Cortical Origin of Frontal Asymmetry for Major Depressive Disorder

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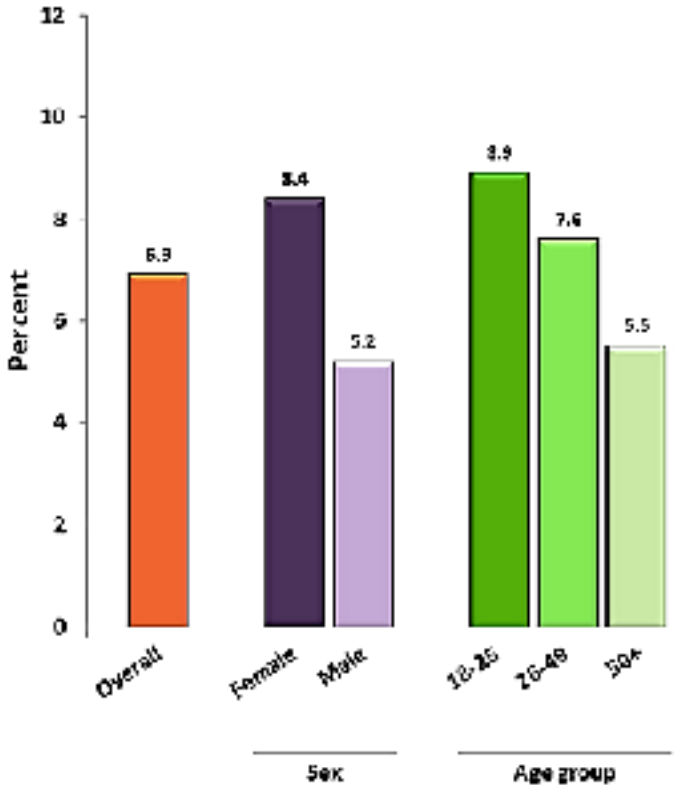
Outline

- **Introduction**
- Methods
  - Data Collection
  - Analysis
- Results
  - EEG, MEG, MEG Cortical Space
- Discussion

MDD is Common and Poorly treated

- 'Depression' refers to a spectrum of disturbances in mood that last for several weeks
- Lifetime prevalence about 12%
- Elevated mortality and comorbidity rate
- Current treatments are insufficient

Prevalence of MDD Episodes among U.S. Adults



Source: World Health Organization, Mental Health Gap Action Programme, 2014

HAM-D Psychometric

THE HAMILTON RATING SCALE FOR DEPRESSION

(to be administered by a health care professional)

Patient's Name

Date of Assessment

To rate the severity of depression in patients who are already diagnosed as depressed, administer this questionnaire. The higher the score, the more severe the depression.

For each item, write the correct number on the line next to the item. (Only one response per item)

1. **DEPRESSED MOOD** (Sadness, hopeless, helpless, worthless)

_____

0= Absent
1= These feeling states indicated only on questioning
2= These feeling states spontaneously reported verbally
3= Communicates feeling states non-verbally—i.e., through facial expression, posture, voice, and tendency to weep
4= Patient reports VIRTUALLY ONLY these feeling states in his spontaneous verbal and non-verbal communication

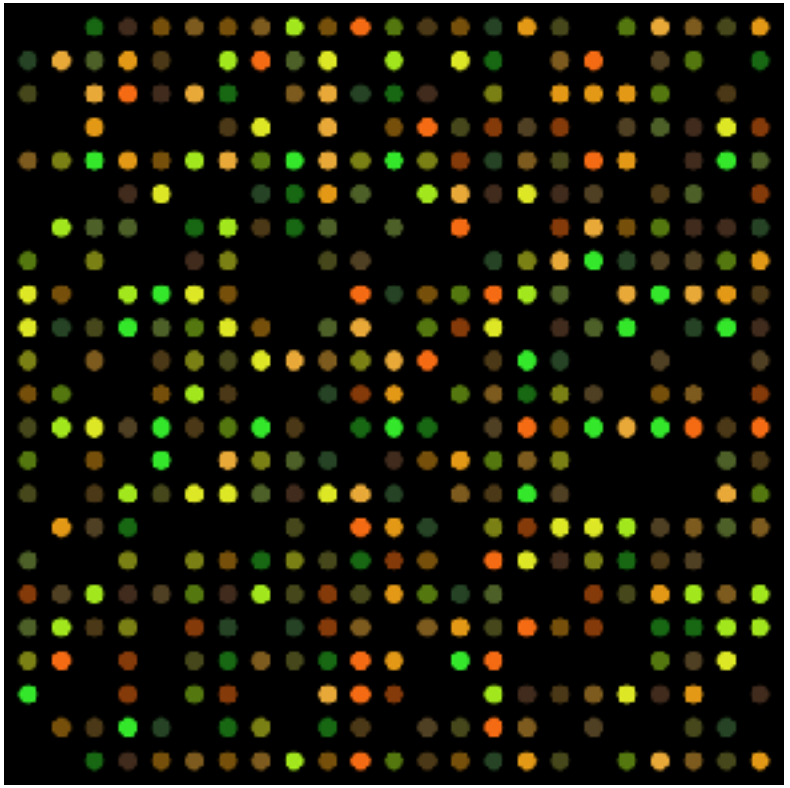
2. **FEELINGS OF GUILT**

0= Absent
1= Self reproach, feels he has let people down
2= Ideas of guilt or rumination over past errors or sinful deeds
3= Present illness is a punishment. Delusions of guilt
4= Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations

Source: Strik J, *et al. Psychosomatics.* 2001; 42:423–428

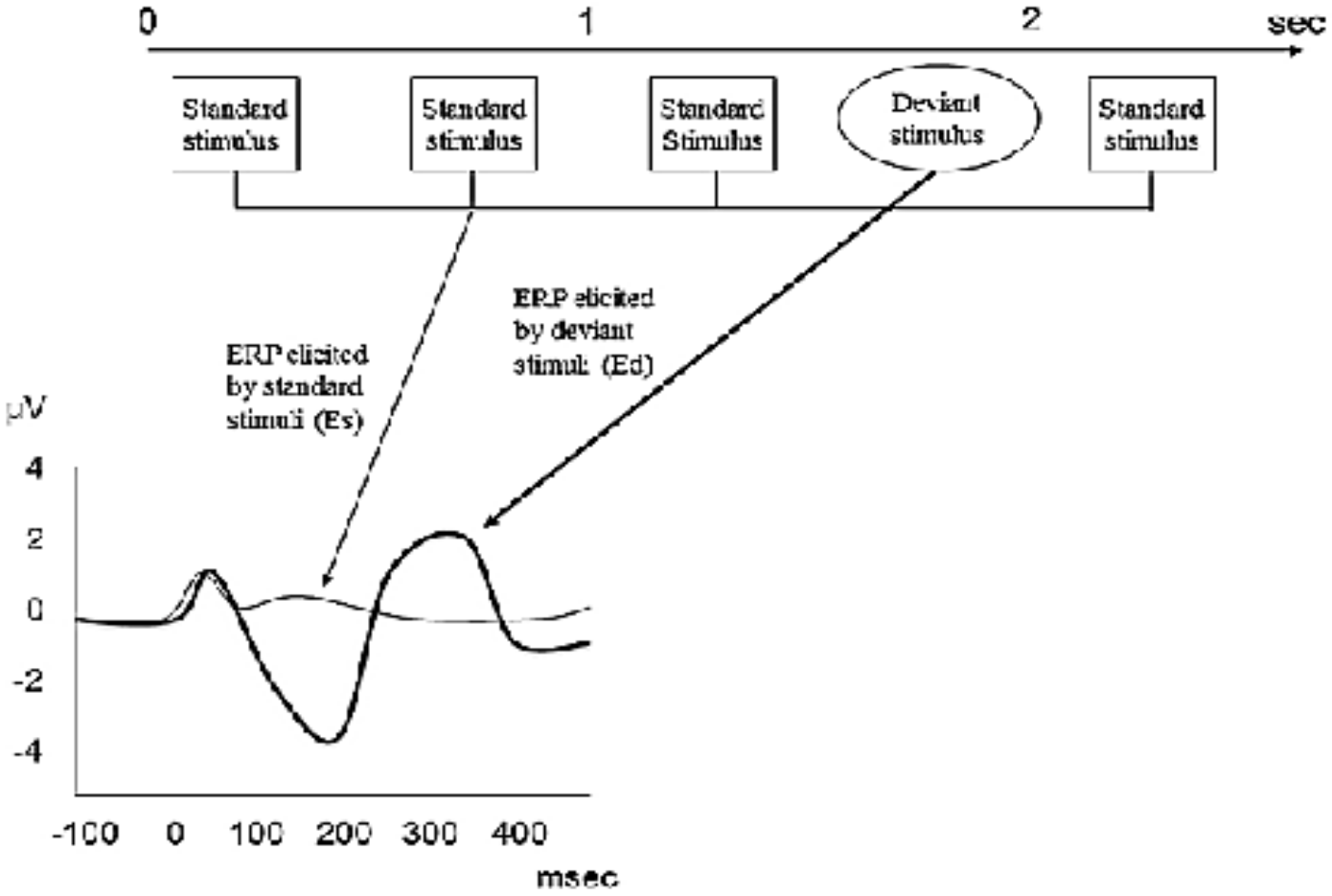
Biomarkers are potential objective diagnostic and prognostic tools

- Biomarkers offer 'biological cues'
- Existing Biomarkers
  - Pathophysiological
  - Electrophysiological
- Problems with existing biomarkers
  - Lack validity
  - Unrealistic for clinical setting



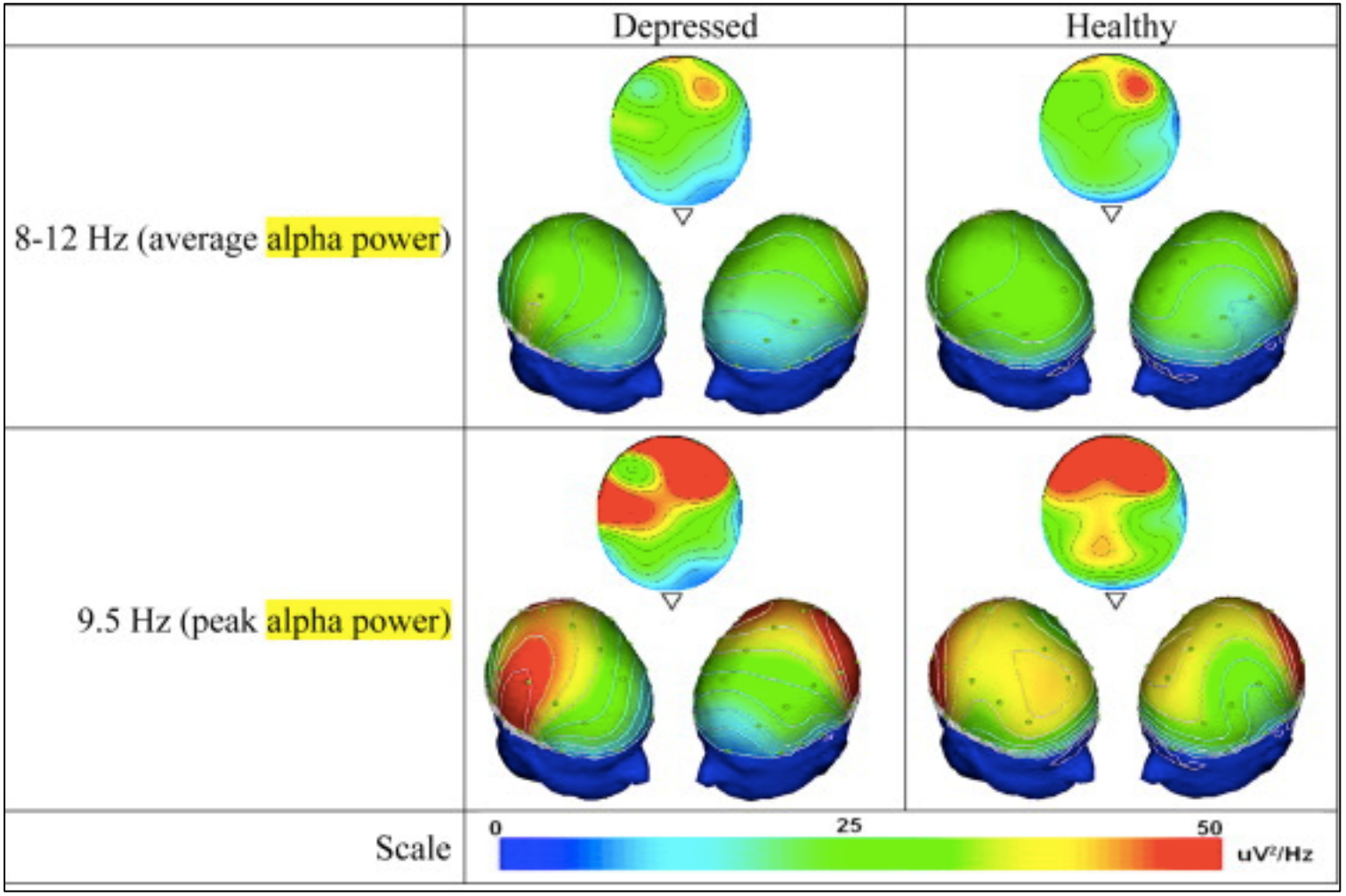
Source: Pajer *et. al*, *Translational Psychiatry.* 2012 **2**, e101; doi: 10.1038/tp.2012.26

