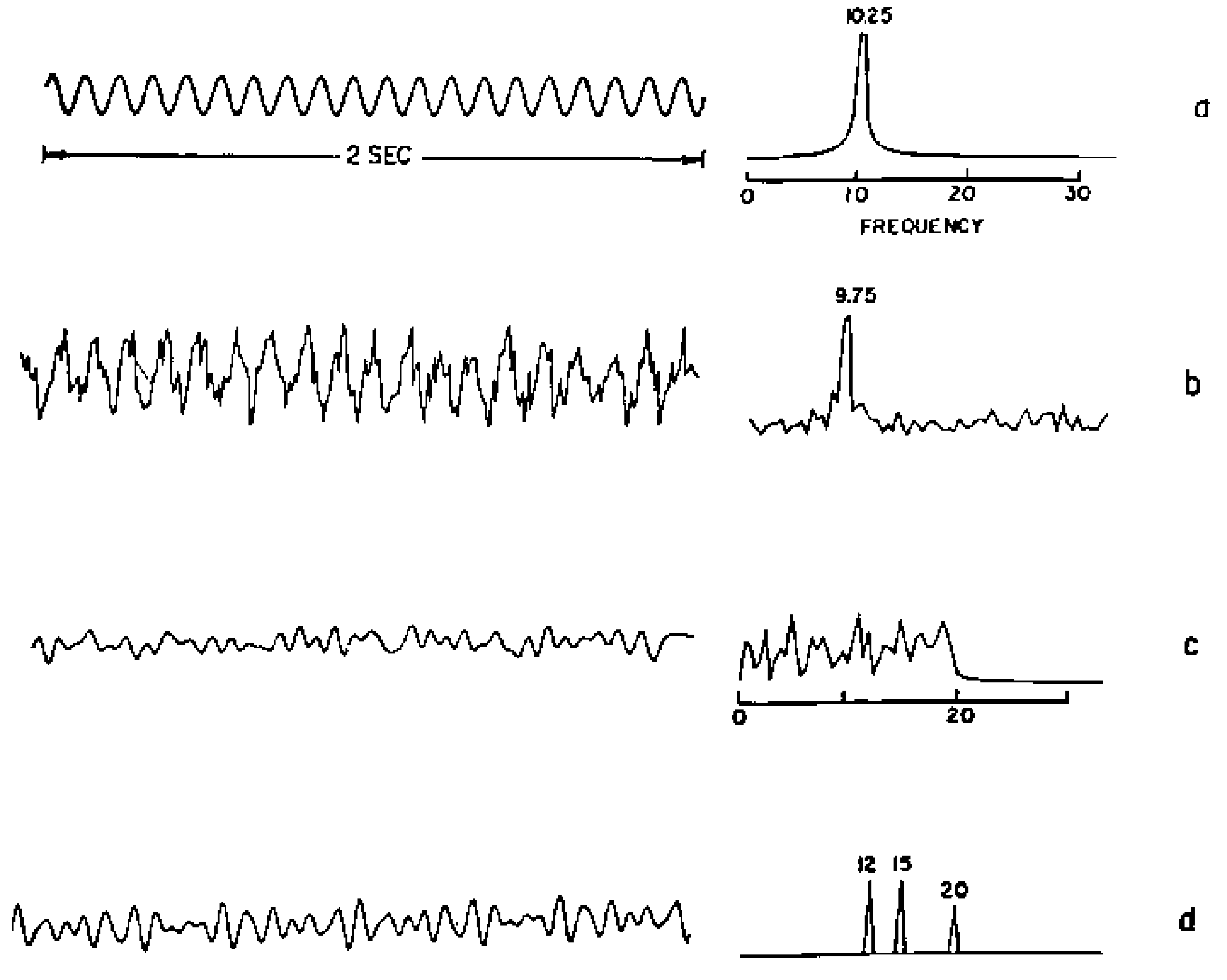
Frequency-domain EEG applications and methodological considerations

Announcements 3/22/21

- Paper/Proposal Guidelines available on course webpage (link in D2L too)
  - Two paragraph prospectus due (on D2L) no later than Monday April 19
- Lab meets Wednesday!
- Class Feedback and Q&A

