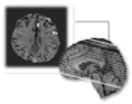
Neuroscience 2005
Functional Brain Imaging



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

www.fmri.org

A Brief Outline

I. The Principle of functional specificity
- A. Single Areas
- B. Multiple Areas

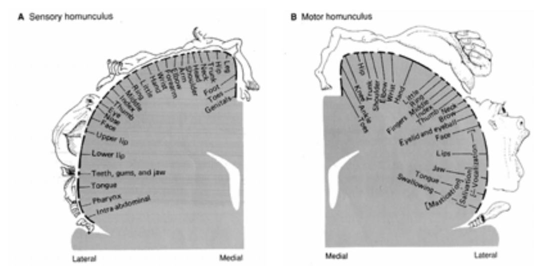
II. Brain Mapping Techniques
- A. Lesion- Based Methods
  1. Visual field loss
  2. Aphasia
  3. Personality Changes
- B. Cardiovascular Based Methods
  1. Positron Emission Tomography, PET
  2. Functional Magnetic Resonance Imaging, fMRI
- C. Electromagnetic-Based Methods
  1. SSEP Somatosensory Potentials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

III. Future Directions of Brain Mapping

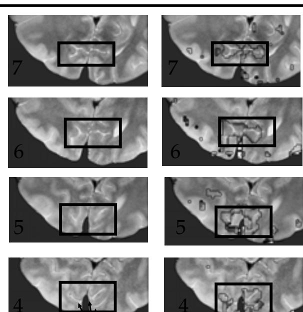
I. The principle of functional specificity

A. Specializations of single brain areas

Homunculus: Map of Sensory/Motor Function



Primary Visual Cortex

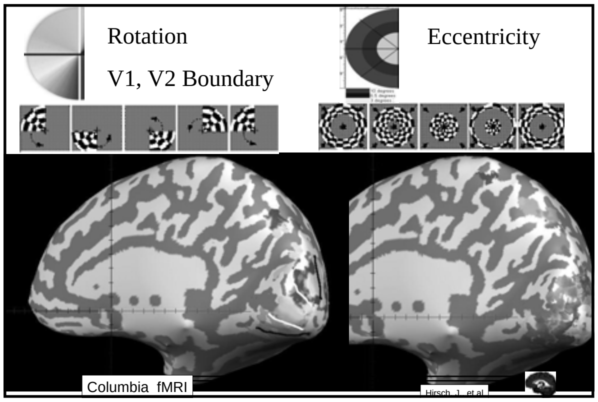


Flashing LED Display

Calcarine Sulcus

FUNCTIONAL SPECIFCITY BASED ON RETINOTOPY

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

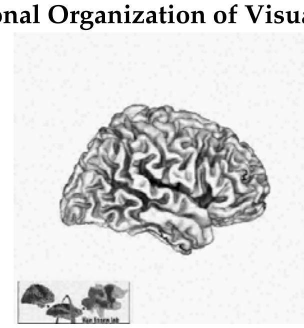


I. Principle of functional specificity

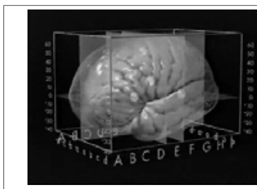
A. Specializations of single brain areas

B. Specializations of multiple brain areas

Functional Organization of Visual Cortex



BRAIN MAP OF OBJECT NAMING (MANY SUBJECTS)



Anatomical Region	Hemis	Area	Centers of mass		
			x	y	z
Superior Temporal Gyrus	L	Wernicke	57	-26	9
Inferior Frontal Gyrus	L	Broca	49	10	25
Inferior Frontal Gyrus	L	Broca	40	25	8
Medial Frontal Gyrus	L	Sup. Motor	9	-6	53

Connectivity Principle: Neural circuits in the brain connect working parts to execute complex tasks.