Electrophysiological measures are potential biomarkers



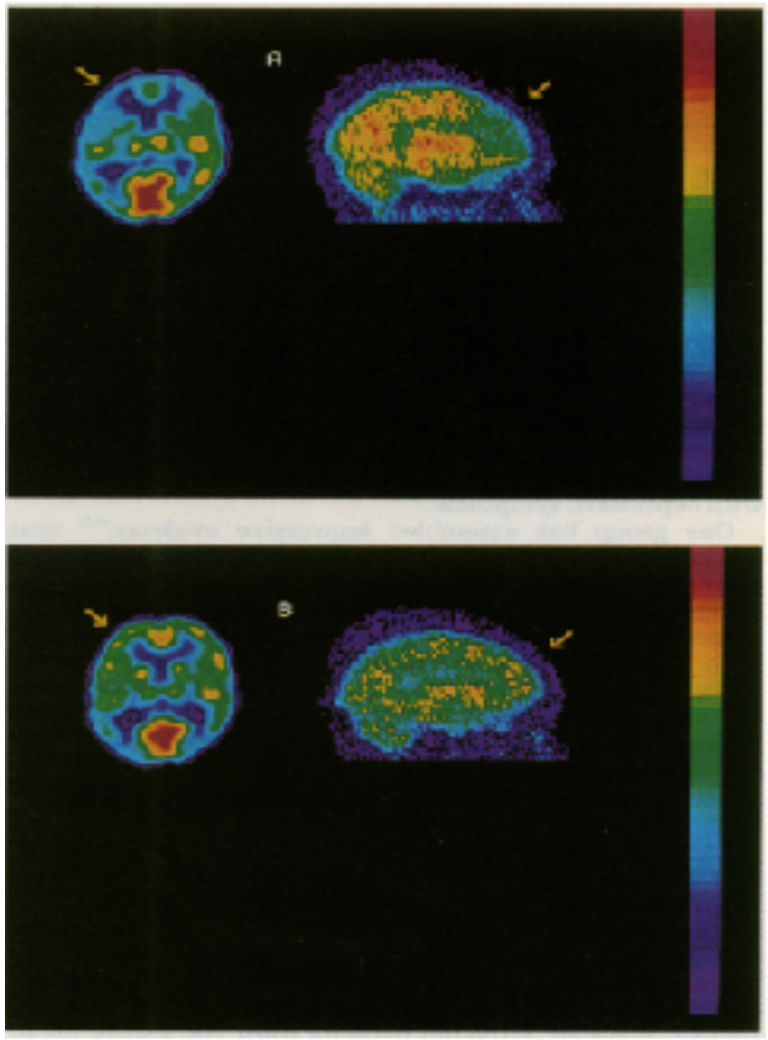
Source: Nagai *et. al*, 2013

Frequency Domain EEG demonstrates Frontal Asymmetry



Source: Gollan *et. al*, 2014 Biological Psych. Figure 1

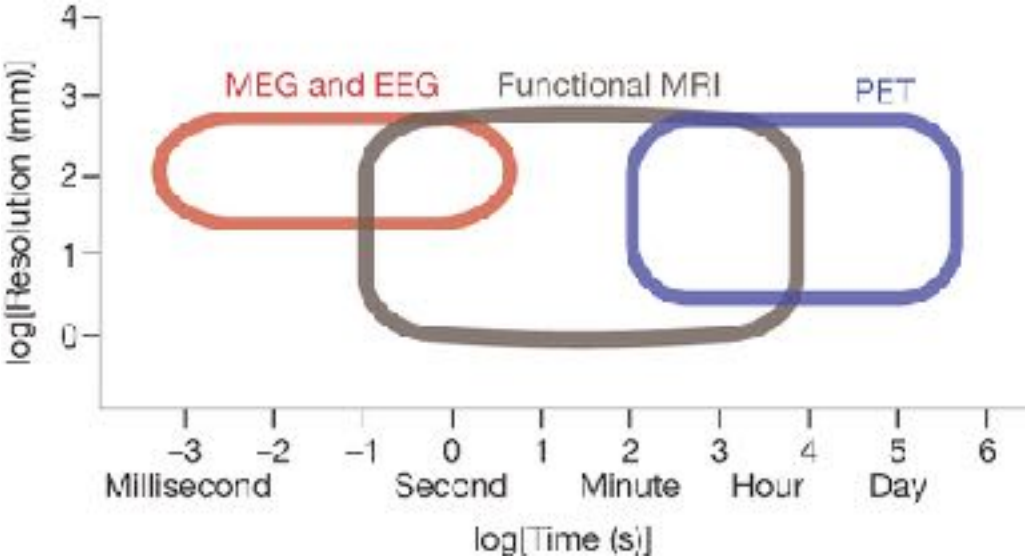
Positron Emission Tomography findings of Frontal Asymmetry



Baxter *et. al* Arch Gen Psychiatry—Vol 46, March 1989

- PET allows noninvasive, quantitative measures ; reliable with respect to source localization
- ⬇ Glucose Metabolic Rates and Cerebral Blood Flow in LEFT dorsal lateral prefrontal cortex (DLPFC) = ⬆ Severity of Depression

Functional neuroimaging methods and their temporal and spatial resolution.



Source: A Meyer-Lindenberg *Nature* **468**, 194-202 (2010)

MEG and EEG Differ in Their Orientation Sensitivity

- MEG only detects currents tangential relative to the volume conductor model
- EEG detects both tangential and radial currents
- Therefore:
  1) MEG signal maxima are detected over their neuronal generators
  2) The relation between EEG scalp electrodes and the underlying neuronal generators is complex

