Neuroscience in Prevention Science: Neuroimaging

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Overview

I. Background

(What is neuroimaging?)

II. Utility of neuroimaging

(Why use neuroimaging?)

III. Regions of interest

(Where to look?)

IV. Neuroimaging methods

(How is it done?)

I. Background

Introduction to common types of neuroimaging

What is neuroimaging?

Neuroimaging: a variety of techniques used to visualize brain structure and function *in vivo*

What is neuroimaging?

Neuroimaging examines links between *behavior* and *brain structure and function*

Common methods:

Structural

- Magnetic resonance imaging (MRI)
- Computerized Tomography (CT)

Functional

- Functional MRI (FMRI)
- Positron Emission Tomography (PET)
- Electroencephalography (EEG)

What is neuroimaging?

Neuroimaging examines links between *behavior* and *brain structure and function*

Common methods:

Structural

- Magnetic resonance imaging (MRI)

Unprecedented spatial resolution

Functional

- Functional MRI (FMRI)

Good balance between spatial and temporal resolution that is needed to study cognitive functions in the timeframe that they occur

Common MRI Methods

Structural MRI

Brain morphometry

- e.g., regional gray matter volume, thickness, area

Functional MRI (FMRI)

Task-based FMRI

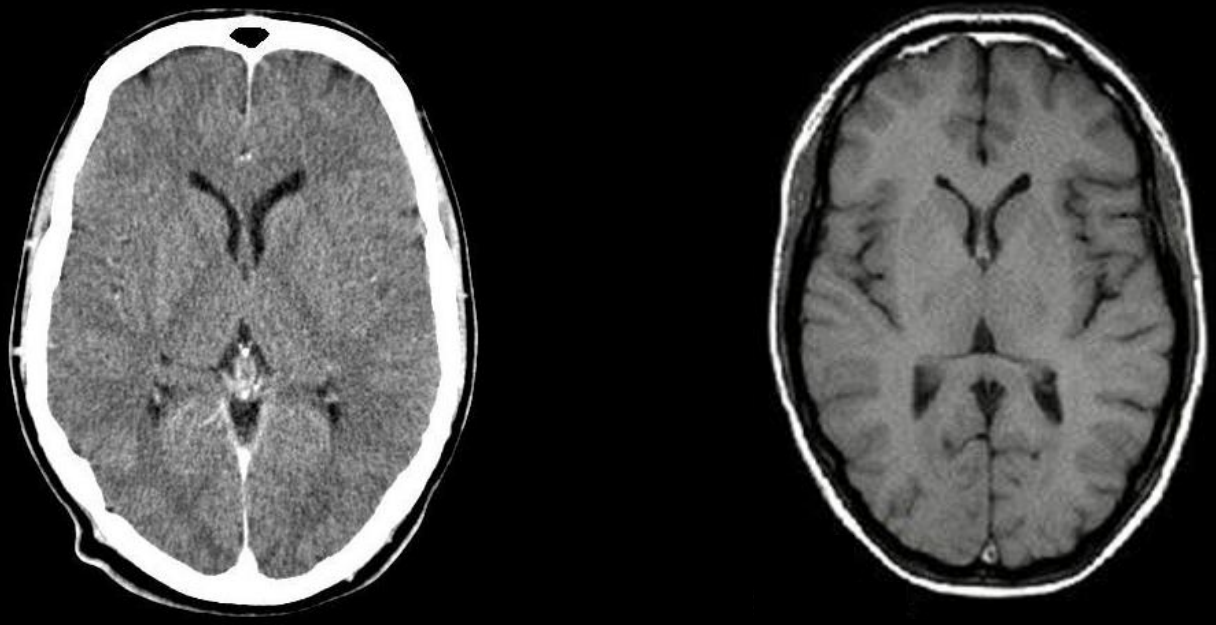
Brain's functional response to targeted challenges

Resting state functional connectivity

Correlations over time between brain networks at rest, without specific task demands

Structural MRI

Best method to produce high-resolution images of brain anatomy *in vivo*

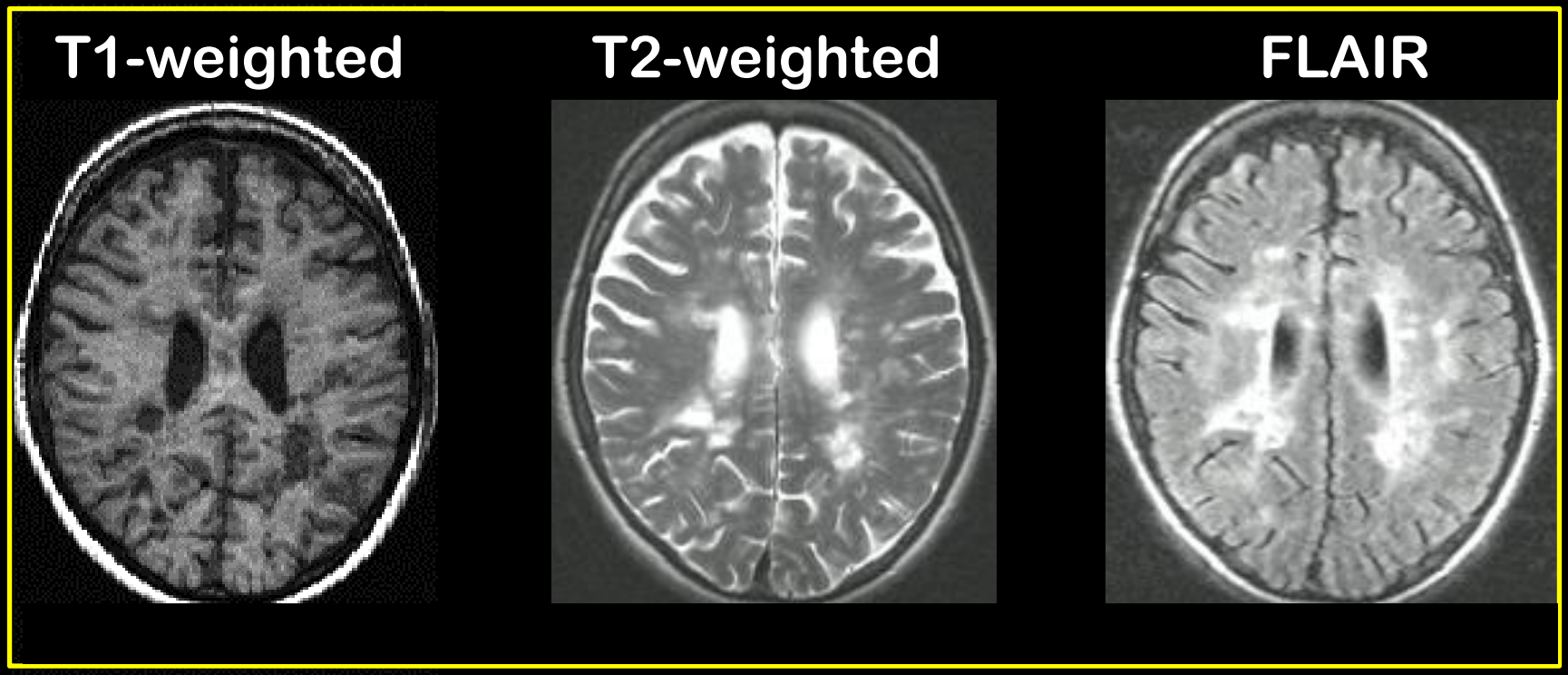


CT versus MRI

Structural MRI

Common research applications

- Lesion quantification (Multiple Sclerosis example below)
- Whole brain & regional *morphometry* (size, shape)
  - Usually volume and cortical thickness



Structural MRI:
Morphometry in prevention science

Types of questions that might be addressed:

Does cortical thickness in cognitive control networks predict risk behaviors?

Do brain nuclei linked to emotional processing vary in size as a function of stress exposure?

Can the effects of prevention programs be monitored using such structural markers?