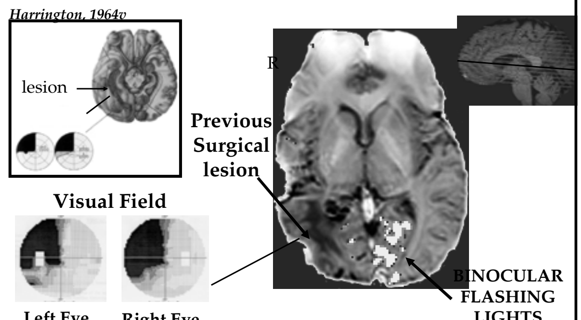
Hirsch, R-Moreno, Kim, Interconnected large-scale systems for three fundamental cognitive tasks revealed by functional MRI. Journal of Cognitive Neuroscience, 13(3), 389-405, 2001.

II. Brain Mapping Techniques

A. Lesion-Based Methods

1. Visual Field Loss

Harrington, 1964v

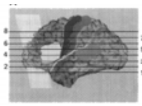
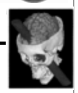


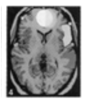
THE BRAIN IS ORGANIZED BY DEDICATING SPECIFIC AREAS TO SPECIFIC FUNCTIONS

2. Aphasia

Neuroscience and Medicine

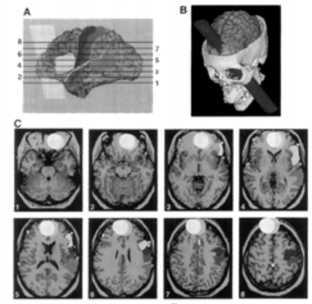
	Year
BROCA Aphasia and lesions in GFi	1841
HARLOW Phineas Gage	1861
WERNICKE Aphasia and lesions in GTs	1874



3. Personality Changes

Phineas Gage



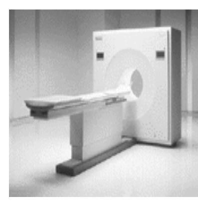
Damasio, H., et al; Science 264: 1102-1105, 20 May 1994

II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. Positron Emission Tomography, PET

TECHNICAL MILESTONES IN IMAGING



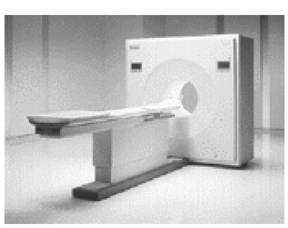
1971	**DAMADIAN** Discovery that biological tissues have different relaxation rates
1971	**HOUNSFIELD CORMACK** Invention of Computed Tomography
1972	**LAUTERBUR** First MR image
1976	**MANSFIELD** First MRI of a body part invention of EPI (scans whole brain in secs.)
1977	**TER-POGOSSOAN SOKOLOFF** First PET studies of brain metabolism

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.

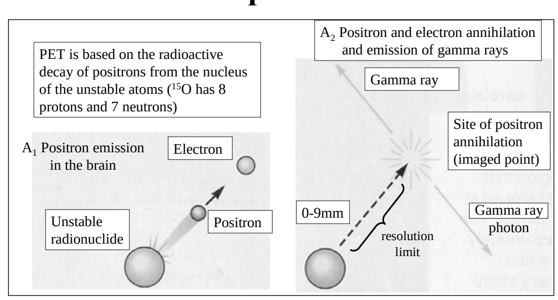
^{18}F – deoxyglucose behaves like deoxyglucose and indicates metabolic activity (half-life = 110 minutes) integration time ≈ 20 minutes



PET SCANNER

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

Principle of PET



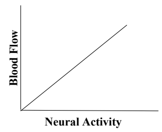
From: Principles of Neural Science (4th. Ed.) Kandel, Schwartz, & Jessell, p. 377.

