: (measured by MEG)

from: www.Aston.ac.uk/psychology/meg/meg/intro/magfield.htm

II. Brain Mapping Techniques

C. Electromagnetic - Based Methods

- Somatasensory Evoked Potential, SSEP
- Direct Cortical Stimulation
- Magnetoencephalography, MEG
  a. Source of signal
  b. Measurement techniques

Magnetoencephalography, MEG

Tiny magnetic fields produced by brain activity (10^{-13} Teslas) can be measured using Superconducting Quantum Interference Devices (SQUIDs).

SQUIDS operate at superconducting temperatures (-269°C). Sensors are placed in a dewar containing liquid helium.

Stimulus – evoked neuromagnetic signals are recorded by an array of detectors.

The spatial location of the source is inferred by mathematical modeling of the magnetic field pattern.

II. Brain Mapping Techniques

C. Electromagnetic - Based Methods

- Somatasensory Evoked Potential, SSEP
- Direct Cortical Stimulation
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  a. Source of signal
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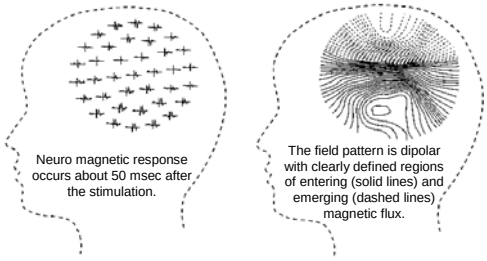
Somatosensory evoked magnetic signals in response to tactile stimulation of the contralateral index finger

Isofield contour maps at the time of maximal response (50 msec) to the tactile stimulation



Neuro magnetic response occurs about 50 msec after the stimulation.

The field pattern is dipolar with clearly defined regions of entering (solid lines) and emerging (dashed lines) magnetic flux.

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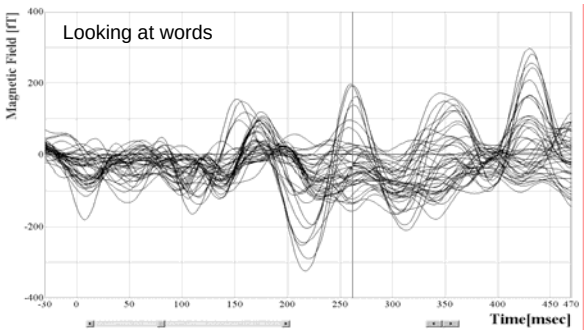
Magnetic field strength in left hemisphere sensors over time



Liina Pylkkanen, Alec Marantz, 2002

Columbia fMRI

Hirsch, J., et al

II. Brain Mapping Techniques

C. Electromagnetic - Based Methods

- **Somatasensory Evoked Potential, SSEP**
- **Direct Cortical Stimulation**
- **Magnetoencephalography, MEG**
- **Electroencephalography, EEG**
  - **a. Source of signal**
  - **b. Measurement techniques**

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Electroencephalography

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  - **c. Computation for analysis**

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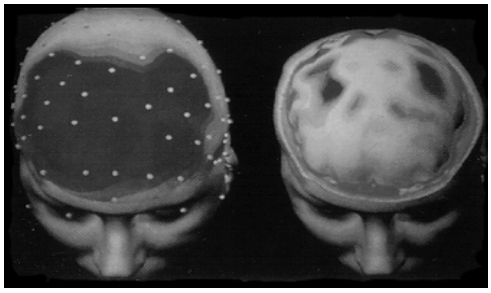
Electroencephalography

Electrode Array for EEG

Averaged Activity profiles during bilateral finger movement



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C. Integration of Brain Mapping Technique

Mapping specific functions to understand a neural system

- **Normalized Brain**
- **Inferences to general population [Random effects]**

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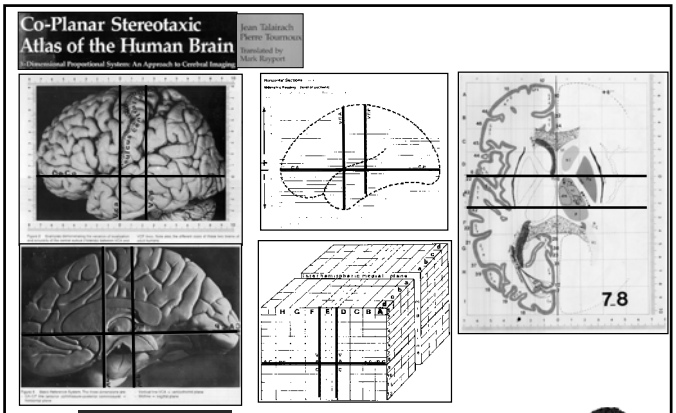

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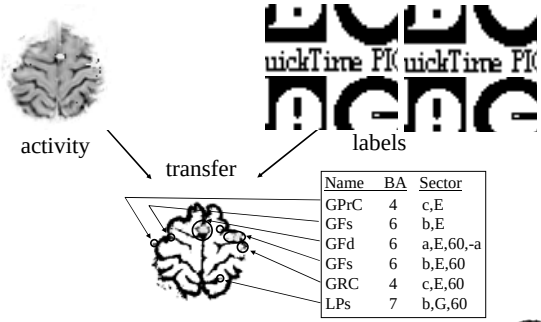
Labeling of Active Brain Areas

Functional Brain

Atlas Brain



Name	BA	Sector
GPrC	4	c,E
GFs	6	b,E
GFd	6	a,E,60,-a
GFs	6	b,E,60
GRC	4	c,E,60
LPs	7	b,G,60

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Anatomical Region	BA	Center of mass x	y	z
Medial Frontal Gyrus	6	9	- 6	53
Superior Temporal Gyrus	22	57	- 25	9
Inferior Frontal Gyrus	44	49	10	25
Inferior Frontal Gyrus	45	40	25	8

Hirsch, R-Moreno, Kim, Interconnected large-scale systems for three fundamental cognitive tasks revealed by functional MRI. Journal of Cognitive Neuroscience, 13(3), 389-405, 2001.

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Functional MRI Research Center

Department of Radiology
Center for Neurobiology and Behavior
Columbia University Medical Center

Mission

To establish a collaborative and multi-investigator neuroimaging research environment focused on education, medical applications, and the study of brain, behavior, and therapy-induced cortical effects aimed at the systems of the brain that underlie cognition, perception, and action.

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