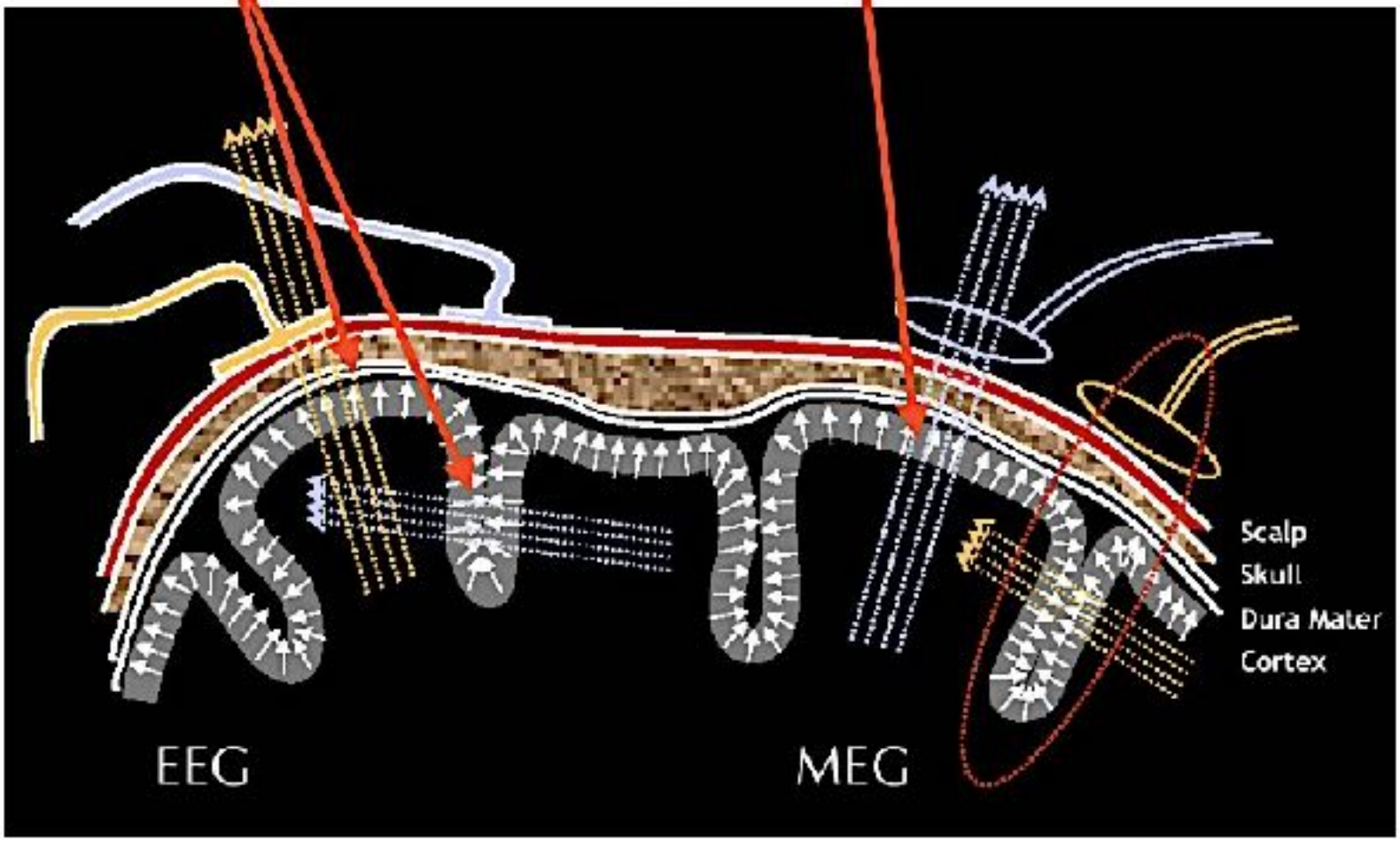
MEG

EEG

Source: http://www.allgpsy.unizh.ch/graduate/mat/180102/Lecture1.pdf

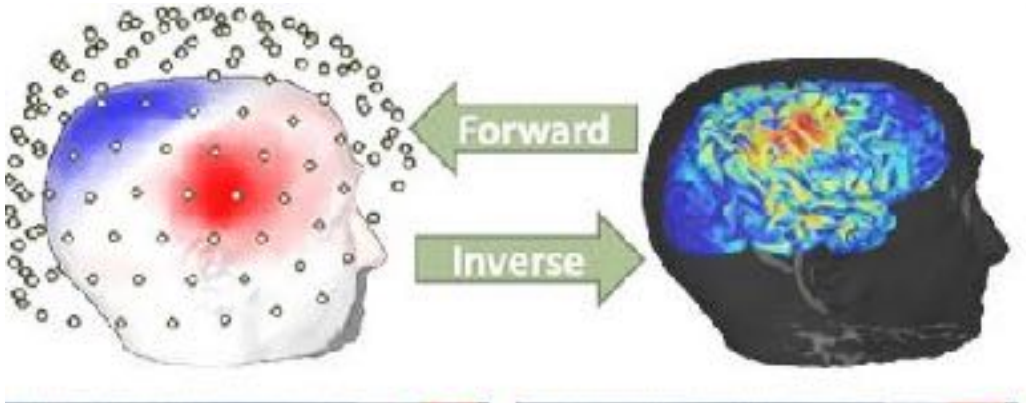
EEG picks up tangentially and radially oriented currents equally.

Currents oriented perfectly radial to the skull are missed in MEG. But there is very little signal that is so perfectly radial.



Source: http://www.allgpsy.unizh.ch/graduate/mat/180102/Lecture1.pdf

Cortical Space



Source: François Tadel and Sylvain Baillet, McConnell Brain Imaging Centre, *Visualizations of brain activity estimated from MEG/EEG scalp recordings.*

Aims

- *Aim 1*: Is there a relationship between cortex neurophysiological characteristics measured with EEG/MEG and the severity/progression of MDD

- *Aim 2*: Better understand the cortical origin of frontal asymmetry for MDD patients using EEG/MEG data

Hypotheses

- *Hypothesis 1 A/B*: EEG/MEG and Cortical Space results differ between the MDD patient and the healthy control and with clinical improvement.

- *Hypothesis 2 A*: EEG/MEG frontal asymmetry is generated in the frontal cortex , specifically in the superior, middle, and/or inferior frontal sulcus