Cerebral Blood Flow is Coupled to Neural Activity

Year

1881 — **MOSSO**
Blood flow and cognitive events

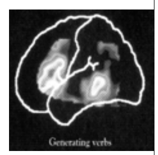
1890 — **ROY & SHERRINGTON**
Relationship between neural activity and vascular changes

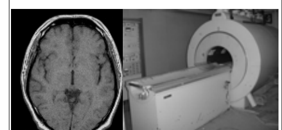


NEUROIMAGING: PET | Year | **STRUCTURAL IMAGING: MRI**

1981 — **HILAL**
First clinical MRI scanner

1984 — **PETERSON/FOX POSNER/RAICHLE**
PET study of human language
Radiolabeled blood flow and neural events





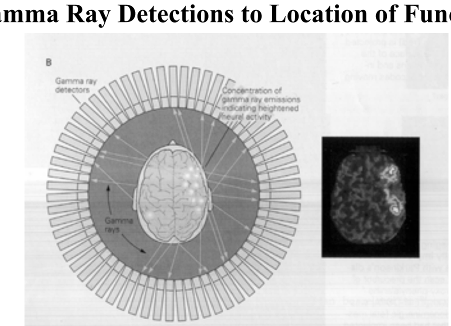
II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. Positron Emission Tomography, PET

- Source of signal and principles
- 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

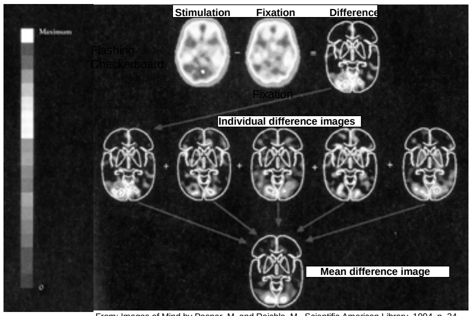
II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. Positron Emission Tomography, PET

- Source of signal and principles
- Measurement techniques
- 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

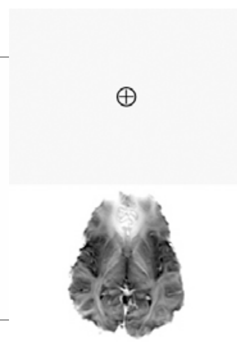
B. Cardiovascular Based Methods

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

FUNCTIONAL MRI: fMRI

OGAWA
Blood Oxygen dependent signal
EPI/MRI and neural events

1990



BELLIVEAU
Cortical map of the human visual system: fMRI

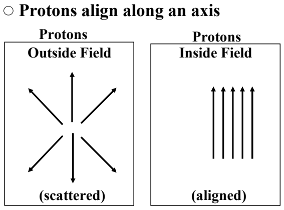
1992

II. Brain Mapping Techniques

1. Functional Magnetic Resonance Imaging, fMRI
   - Source of signal and principles

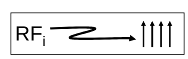
MAGNETIC FIELD 1:

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

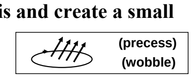


MAGNETIC FIELD 2:

- Created when a radio frequency pulse (63.3 mgHz) is applied to aligned protons



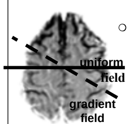
- Protons precess around the axis and create a small current (MRI signal)



MAGNETIC FIELD 3:

- A detectable radio frequency is emitted by the protons as they relax into their aligned state

- The Radio frequency (RF_o) is dependent upon field strength and therefore indicates location of origin

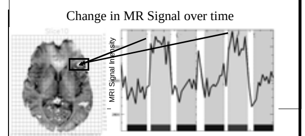


- Application of magnetic field gradient (mT)

- Location of signa are recorded

MAGNETIC FIELD 4:

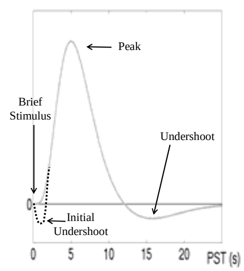
Local signal change of a single voxel over time is due to change in proportions of oxyhemoglobin/deoxyhemoglobin