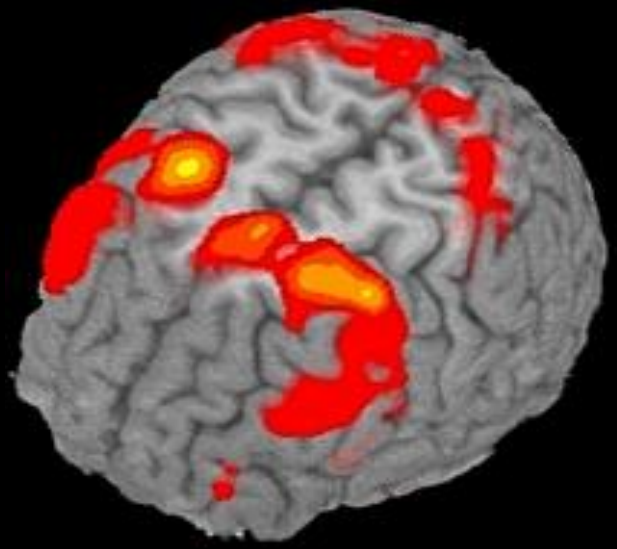
Functional MRI (FMRI)

Two common types of FMRI:

Task-based: **brain response quantified during specific challenges in the MRI scanner**

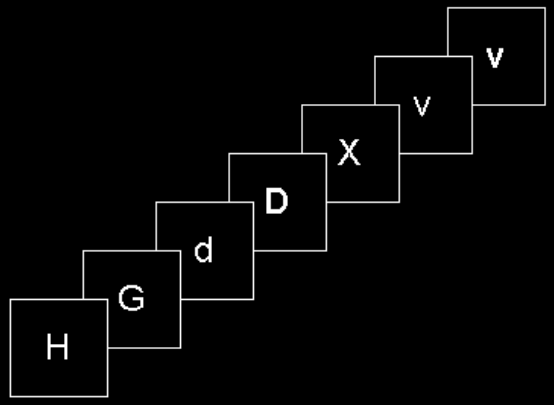
Resting state: **synchronization of brain network nodes measured without specific task demands**

Task-Based FMRI



Task-based FMRI: is used to quantify activity during cognitive, affective, or behavioral challenges

Task-Based FMRI



cognitive, affective, or behavioral challenges

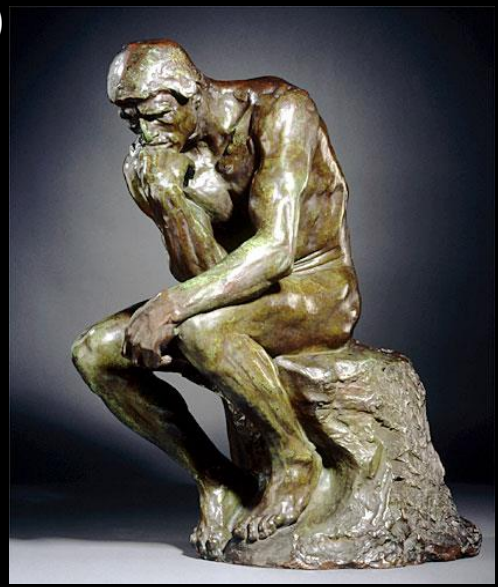
e.g., memory, craving provocation, distress tolerance

Images from: Gilbert & Rabinovich, 1999 and moodsurfing.com

Task-based FMRI

Challenges of potential interest in prevention

- Working memory
  - (e.g., n-Back, Paced Auditory Serial Addition Test (PASAT))
- Distress tolerance
  - (e.g., PASAT, n-Back, cold pressor challenge)
- Cue reactivity
  - (e.g., cigarette, food, emotion provocation)
- Decisions about reward
  - (e.g., delay discounting)
- Inhibitory control
  - (e.g., Stroop, Go/No-go)



Task-Based FMRI in prevention science

Types of questions that might be addressed:

Does brain response in cognitive control networks predict risk behaviors?

Does reactivity in networks associated with emotion vary as a function of stress exposure?

Can the outcomes of prevention programs be evaluated using brain response to stressors?

Resting State FMRI
Functional Connectivity

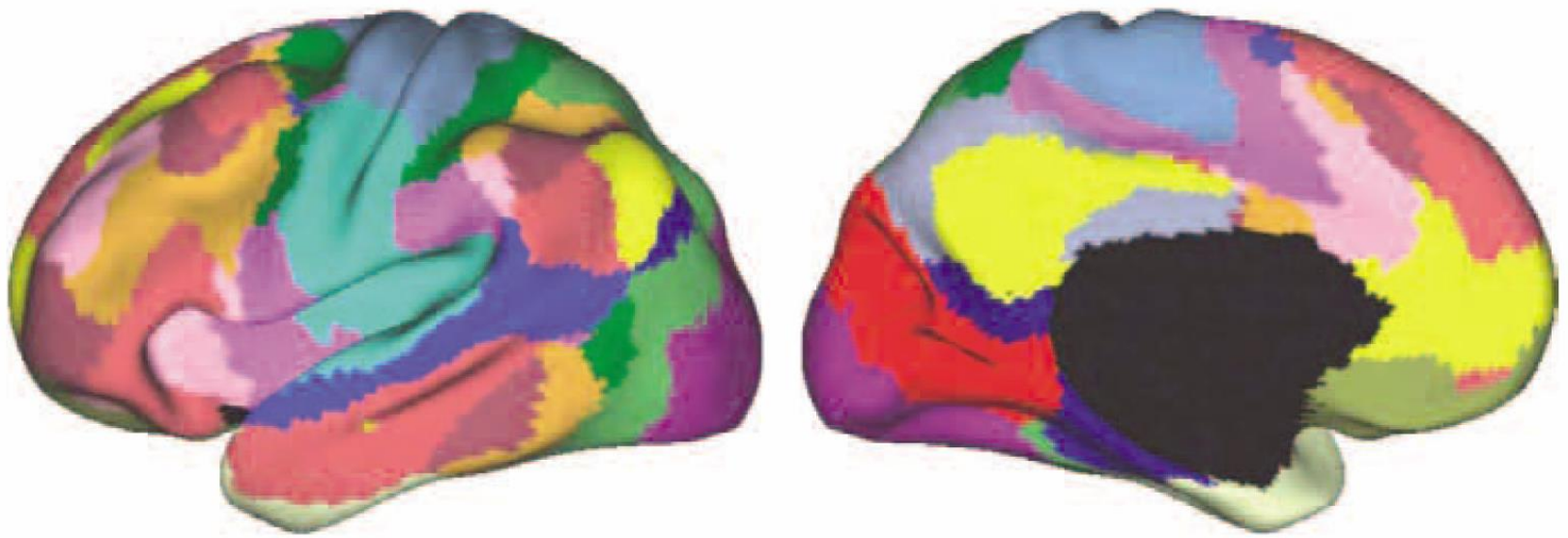
Used to examine FMRI signal for covariance among nodes of brain networks over time

No specific task demands

- No particular network is challenged
- But any network can be examined

Resting State Functional Connectivity

Reveals the brain's intrinsic functional networks



Synchronous regions have same color

(Original sample size 500; replicated in another sample of 500)

Yeo et al., 2011

Functional connectivity in prevention science

Types of questions that might be addressed:

Does synchronization of cognitive control networks predict risk behaviors?

Does the the strength connectivity between cognitive control and emotion networks vary as a function of stress exposure?

Do prevention programs alter interactions between these networks?

II. Utility of Neuroimaging

Why use neuroimaging?

Visualize brain structure and function *in vivo*

Before neuroimaging, understanding of brain function relied on cases of dysfunction (e.g., stroke, brain injury)

1) Abnormal behavior was noted

2) Brain structure was examined post-mortem

Preserved brain of Paul Broca's famous patient Louis Leborgne

Dronkers et al., 2007

Advantages of MRI and FMRI over other neuroimaging techniques

- Non-invasive
- No radioactive tracers or contrast agents
- High spatial and temporal resolution
- Multi-sequence protocols are possible
  - functional and structural available in one session
- Whole-brain scans
- Availability of MRI

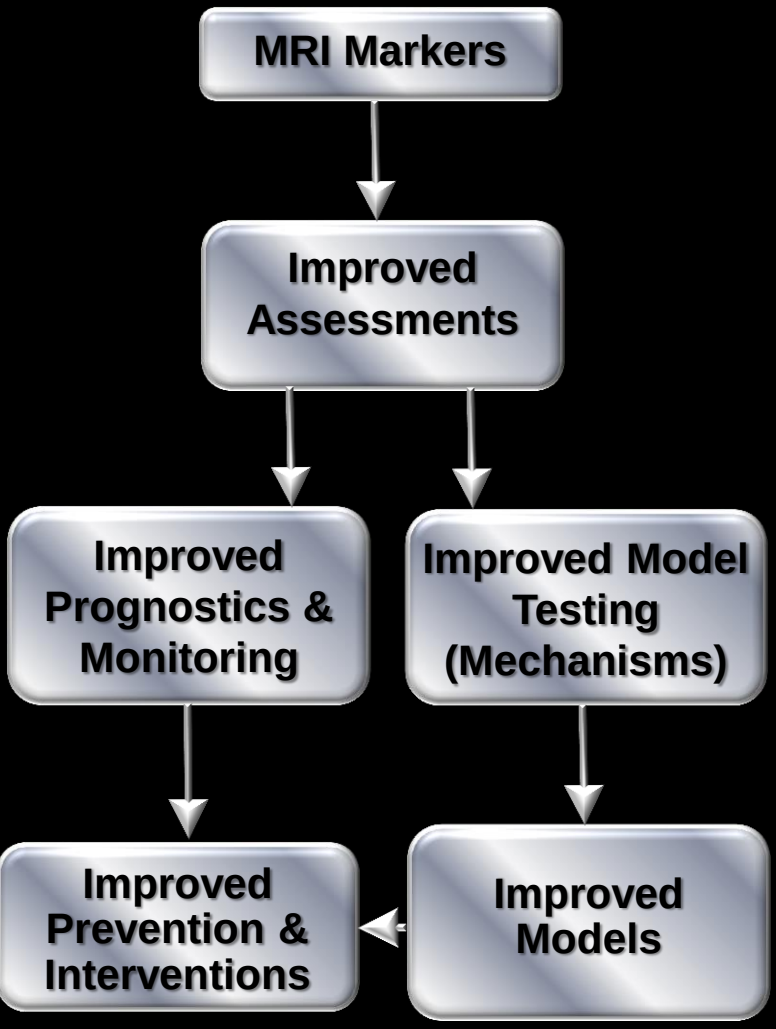
Why use MRI in Prevention Science?