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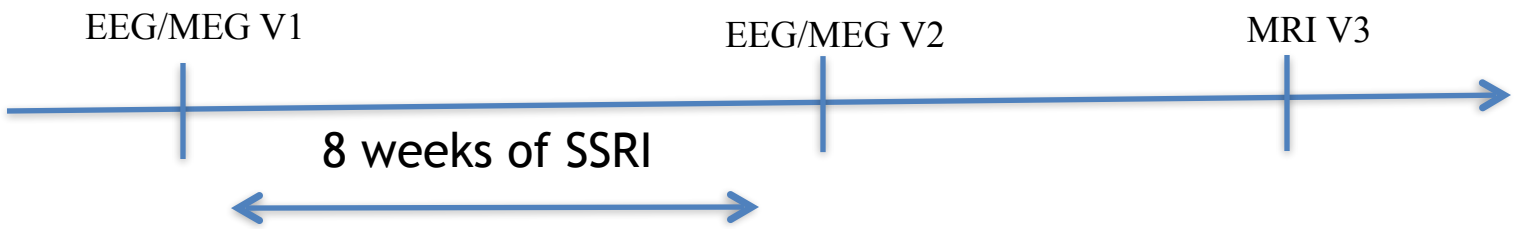
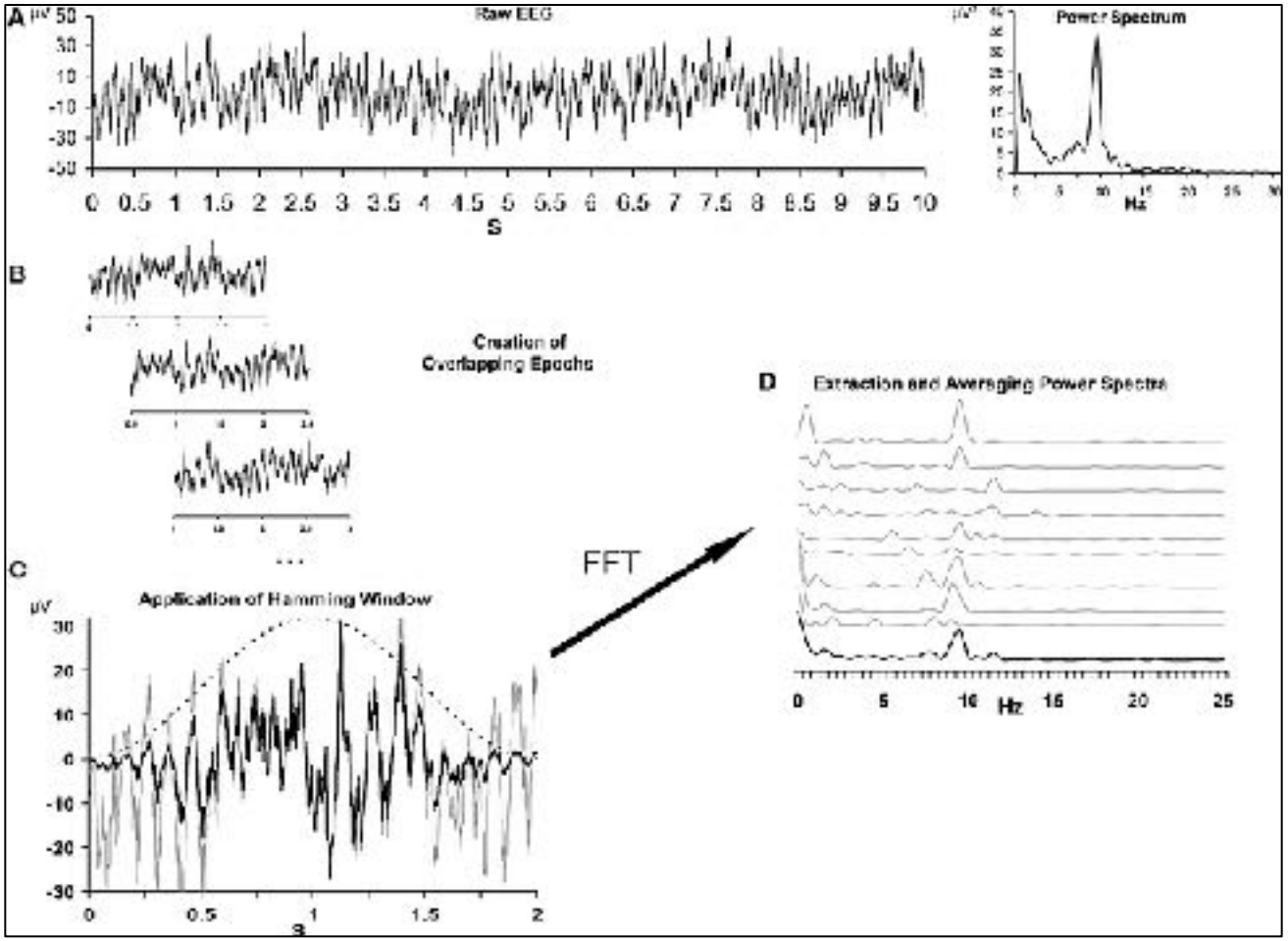
Data Collection

- MGH Depression and Clinical Research Program (DCRP)
  - EEG/MEG visit 1, EEG/MEG visit 2, and MRI visit
  - MDD subjects given FDA approved escitalopram (SSRI) for 8 weeks



EEG/MEG Frequency Domain Analysis



Source: Allen *et. al,* 2004

Fieldtrip MATLAB Toolbox

- Introduction

- Multi-taper
  - https://www.youtube.com/watch?v=vwPpSglPJTE

MNE Python Script

#Import Modules

import numpy as np #**for computing PSDs**
import mne **# for generating PSDs plots**
import matplotlib.pyplot as plt **# for plotting PSDs**

#Import Functions

from mne import io, read_proj, read_selection

from mne.time_frequency import compute_raw_psd

from mne.minimum_norm import read_inverse_operator, compute_source_psd

 # Load Data

 # Input from preprocessed _raw.fif files

raw_fname='/space/tmsh/1/users/dietta/Wyss_MDD/EEG_MEG/W113/131028/raw_maxf/W113HS2_EO6_SSSmctreocg8_raw.fif‘

raw=io.Raw('/')space/tmsh/1/users/dietta/Wyss_MDD/EEG_MEG/W113/131028/raw_maxf/W113HS2_EO6_SSSmctreocg8_raw.fif

 # Set Analysis Parameters

Pxx, freqs = plt.psd

 # Computation of Bipolar Montage sensitive to left-right axis

(raw_df[ch_names_diff[i][0]] - raw_df[ch_names_diff[i][1]]

 # Set Analysis Parameters for FFT

NFFT=1004 # number of point in the buffer # (fmax-= 504) (**Nyquist frequency would ½ (sampling rate)**
Fs=1004 **# sampling frequency (data points per second)**
Frequency resolution is 1 Hz bins
Nooverlap = 0 # **no overlap between windows**