Frequency-domain EEG applications and methodological considerations



Time Domain

Frequency Domain

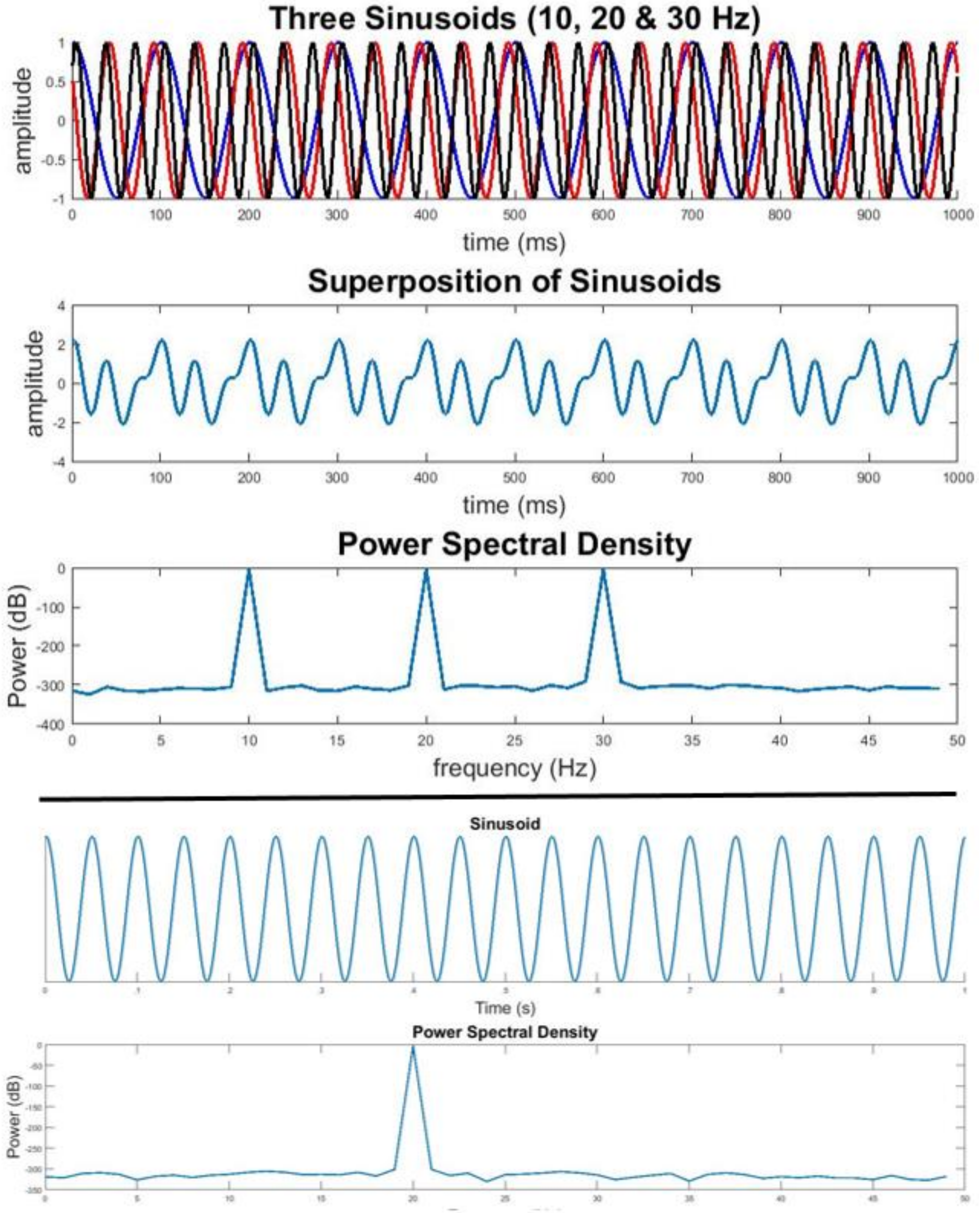
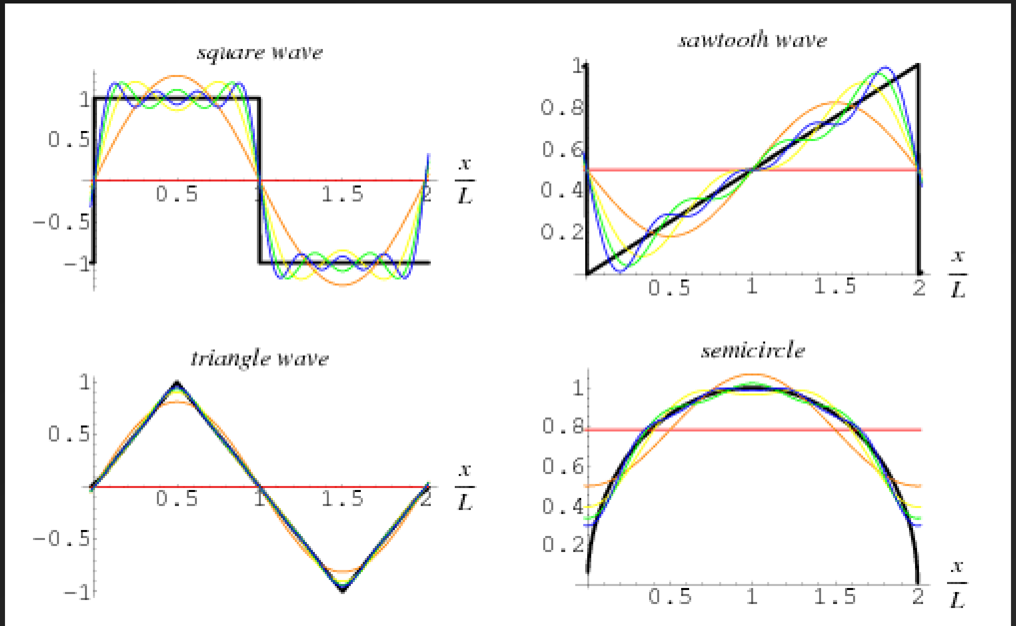