Improved assessment

Improved

- Testing of brain-behavior models
- Risk assessment (diagnostics / prognostics)
- Monitoring of course
- Outcome evaluation

Why use MRI in Prevention Science?



How are assessments improved?

Improved sensitivity

- Direct and objective quantification of difficult to measure states
  - e.g., effort, fatigue, mood, craving, hunger, withdrawal, malingering

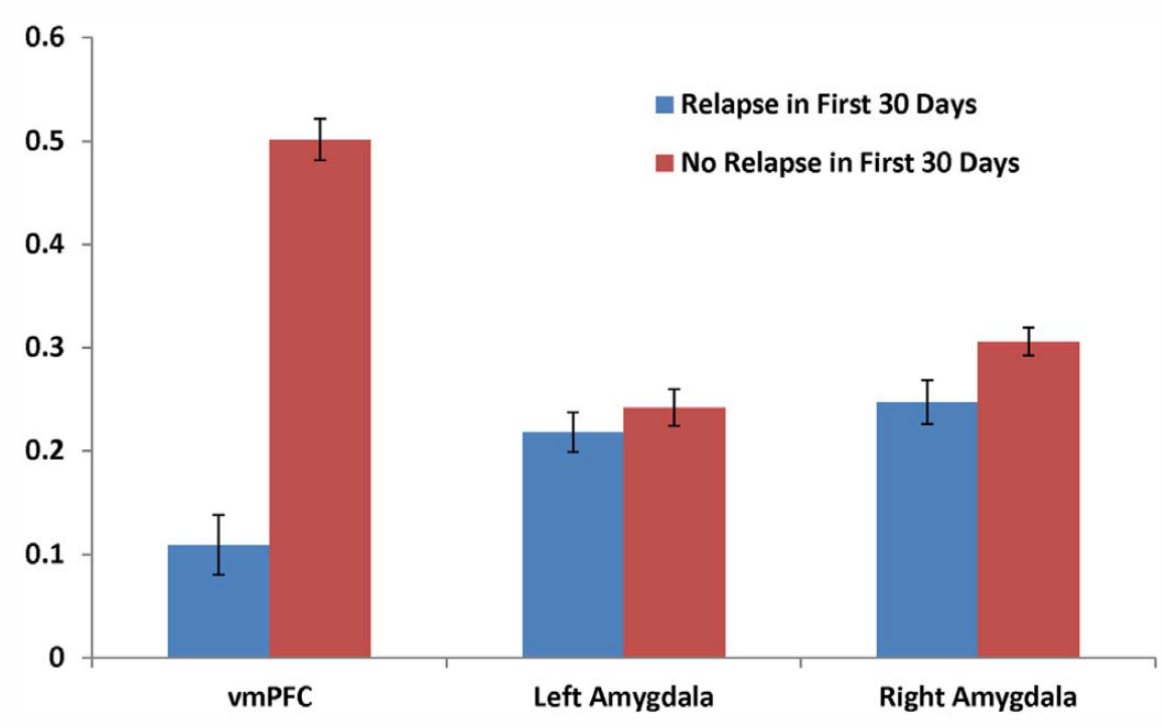
Complementary information

- Brain markers may provide previously unavailable information

Complements best outcome predictor

Response to warning labels in the VMPFC adds to predictive utility of dependence severity alone

- Improved predictive validity
- Localization of effect



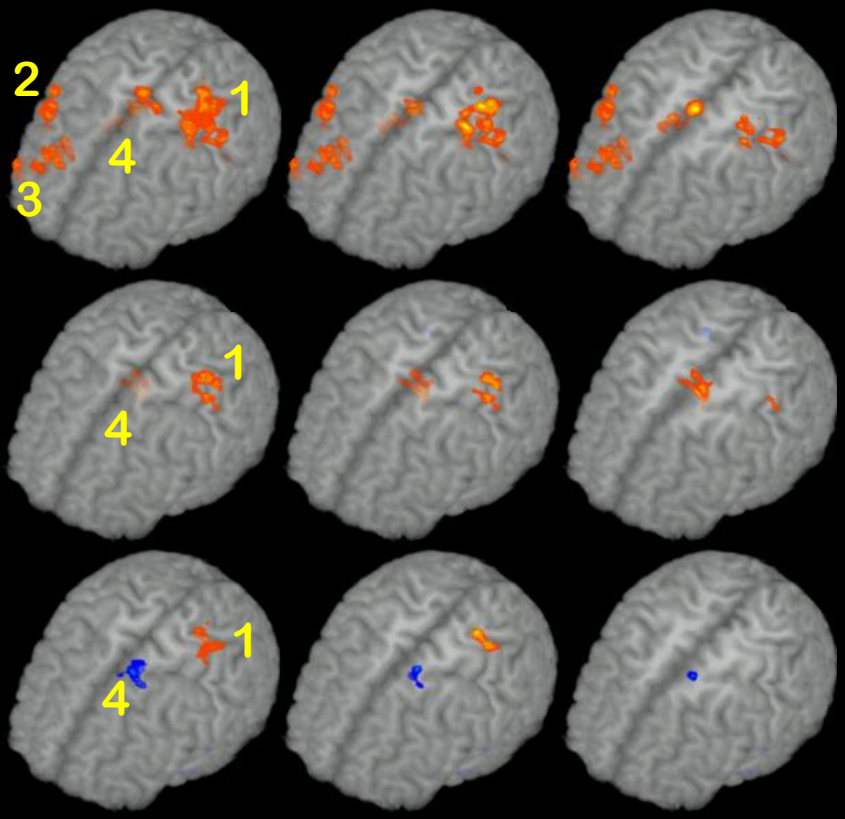
Owens et al., 2017

Overactivation: group contrasts of n-Back

1-Back

2-Back

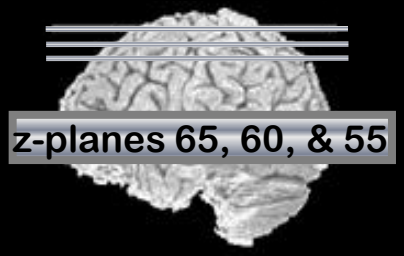
3-Back



Red = Greater activity in the Multiple Sclerosis group

Blue = Greater activity in the control group

Performance accuracy did not differ



	Region	Center Coordinates x	y	z
1	Postcentral gyrus	-42	25	57
2	Caudal middle frontal gyrus	48	22	39
3	Rostral middle/superior frontal gyrus	23	40	43
4	Medial/superior frontal gyrus (caudal)	05	05	55

Sweet et al., 2006

III. Regions of Interest

Where to look for neural correlates in prevention research?