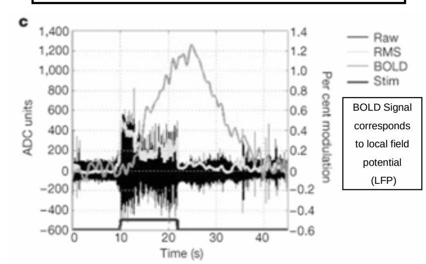
PHYSIOLOGY	PHYSICS
NEURAL ACTIVATION IS ASSOCIATED WITH AN INCREASE IN BLOOD FLOW (Roy & Sherrington, 1890) RESULT: REDUCTION IN THE PROPORTION OF DEOXY HGB IN THE LOCAL VASCULATURE	DEOXY HGB IS PARAMAGNETIC (Linus Pauling, 1936) AND DISTORTS THE LOCAL MAGNETIC FIELD CAUSING SIGNAL LOSS RESULT: LESS DISTORTION OF THE MAGNETIC FIELD RESULTS IN LOCAL MR SIGNAL INCREASE

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)



BOLD ORIGIN



BOLD Signal corresponds to local field potential (LFP)

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

II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. Positron Emission Tomography, PET
2. Functional Magnetic Resonance Imaging, fMRI
   - Source of signal and principles
   - Measurement techniques

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:

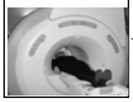
[26] axial slices

Resolution [1.5 x 1.5 x 4.5] mm

Each voxel is analyzed seperately

COMPUTATIONS FOR *f*UNCTIONAL IMAGE PROCESSING

Acquisition



RECONSTRUCTION

ALIGNMENT

VOXEL BY VOXEL ANALYSIS

GRAPHICAL REPRESENTATION

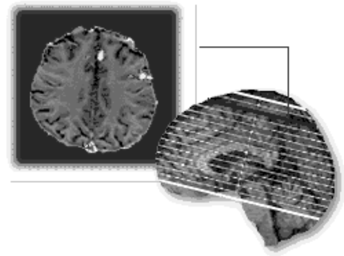
Functional Brain Map

Columbia fMRI

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

Brain Map of Object Naming

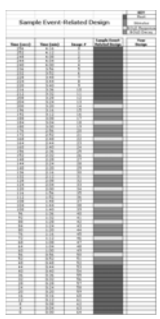
(Single Subject)



Columbia fMRI

Hirsch, J., et al

Block Design | **Event-Related Design**



Columbia fMRI

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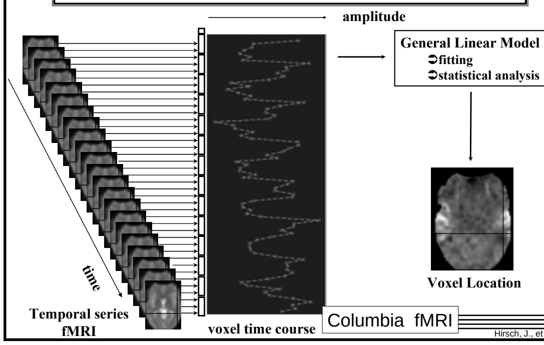
One voxel = One test (t, F, ...)



Columbia fMRI

Hirsch, J., et al

II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. **Positron Emission Tomography, PET**
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   - **Source of signal and principles**
   - **Measurement techniques**
   - **Computations 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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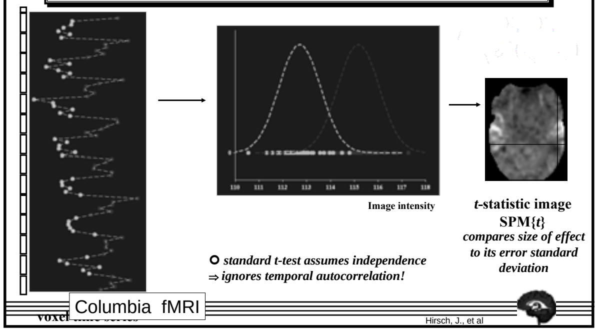
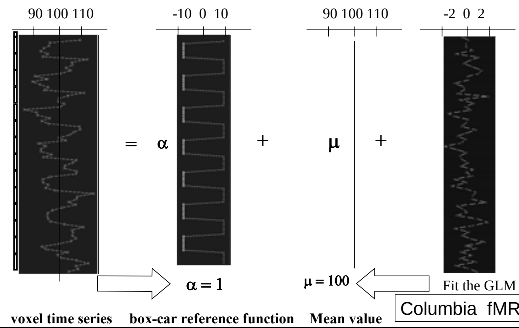
two-sample *t*-test