Figure 9: Constructing a complex signal from the superposition of sinusoids (top). The power spectrum of the signal show distinct peaks at the frequencies of the component sinusoids. A single sinusoid corresponds to a single peak in the power spectrum (bottom).

From: Curham & Allen (in press)

Fourier Series Representation

- If a signal is periodic, the signal can be expressed as the sum of sine and cosine waves of different amplitudes and frequencies
- This is known as the Fourier Series Representation of a signal

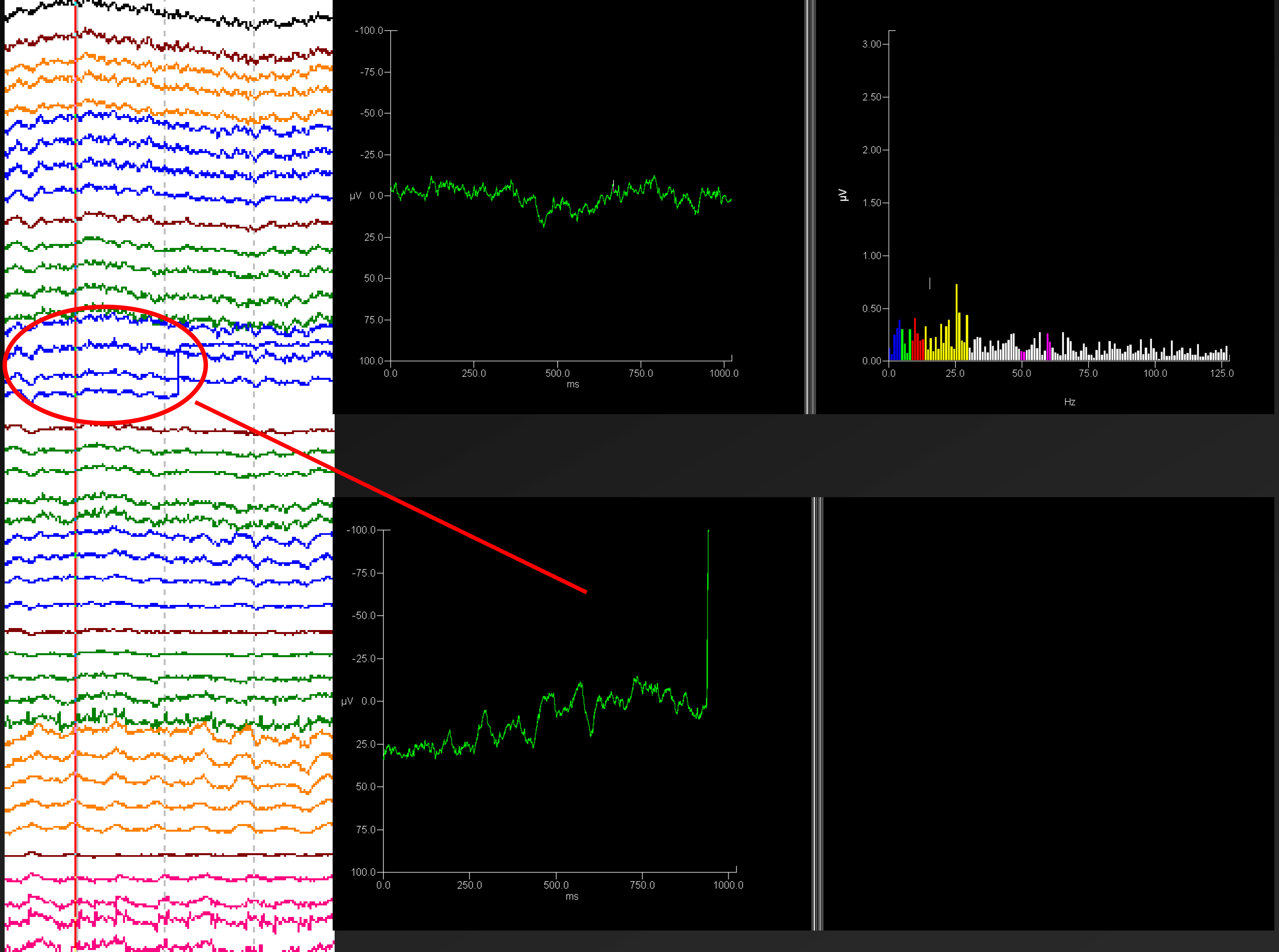


Fourier Series Representation

- Pragmatic Details
  - Lowest Fundamental Frequency is 1/T
  - Resolution is 1/T
- Phase and Power
  - There exist a phase component and an amplitude component to the Fourier series representation
    - Using both, it is possible to completely reconstruct the waveform.

Pragmatic Concerns

- Sample fast enough so no frequencies exceed Nyquist
  - signal bandwidth must be limited to less than Nyquist
  - Violation = ERROR
- Sample a long enough epoch so that lowest frequency will go through at least one period
  - Violation = ERROR
- Sample a periodic signal
  - if subject engaging in task, make sure that subject is engaged during entire epoch
  - Violation = ??, probably introduce some additional frequencies to account for change



-100.0
-75.0
-50.0
-25.0
µV 0.0
25.0
50.0
75.0
100.0
0.0
250.0
500.0
750.0
1000.0
ms
3.00
2.50
2.00
1.50
µV
1.00
0.50
0.00
0.0
25.0
50.0
75.0
100.0
125.0
Hz

Demo of EEG Data

- CNT Data to Frequency Domain Representation

Frequency-domain EEG applications and methodological considerations

Applications

- Emotion Asymmetries
  - Lesion findings
    - Catastrophic reaction (LH)
    - RH damage show a belle indifference
  - EEG studies
    - Trait (150+ studies)
    - State (oodles more studies)