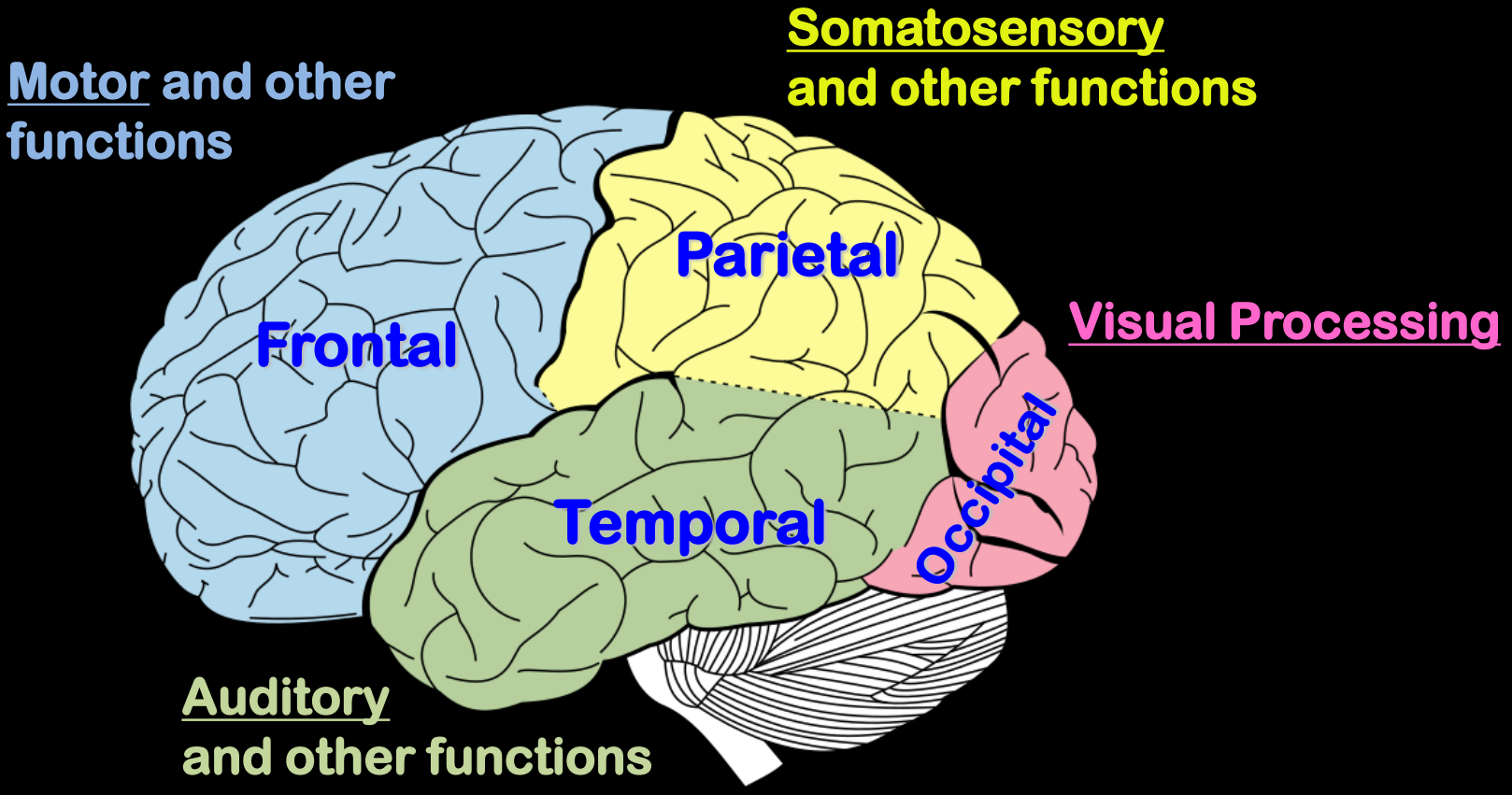
The gray matter, where the cell bodies of neurons are located

Two types of gray matter

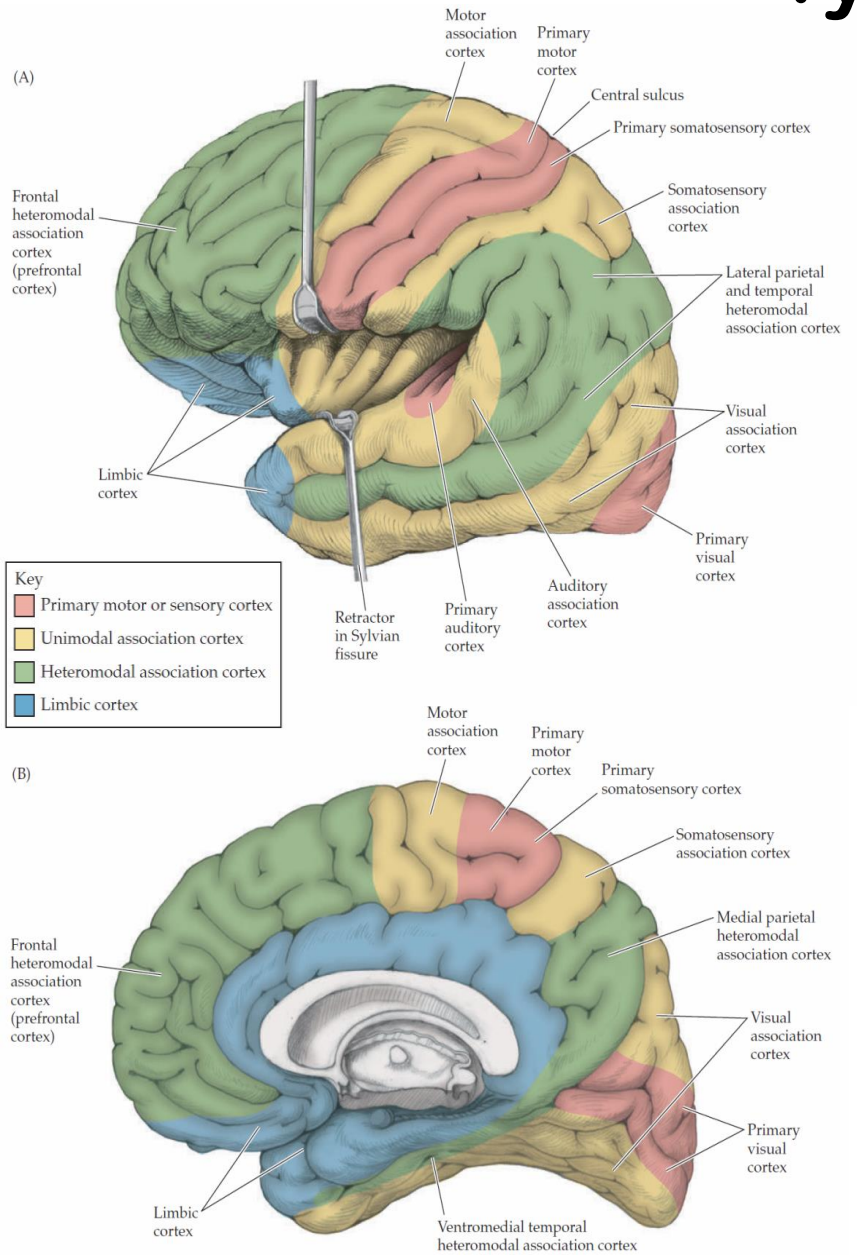
1) Cortical regions (brain surface)

2) Subcortical nuclei (below the surface)