Regression



II. Brain Mapping Techniques

B. Cardiovascular Based Methods

1. **Positron Emission Tomography, PET**
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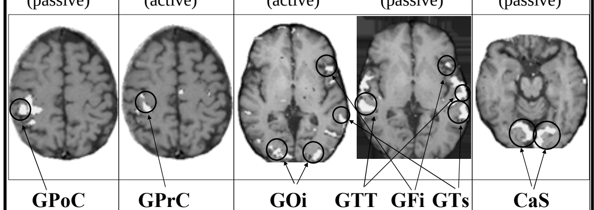
   - **Source of signal and principles**
   - **Measuremnet techniques**
   - **Computation for analysis**
   - **Individual brain maps**

Standard Brain Mapping Tasks

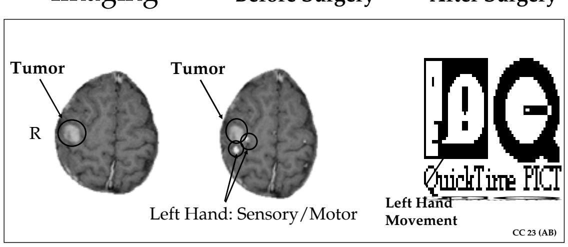
SENSORY	MOTOR	LANGUAGE		VISION
Touch	Finger Thumb Tapping	Picture Naming	Listening to Words	Reversing Checkerboard
(passive)	(active)	(active)	(passive)	(passive)



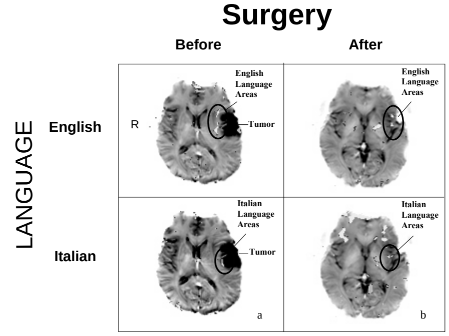
From Hirsch, J., et al; Neurosurgery 47: 711-722, 2000

Conventional Imaging | Functional Imaging

Before Surgery **After Surgery**



Surgery



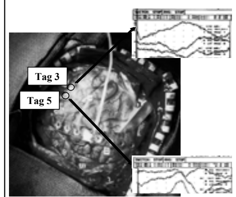
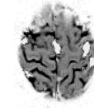
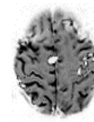
II. Brain Mapping Techniques

C. Electromagnetic - Based Methods
1. Somatosensory Evoked Potential, SSEP
2. Direct Cortical Stimulation

Columbia fMRI

Hirsch, J., et al

Sensory Motor Mapping

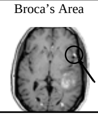
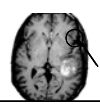
Craniotomy	SSEP	Direct Cortical Stimulation	Localization fMRI
		"Twitching of hand, focal seizure involving arm"	
		"Twitching in 1st three digits"	

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.

Columbia fMRI

Hirsch, J., et al

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.

Columbia fMRI

Hirsch, J., et al

II. Brain Mapping Techniques

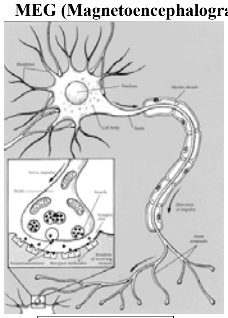
C. Electromagnetic - Based Methods
1. Somatasensory Evoked Potential, SSEP
2. Direct Cortical Stimulation
3. Magnetoencephalography, MEG
- **Source of signal and principles**

