Neuroscience in Prevention Science: Neuroimaging

Lawrence H. Sweet, Ph.D.
Gary R. Sperduto Professor in Clinical Psychology
Director, Clinical Neuroscience Laboratory and Center for Translational & Prevention Science - Neurocognitive Core
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 \textit{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

T1-weighted  T2-weighted  FLAIR
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: is used to quantify activity during cognitive, affective, or behavioral challenges
Task-Based FMRI

- MRI is best known as a method to produce high-resolution images of anatomy including the brain (atrophy, lesions, tumors).

Task-based FMRI: is used to quantify activity during 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 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 \textit{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?

MRI Markers

Improved Assessments

Improved Prognostics & Monitoring

Improved Prevention & Interventions

Improved Model Testing (Mechanisms)

Improved Models
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

Red = Greater activity in the Multiple Sclerosis group

Blue = Greater activity in the control group

Performance accuracy did not differ

Center Coordinates

<table>
<thead>
<tr>
<th>Region</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Postcentral gyrus</td>
<td>-42</td>
<td>25</td>
<td>57</td>
</tr>
<tr>
<td>2 Caudal middle frontal gyrus</td>
<td>48</td>
<td>22</td>
<td>39</td>
</tr>
<tr>
<td>3 Rostral middle/superior frontal gyrus</td>
<td>23</td>
<td>40</td>
<td>43</td>
</tr>
<tr>
<td>4 Medial/superior frontal gyrus (caudal)</td>
<td>05</td>
<td>05</td>
<td>55</td>
</tr>
</tbody>
</table>

z-planes 65, 60, & 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

- **Motor** and other functions
- **Somatosensory** and other functions
- **Visual Processing**
- **Frontal**
- **Parietal**
- **Temporal**
- **Occipital**

**Auditory** and other functions
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

- Corpus callosum
- Fornix
- Pineal gland
- Cingulate gyrus
- Parahippocampal gyrus
- Hippocampus
- Anterior group of thalamic nuclei
- Hypothalamus
- Mamillary body
- Amygdaloid body
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.
MRI signal

Hydrogen protons are abundant in H\textsubscript{2}O 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 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

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

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

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

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