1) Cortical Function: Simplified Localization by Lobe



Types of Cortical Regions



Primary (motor and sensory)
Unimodal (motor or one sense)
Heteromodal
Limbic

Most relevant in prevention

Limbic cortex

Emotional and motivational processing

Heteromodal association areas

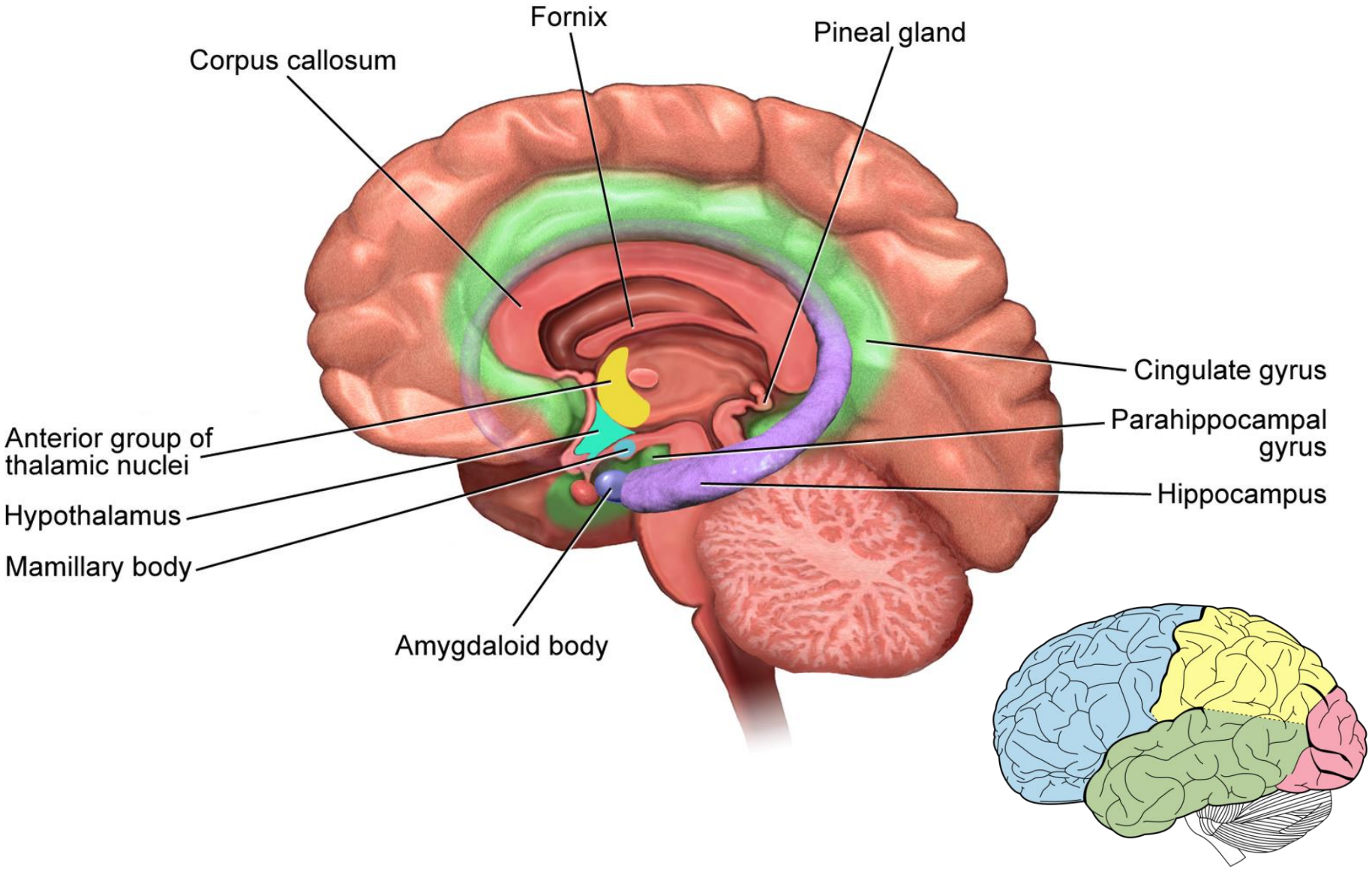
Higher order cognitive functions

Blumenfeld, 2010

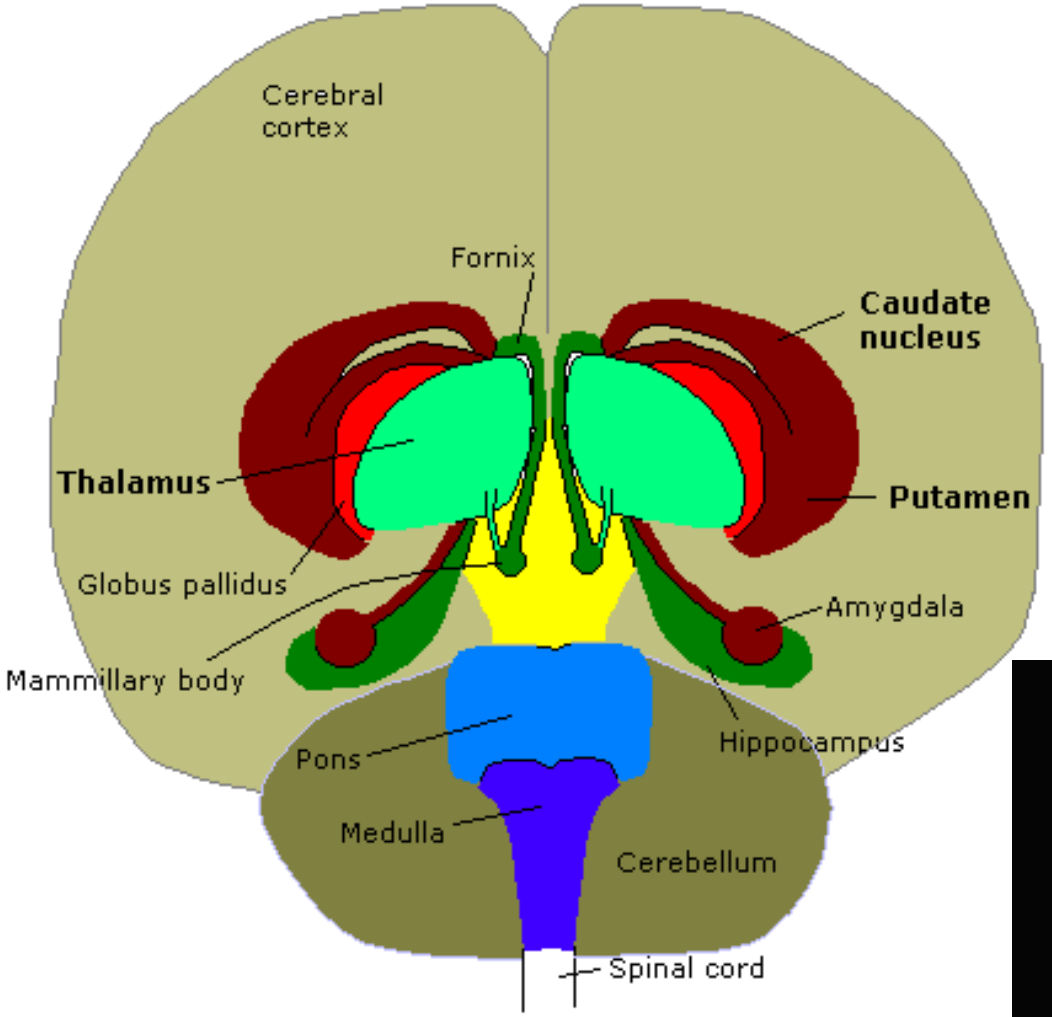
Some Prefrontal Functions

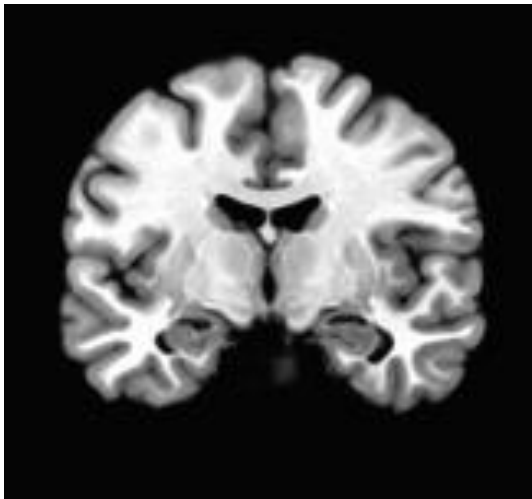
- Executive functions
  - Working memory
  - Planning
  - Divergent thinking / Abstraction
  - Inhibitory control / Regulation
  - Multi-tasking
  - Decision-making
  - Selective and sustained attention
- Social functions
- Emotional functions

2) Subcortical Nuclei



Subcortical Nuclei





Subcortical Nuclei

- Amygdala (emotion and reward)
- Basal forebrain (reward and motivation)
  - Ventral striatum
  - Septal nuclei
- Basal Ganglia (starting, stopping, switching)
- Hippocampus (memory)

IV. Neuroimaging Methods

How is it done?

MRI and FMRI use a large magnetic field, radio wave pulses, and sensitive antennas to quantify brain structure and function