Types of Studies

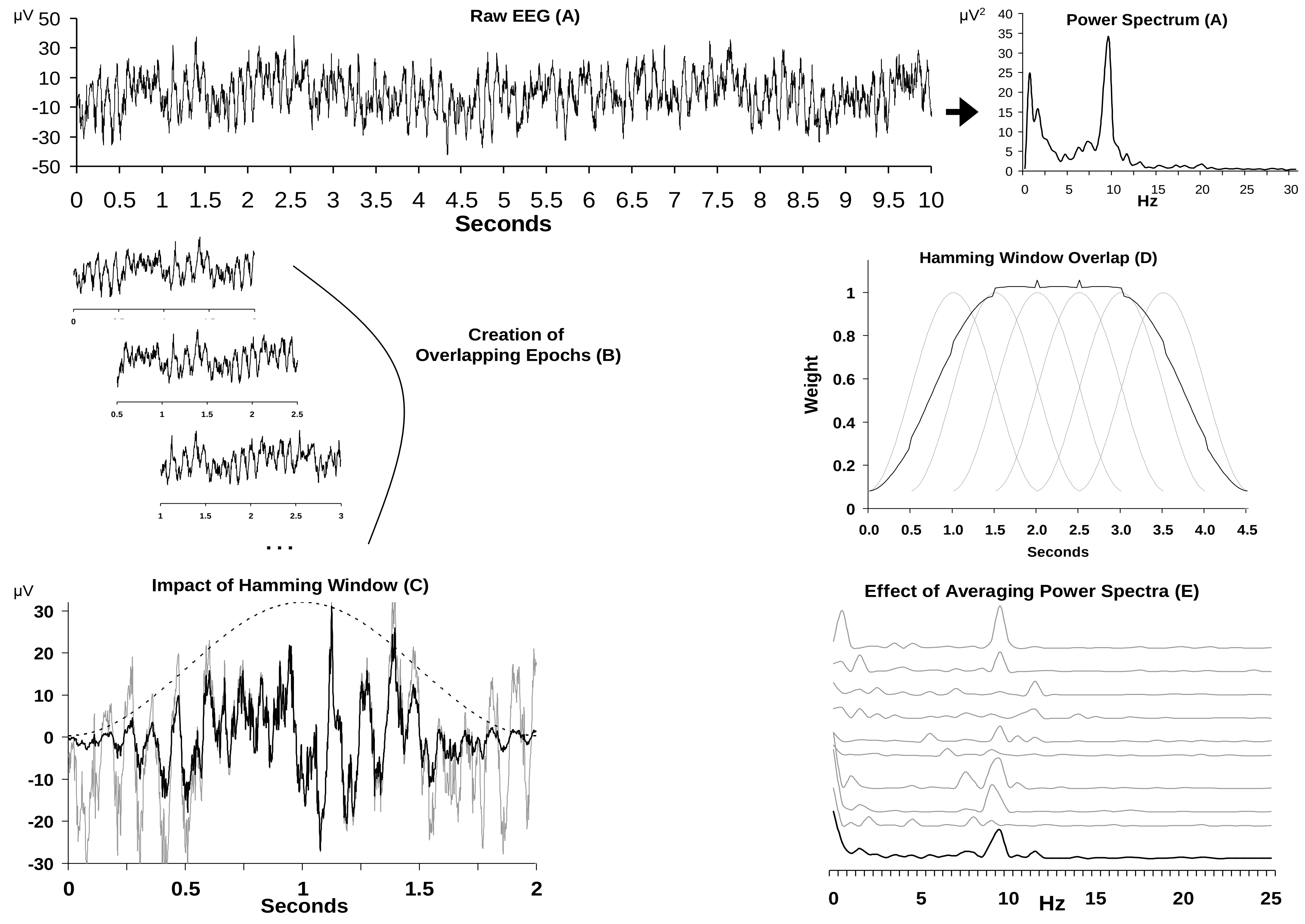
- Trait
  - Resting EEG asymmetry related to other traits (e.g. BAS)
  - Resting EEG asymmetry related to psychopathology (e.g. depression)
  - Resting EEG asymmetry predicts subsequent emotional responses (e.g. infant/mom separation)
- State
  - State EEG asymmetry covaries with current emotional state (e.g., self report, spontaneous emotional expressions)

For reviews:
Allen, Coan, & Nazarian 2004
Allen & Reznik, 2015
Reznik & Allen, 2018