Columbia fMRI

Hirsch, J., et al

Methods to Measure Electromagnetic Activity:

MEG (Magnetoencephalography) - EEC (Electroencephalography)



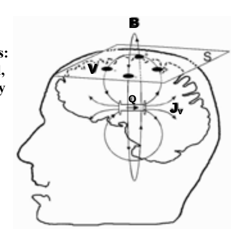
- **Signal Source: Electrical Activity of nerve cells.**
- **What is measured on the surface of the head is the result of mostly postsynaptic potentials (excitatory or inhibitory)**
- **Many nerve cells are aligned in palisades (e.g. pyramidal cells) and post-synaptic electrical fields sum with increasing 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**

Columbia fMRI

Hirsch, J., et al

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

Columbia fMRI

Hirsch, J., et al

II. Brain Mapping Techniques

C. Electromagnetic - Based Methods

1. Somatasensory Evoked Potential, SSEP
2. Direct Cortical Stimulation
3. Magnetoencephalography, MEG
   - Source of signal and principle
   - 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.

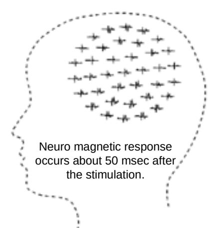
The spatial location of the source is inferred by mathematical modeling of the magnetic field pattern.

II. Brain Mapping Techniques

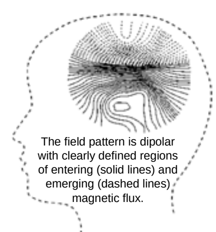
C. Electromagnetic - Based Methods

1. Somatasensory Evoked Potential, SSEP
2. Direct Cortical Stimulation
3. Magnetoencephalography, MEG
   - Source of signal
   - Measurement techniques
   - Computation for analysis

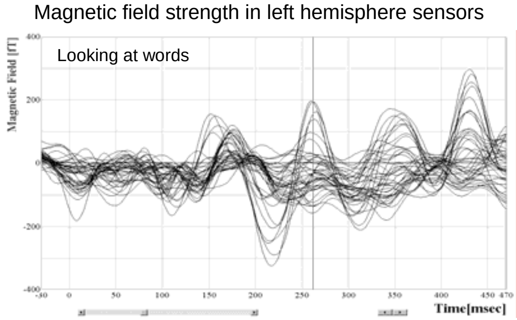
Somatosensory evoked magnetic signals in response to tactile stimulation of the contralateral index finger



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



Magnetic field strength in left hemisphere sensors



Liina Pylkkanen, Alec Marantz, 2002

II. Brain Mapping Techniques

C. Electromagnetic - Based Methods

1. Somatasensory Evoked Potential, SSEP
2. Direct Cortical Stimulation
3. Magnetoencephalography, MEG
4. Electroencephalography, EEG
   - Source of signal and principles
   - Measurement techniques

Electroencephalography

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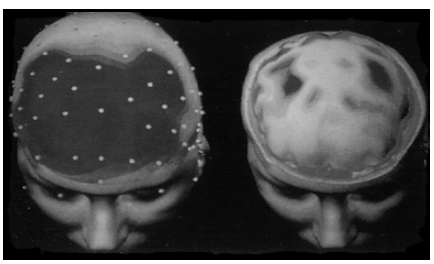
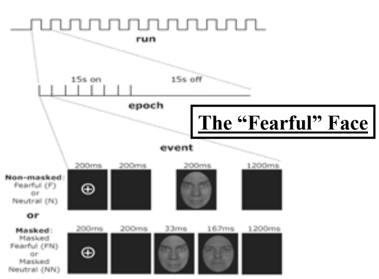
Electroencephalography

Electrode Array for EEG — Averaged Activity profiles during bilateral finger movement