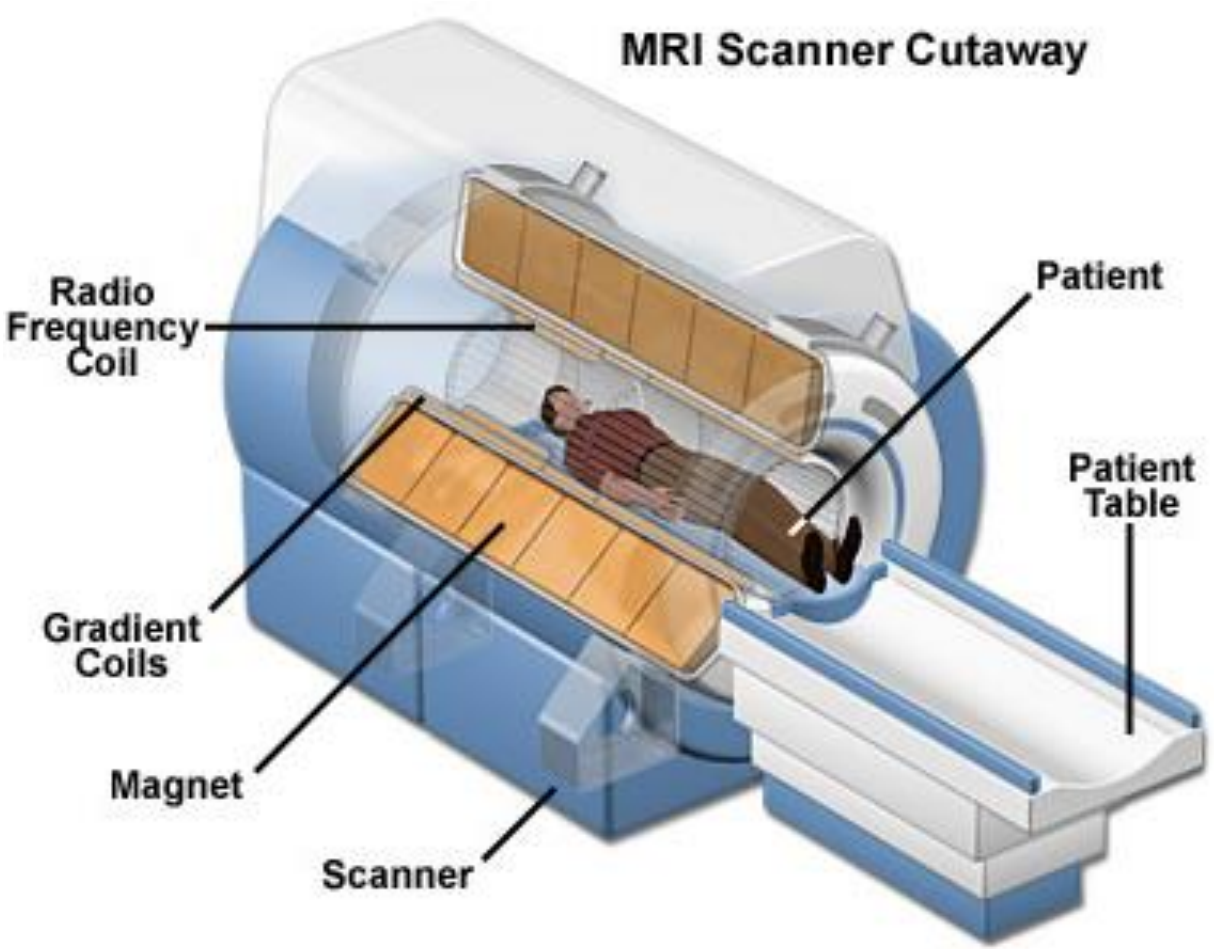


Image source: www.magnet.fsu.edu

MRI signal

Hydrogen protons are abundant in H_2O in humans

1) H protons spin generate magnetic field
   - Act like little magnets
   - Orientations are normally random

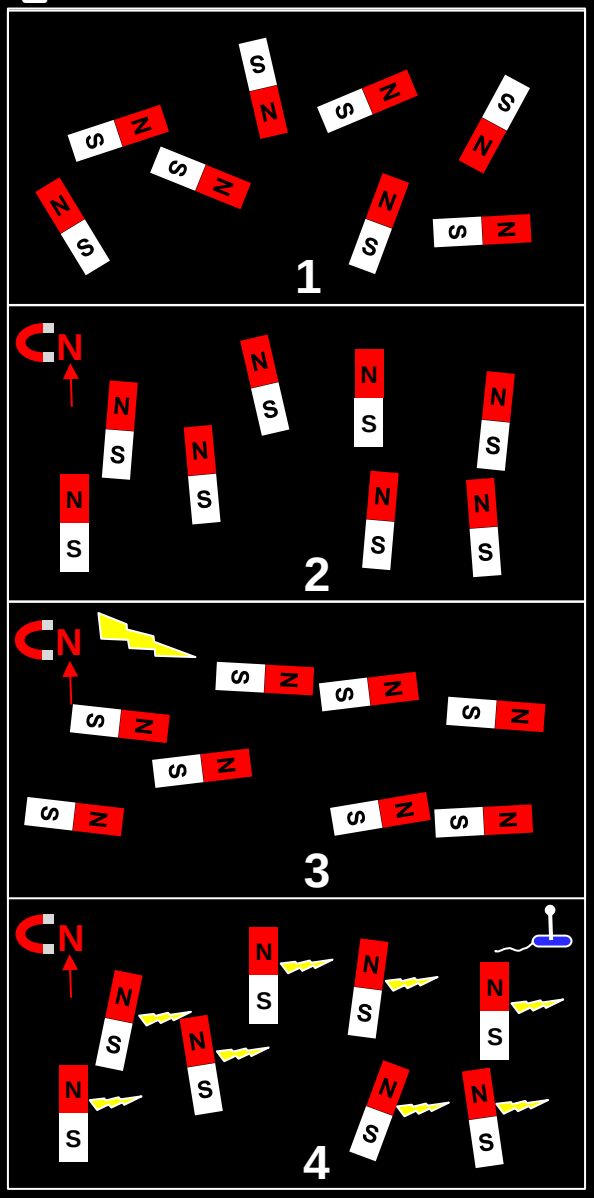
2) Protons align in the strong magnetic field

3) A radio wave pulse perturbs alignment

   - Energy is absorbed (higher energy state)
   - Proton orientation and spins synchronize

4) Relaxation: protons emit radio signal as they return to lower energy states

   - Antenna measures rates of realignment
   - Rates differ by tissue type, providing contrast



FMRI Signal

FMRI detects changes in capillary blood over time

Oxyhemoglobin (with O_2) produces signal normally

Deoxyhemoglobin (without O_2) is magnetic and suppresses signal

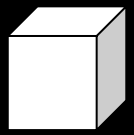
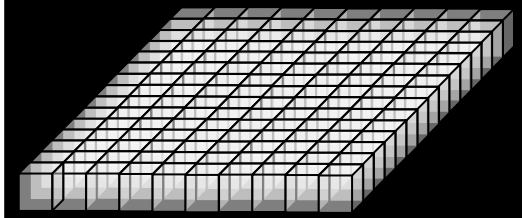
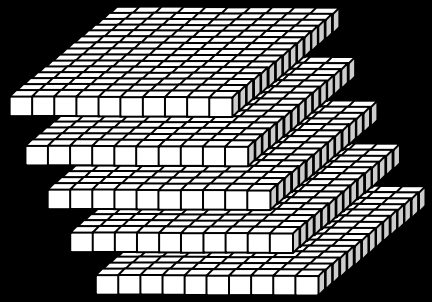
As the ratio of oxyhemoglobin to deoxyhemoglobin increases, FMRI signal is stronger

- Oxyhemoglobin is delivered in excess of neural demand where the brain is most active

- Task-based FMRI is always a contrast of this ratio during challenge compared to this ratio during a control condition (i.e., always relative)

MRI Data

Summed per voxel, a 3-dimensional pixel

	Voxel	Plane	Volume
MRI:	1 mm^3	256 x 256 voxels	10 million voxels
FMRI:	3 mm^3	64 x 64 voxels	200, 000 voxels
			
	Basic unit of data acquisition and analysis *Spatial resolution* is the voxel size	Acquired in slices comprised of voxels	Slices are stacked to create a volume In FMRI multiple volumes are acquired *Temporal resolution* is the time required to acquire a volume

FMRI Data Analysis

Data preprocessing

- Prepare data for analyses
  e.g., quality control, stereotaxic standardization

Individual level analyses

- Each voxel is examined over time for response to the FMRI challenge (e.g., memory test, smoking cues)

Group level analyses

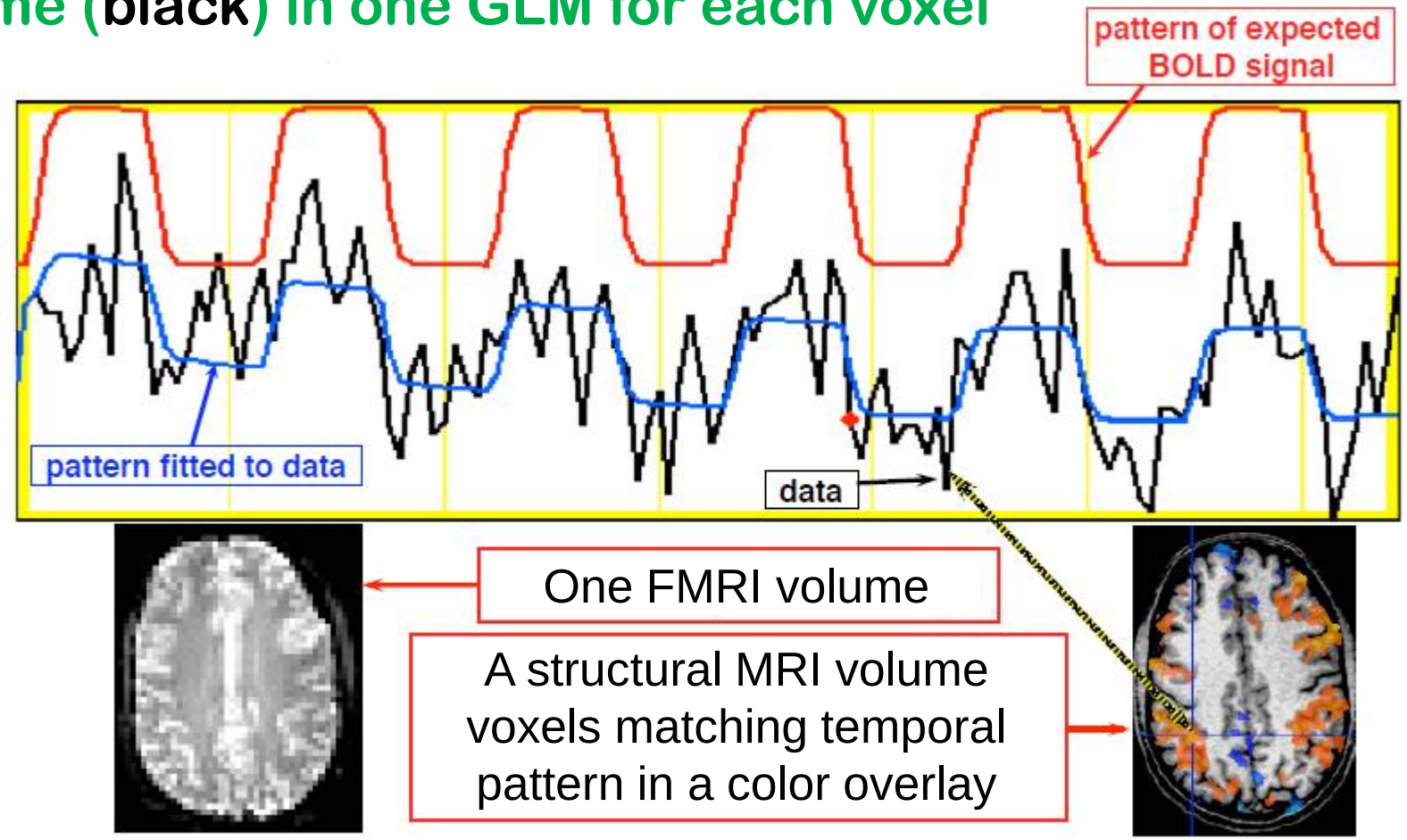
- Voxel by voxel comparisons of individual effects
- Region of interest (summed voxel effects by region)