Trait, Occasion, and State variance

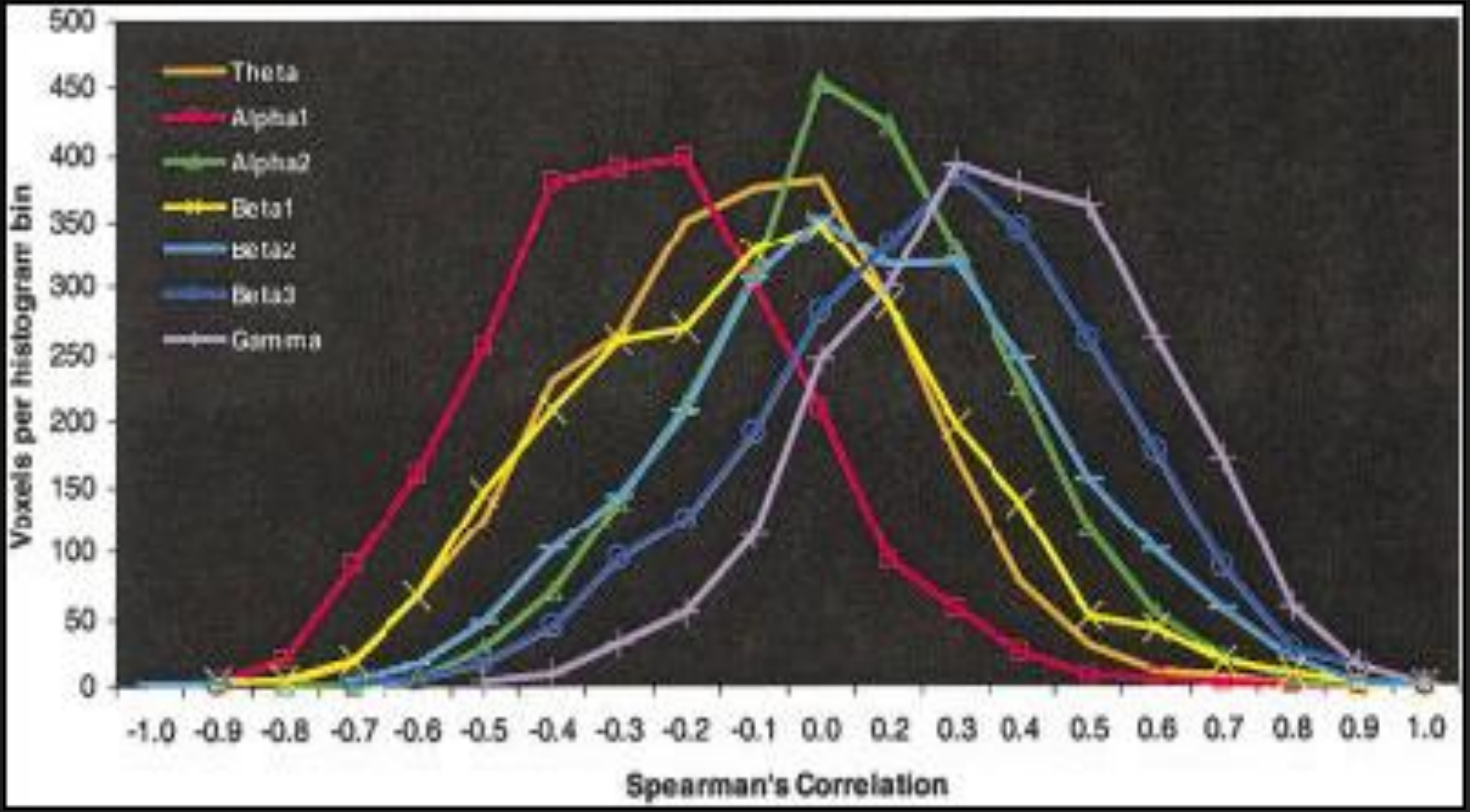
- Three sources of reliable variance for EEG Asymmetry
  - *Stable trait consistency* across multiple assessments
  - *Occasion-specific* variance
    - reliable variations in frontal asymmetry across multiple sessions of measurement
    - may reflect systematic but unmeasured sources such as current mood, recent life events and/or factors in the testing situation.
  - *State-specific* variance
    - changes within a single assessment that characterize
      - the difference between two experimental conditions
      - the difference between baseline resting levels and an experimental condition.
      - conceptualized as proximal effects in response to specific experimental manipulations
      - should be reversible and of relatively short duration
- Unreliability of Measurement (small)