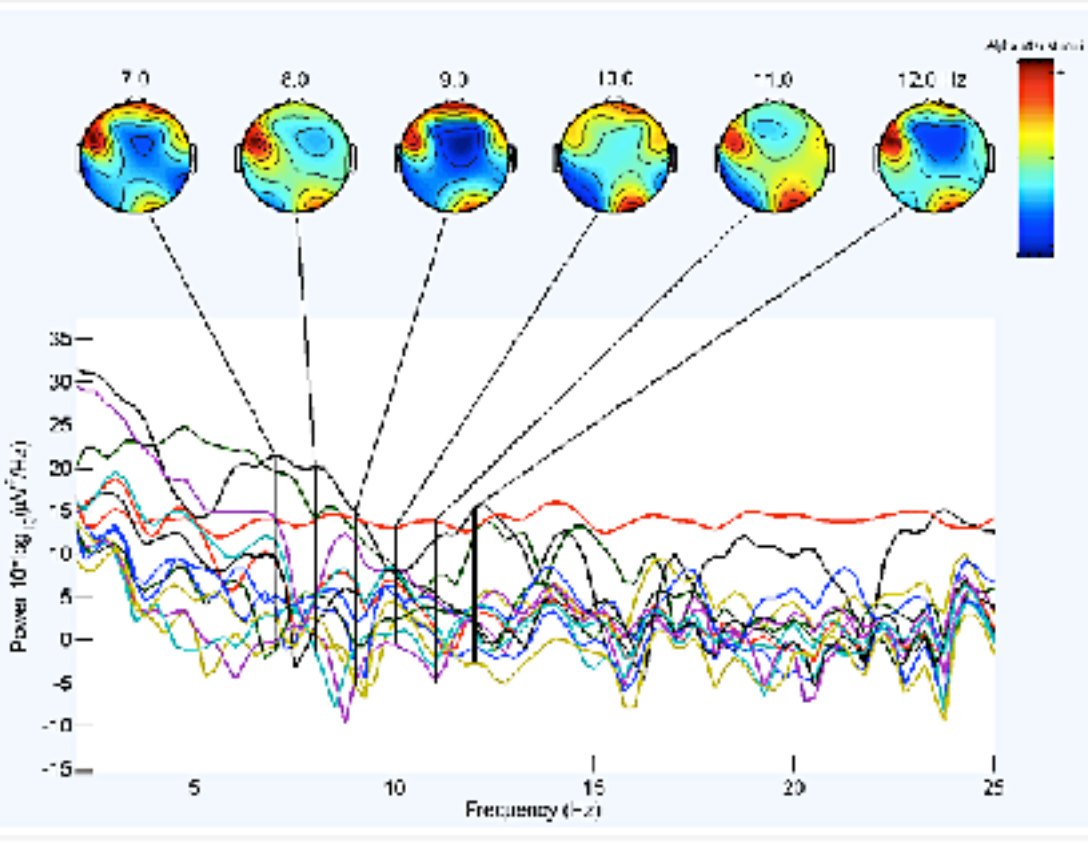
 # Plot PSDs

plt.plot(freqs[freqs <= 100], 10*np.log10(Pxx_list[0][freqs <= 100]), c='r') **# compute and plot LH PSD**

plt.plot(freqs[freqs <= 100], 10*np.log10(Pxx_list[1][freqs <= 100]), c='b') **# compute and plot RH PSD**

Frontal Asymmetry

- Frontal Asymmetry Model: EEG detects less left hemispheric activity relative to the right within the frontal lobe



Source: http://neuroinf.blogspot.com/2014/07/eeg-data-analysis-of-audio-induced-fear.html

Frontal Alpha Asymmetry Scores

- ↑ (more positive) scores indicate relatively greater left frontal activity
- ↓ (more negative) scores indicate relatively greater right frontal activity
- FAA = (LH) – (RH)

MDD SFS	LH	RH
Frequency (Hz)	Power Values (dB/Hz)	
8	-53.10	-48.14
9	-53.11	-48.14
10	-53.86	-49.44
11	-54.30	-51.07
12	-54.68	-53.99
AVG	-53.98	-52.45
Frontal Asymmetry	-1.53	

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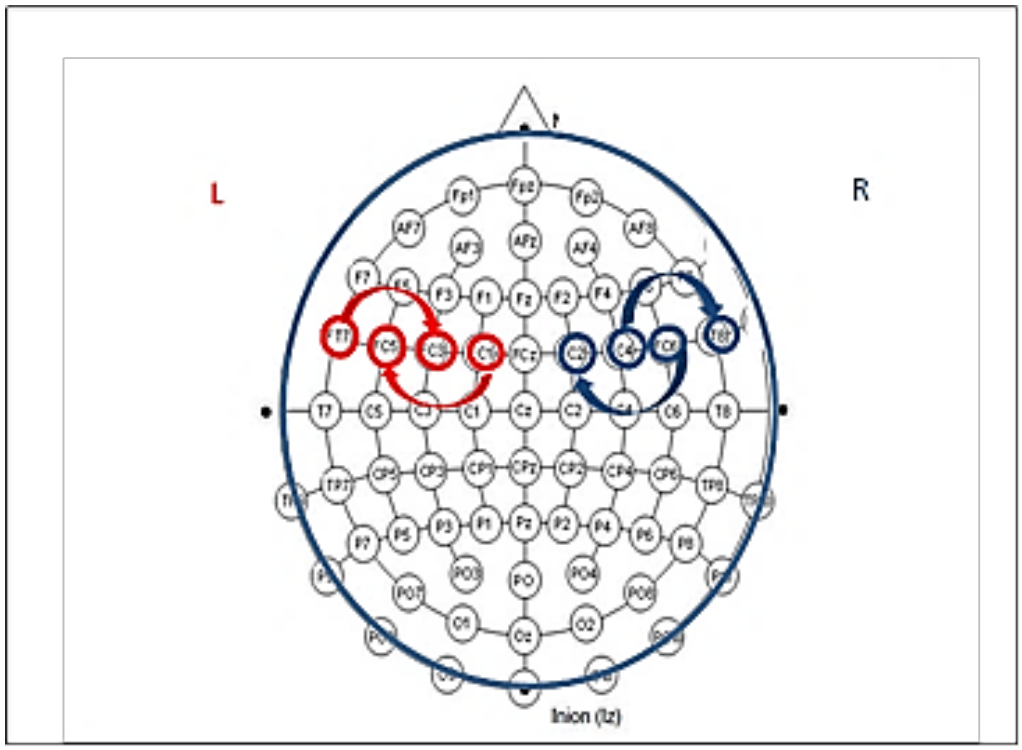
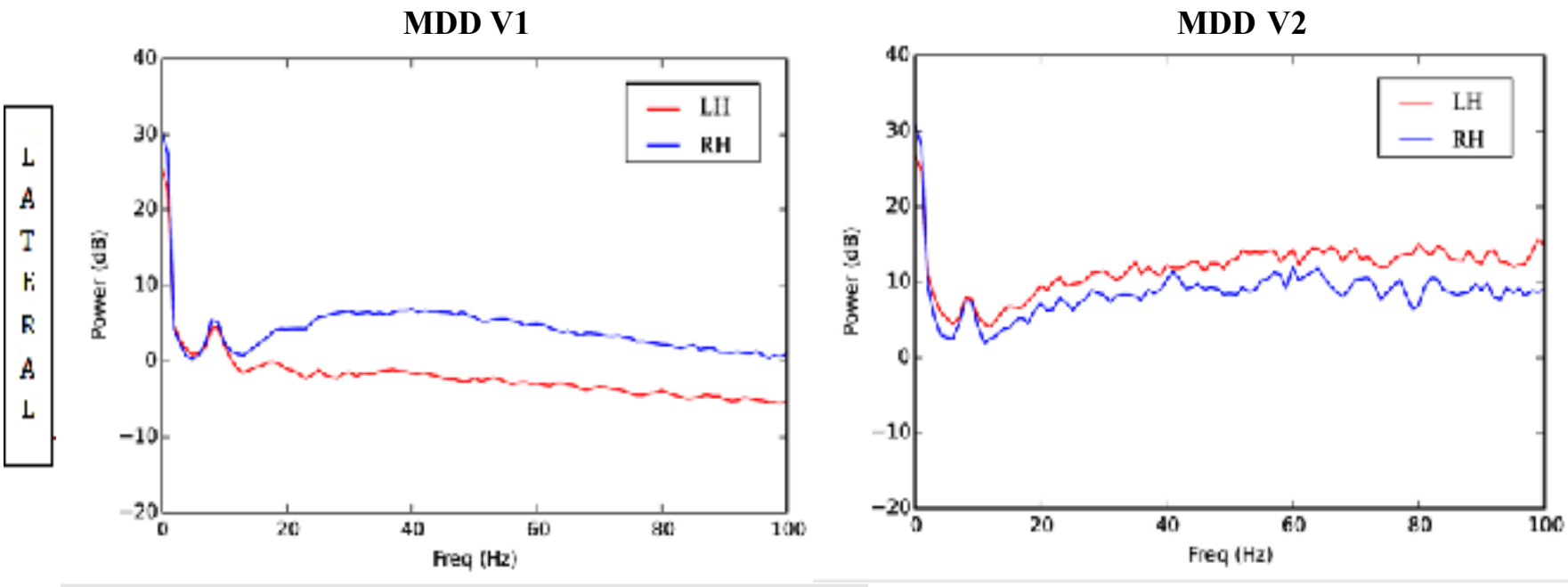
EEG Channels