FMRI Data Analysis

Individual level analyses

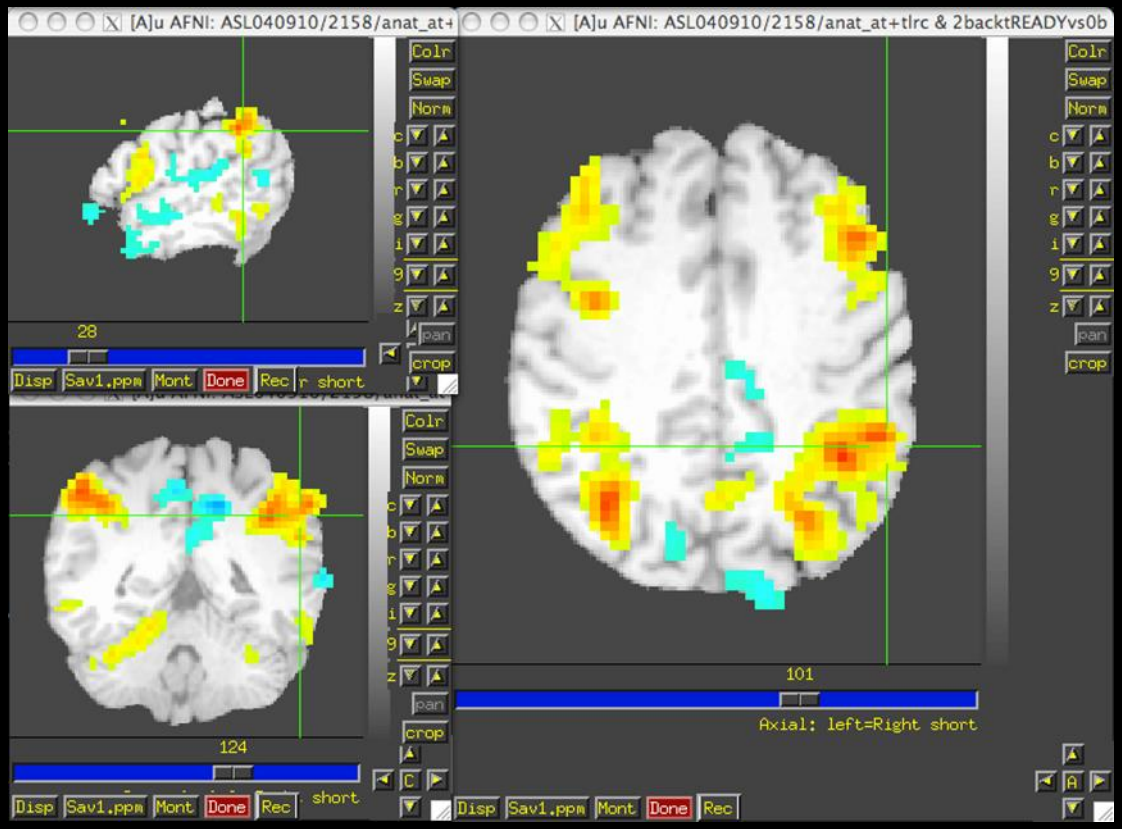
General Linear Modeling (GLM)

The time courses of conditions in the FMRI paradigm are used as predictors (red and blue) of BOLD signal over time (black) in one GLM for each voxel



GLM output provides a partial β coefficient for each condition modeled for each voxel

An example of a β coefficient map representing the 2-Back effect in one person



FMRI Data Analysis

Group level analyses

Major approaches to group level analyses

Voxel-wise analyses

Region of interest analyses

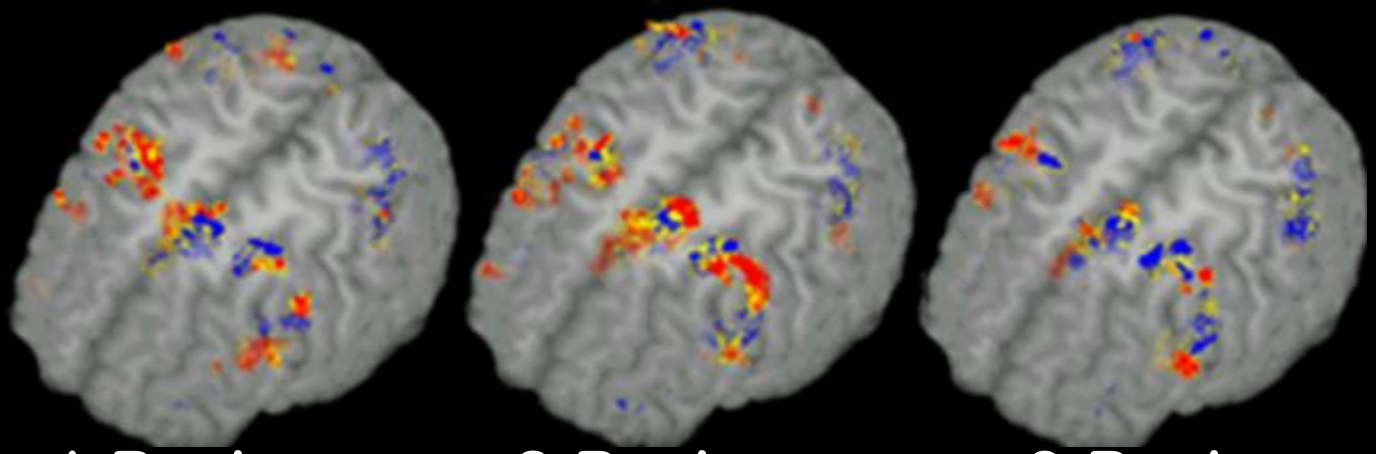
Group Level: Voxel-wise Analyses

Two major types of group level voxelwise analysis

1) Summary maps: combine data by group or condition to get group-level effects

Evaluate whether FMRI challenge elicits valid response

Example of Voxel-wise Group Summary activity

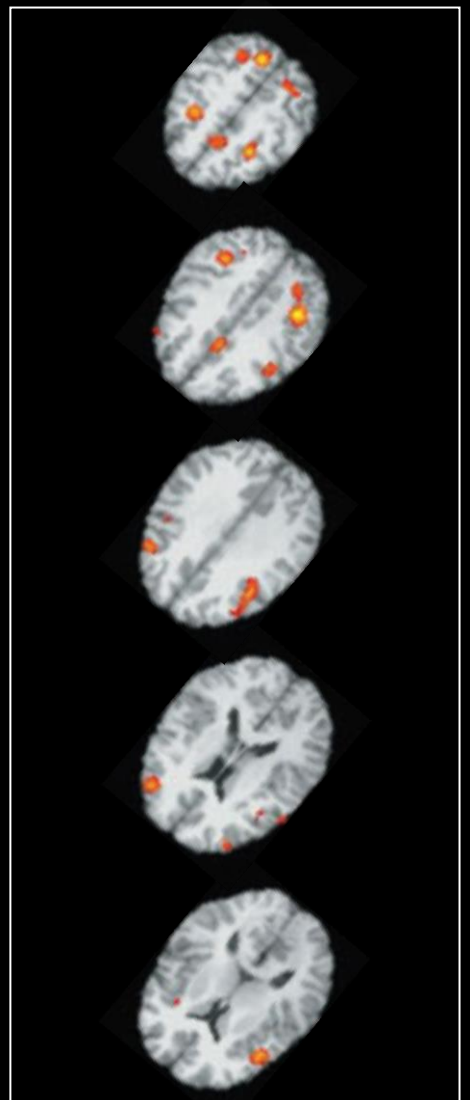


1-Back 2-Back 3-Back

Red = Unique to the MS group

Blue = Unique to the control group

Yellow = Common to both groups



n-Back Meta-analysis
(Owen et al., 2005)