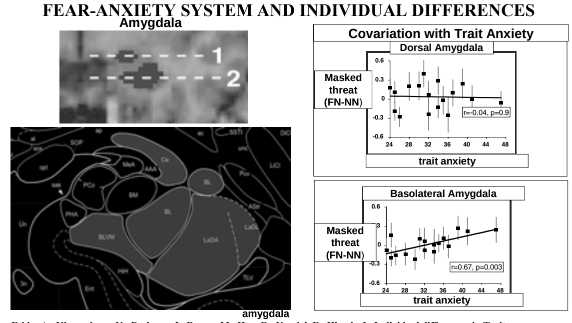
C. Future Directions of Brain Mapping

• NEUROCIRCUITRY FOR ANXIETY



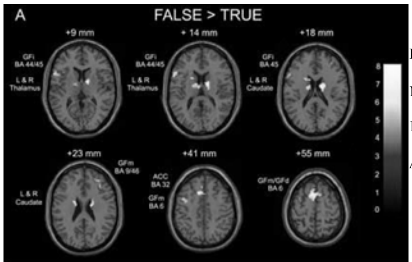
Etkin, A., Klemenhage, K., Dudman, J., Rogan, M., Hen, R., Kandel, E., Hirsch, J., Individual differences in Trait Anxiety Predict the Response of Basolateral Amygdala to Unconsciously Processed Threat, Vol 44, 1043-1055, Neuron, 2004

FEAR-ANXIETY SYSTEM AND INDIVIDUAL DIFFERENCES



Etkin, A., Klemenhage, K., Dudman, J., Rogan, M., Hen, R., Kandel, E., Hirsch, J., Individual differences in Trait Anxiety Predict the Response of Basolateral Amygdala to Unconsciously Processed Threat, Vol 44, 1043-1055, Neuron, 2004.

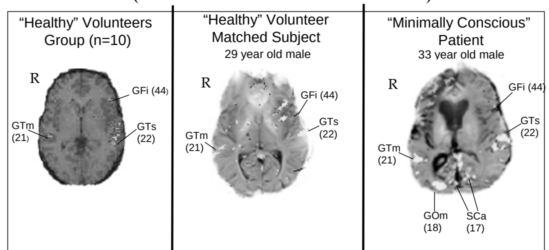
NEUROCIRCUITRY FOR "FALSE ANSWERS"



Inferior Frontal G.
Middle Frontal G.
Medial Frontal G.
Anterior Cingulate G.
Thalamus
Candate

Nunez, J.M., Casey, B. J., Egner, T., Hare, T., Hirsch, J., Intentional False Responding Shares Neural Substrates with Response Conflict and Cognitive Control, in press, NeuroImage, 2005.

• NEUROCIRCUITRY AND DISORDERS OF CONSCIOUSNESS: LISTENING TO NARRATIVES (FORWARD AND/NOT BACKWARD)



Schiff, N.D., Rodriguez-Moreno, D., Kamal, A., Kim, K.H.S., Giancino, J.T., Plum, F., Hirsch, J., fMRI Reveals Large Scale Network Activation in Minimally Conscious Patients, Neurology, 64:3, 514-523, 2005.

•NEURAL ANATOMY OF "MORALITY"

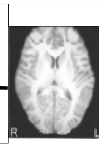
Year

HARLOW

Phineas Gage

1861

2004

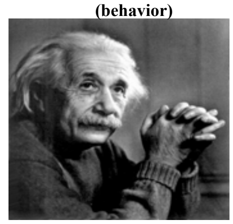


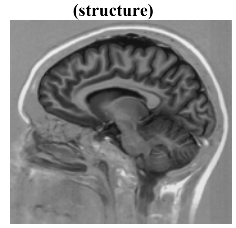
Greene, J.d., Nystrom, L.E., Engell, A.D., Darley, J.M., Cohen, J.D., The Neural Bases of Cognitive Conflict and Control in Moral Judgement,Neuron, 44, 389-400, 2004.

THE MOST FUNDAMENTAL GOAL OF NEUROSCIENCE

TO UNDERSTAND THE RELATIONSHIP BETWEEN THE

Operation of the mind (behavior) **AND** **Neurophysiology of the brain (structure)**





BRAIN-TO-BEHAVIOR PRINCIPLE