Allen, Coan, & Nazarian 2004



Smith, Reznik, Stewart, & Allen, 2017

Alpha Vs Activity Assumption (AAA)



Oakes et al, 2004, *Human Brain Mapping*

Alpha and Activity

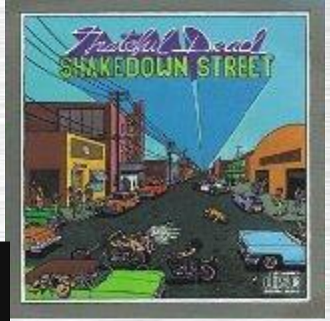
- May be more apt to think of alpha as regulating network activity
- High alpha has inhibitory function on network activity (more in advanced topics)

EEG Asymmetry, Emotion, and Psychopathology

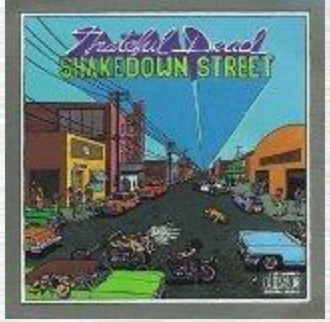
1978


THE POLICE


www.fraps.com
©2009 Google
Eye alt 9168.05 km


Grateful Dead
SHAKEDOWN STREET

1978



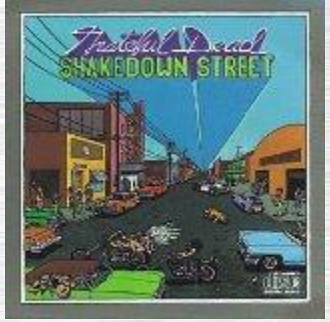
EIGHTEENTH ANNUAL MEETING
SOCIETY FOR PSYCHOPHYSIOLOGICAL RESEARCH

The Eighteenth Annual Meeting of The Society for Psychophysiological Research was held at The Concourse Hotel in downtown Madison, Wisconsin, September 15, 16, 17, and 18, 1978. Members of the Program Committee were: Rafael Klorman and Ted Weerts (Co-Chairmen), Michael Coles, Don Fowles, Linda Gannon, James Ison, J. Richard Jennings, Rathe Karrer, Michael Nelson, Arne Öhman, Leonard Salzman, and David Siddl

As in recent years, the bulk of the research reports were given and discussed informally at Friday and Sunday evenings, September 15 and 17. In addition, research reports were presented sessions on Saturday and Monday mornings, and others were included in the Display and Dis which ran in tandem with the meetings on Saturday from 8:30 to 5:00. Several symposia, workshops were also included in this year's program.

Following are the abstracts of research reports presented and discussed during the Paper Sessi Display and Discussion poster session.