Sample: 15 Multiple Sclerosis Patients
15 Matched Healthy Controls

Results: Each group exhibits brain response to a working memory Challenge that is consistent with prior literature

Sweet et al., *Human Brain Mapping*, 2006

Group Level: Voxel-wise Analyses

Two major types of group level voxelwise analysis

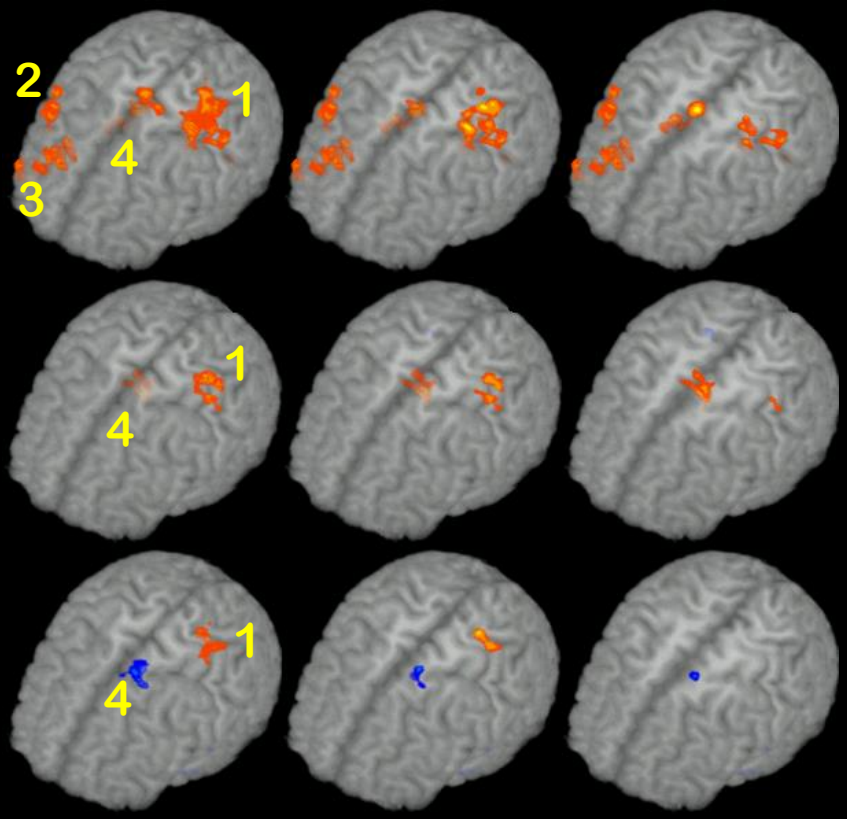
2) Contrast maps: contrast groups or conditions to identify which voxels show the greatest differences

Exploratory and descriptive

- *a priori* hypotheses not likely at voxel level (not functionally meaningful units)

- Useful to localize strongest effects

Example of Voxel-wise Group Contrasts



Red = Greater activity in the Multiple Sclerosis group

Blue = Greater activity in the control group

Performance accuracy did not differ

Sample: 15 Multiple Sclerosis Patients
15 Matched Healthy Controls

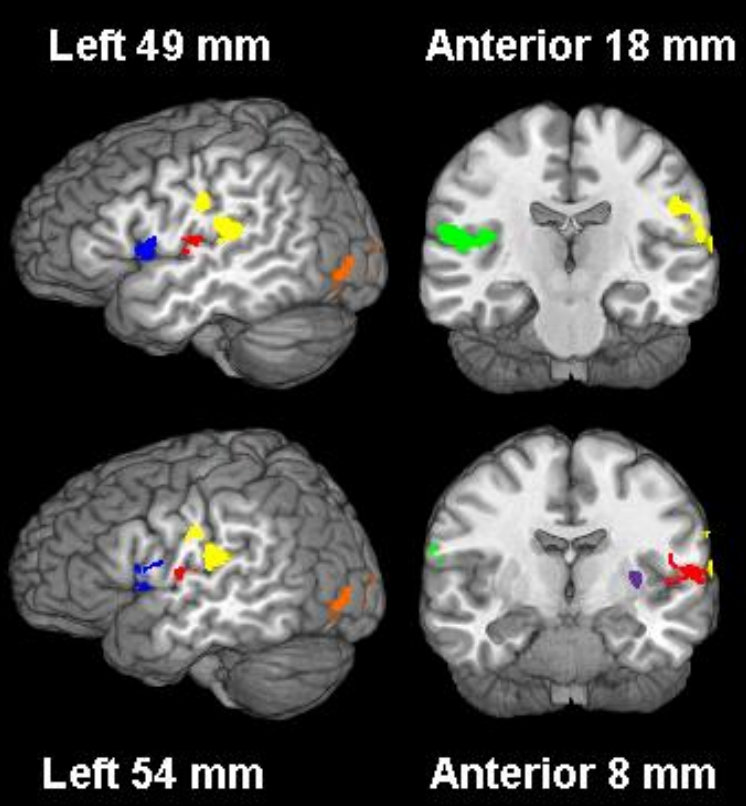
Results: MS patients exhibit greater brain response during working memory despite normal performance accuracy

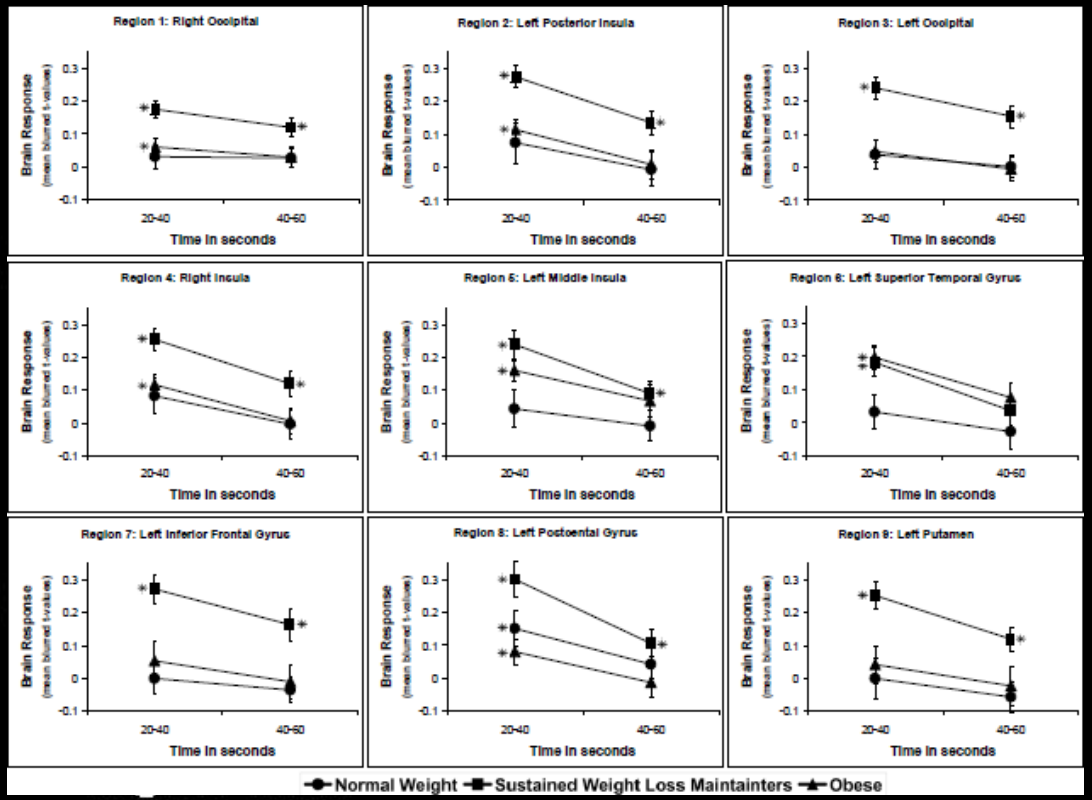
Sweet et al., *Human Brain Mapping*, 2006

Group Level Region of Interest Analyses

Summarize voxel effects across functionally meaningful brain regions

Example of ROI Analyses:
Cue reactivity "Lollipop paradigm"





Sample: 17 Successful Weight-loss Maintainers (SWLM)
16 Obese Controls
17 Normal Weight Controls

Results: SWLM group exhibited greater reactivity and scored higher on dietary restraint

Sweet et al., *Obesity,* 2012