Source: Figure 5

MDD EEG PSD plots

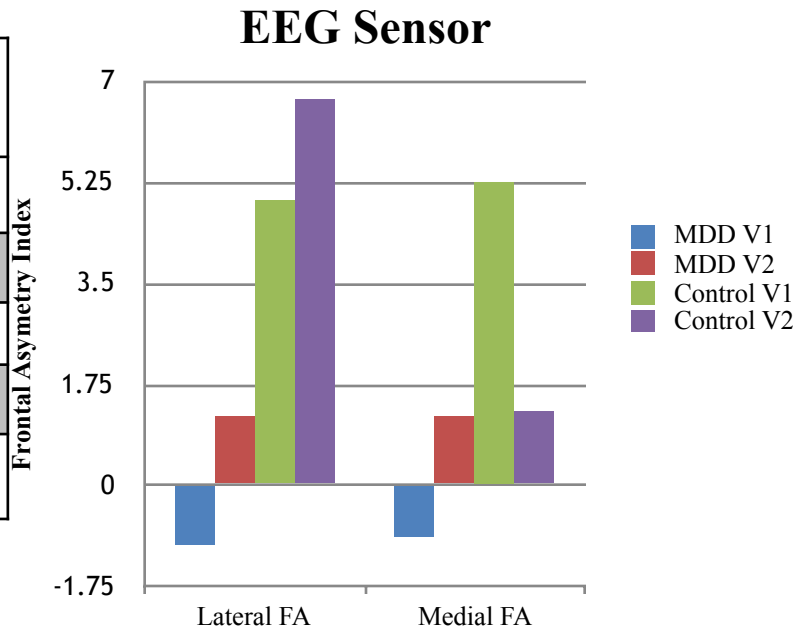


Source: Figure 6

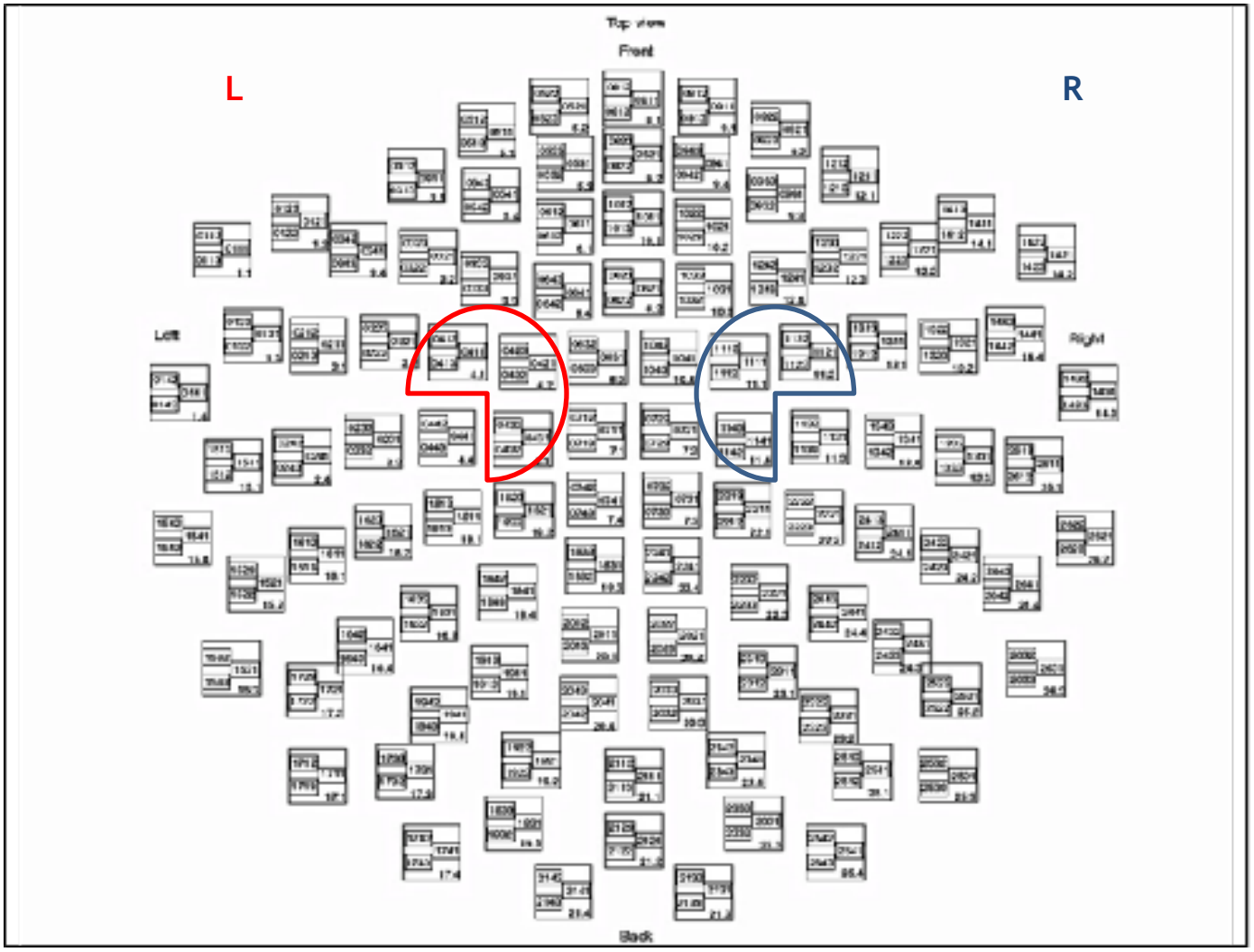
EEG
Sensor Results

EEG Bipolar					
Frequency Band		MDD V1	MDD V2	Control V1	Control V2
	Lateral				
ALPHA (8-13Hz)	Frontal Asymmetry	-1.0	1.21	4.94	6.69
	Medial				
	Frontal Asymmetry	-0.86	1.19	5.25	1.31

Source: Table 3



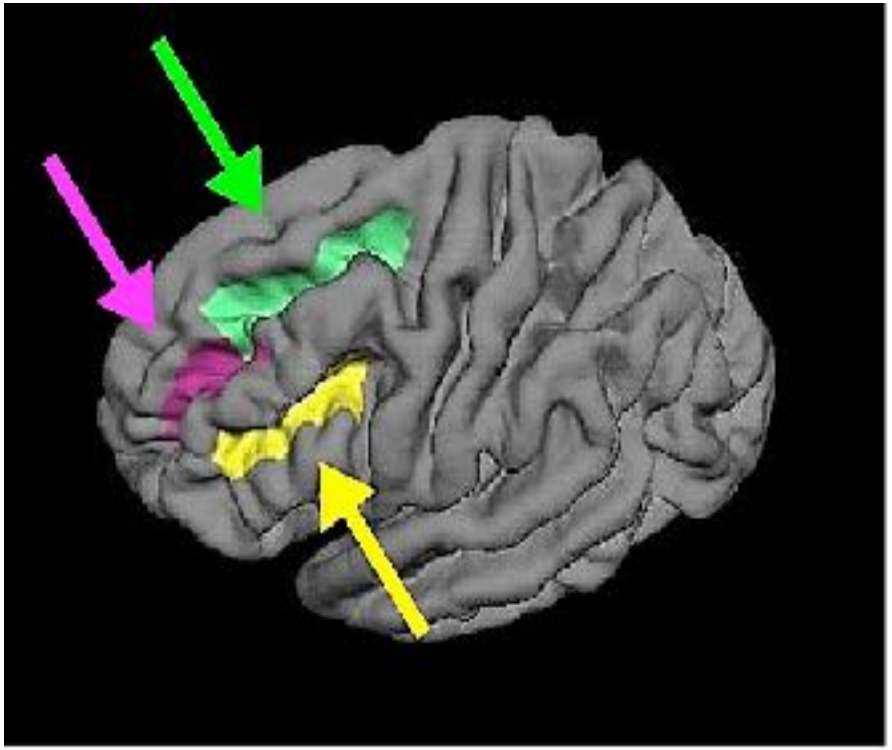
MEG Helmet



Source: Vectorview Manual, 2009

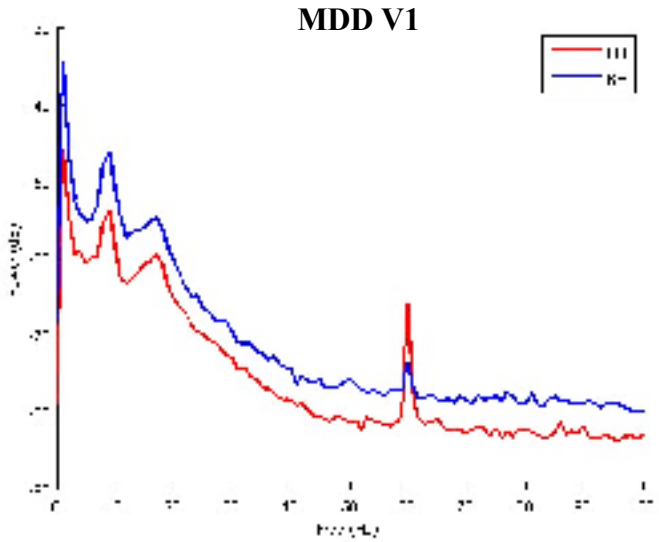
RESULTS CORTICAL SPACE

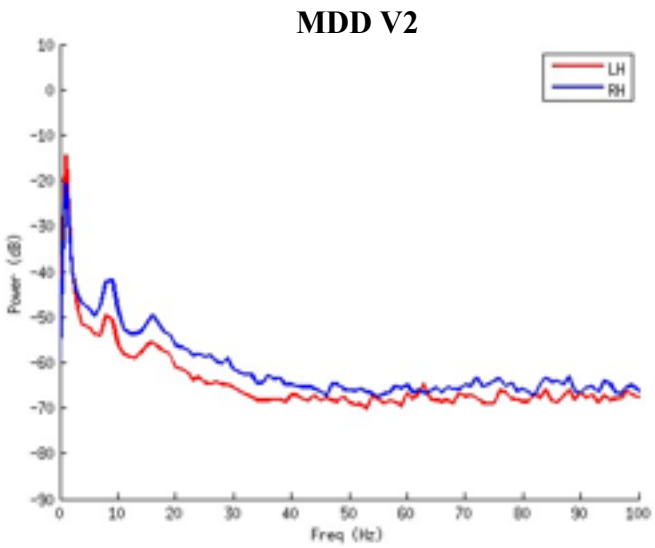
Cortical Labels



Source: Figure 5

MEG Cortical Space Results
Superior Frontal Sulcus





Source: Figure 8

Summary

		MDD V1		MDD V2		HC V1		HC V2	
		LH	RH	LH	RH	LH	RH	LH	RH
EEG Sensor	Lateral								
	Medial								
MEG Source	IFS								
	MFS								
	SFS								

Source: Table 6

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Discussion

- Frontal Alpha Asymmetry exists for MDD patient
- For MDD, FA changes after treatment
- Superior Frontal Sulcus shows evidence of FA
- Supports FA for biomarker in MDD

- Extensions: need more subjects !
- More exploratory questions to be answered
  - Trait versus State
  - Sensitivity and Specificity

Future Directions

- More data
- Better Methods
- Better theoretical interpretations of FA

Thank You!!

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