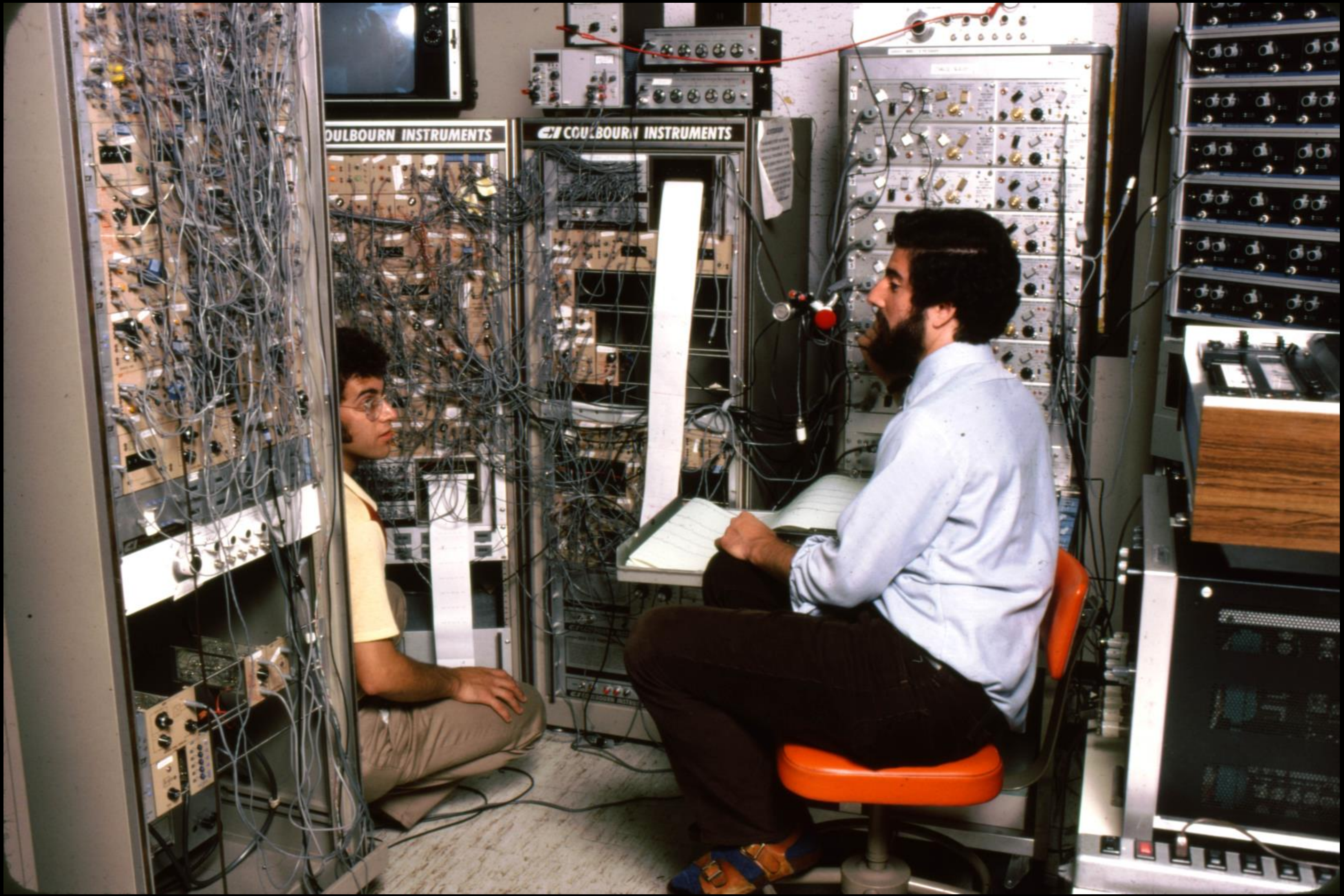
1978



PAPER SESSION II

"During positive affect, the frontal leads display greater relative left hemisphere activation compared with negative affect and vice versa"

3. Davidson, R. J. (State University of New York at Purchase), **Schwartz, G. E.** (Yale University), **Saron, C., Bennett, J.** (State University of New York at Purchase), **& Goleman, D. J. Frontal versus parietal EEG asymmetry during positive and negative affect.** A variety of data suggest that positive and negative affect may be differentially lateralized in the human brain. This report describes an experiment which explored the differential effect of positive versus negative affect on parietal and frontal brain regions. Seventeen right-handed subjects were exposed to portions of a television show judged to vary in emotional content. Subjects were asked to press down on a pressure-sensitive knob according to how much they disliked and to let up according to how much they liked the program, with hand use counterbalanced across subjects. These pressure changes, along with EEG filtered for 8–13 Hz recorded from F_4, F_3, P_4 and P_3 referenced to C_Z were digitized and printed every 30 sec. Two epochs representing the most positively and


OULBOURN INSTRUMENTS
CI COULBOURN INSTRUMENTS

Left Hypofrontality in Depression

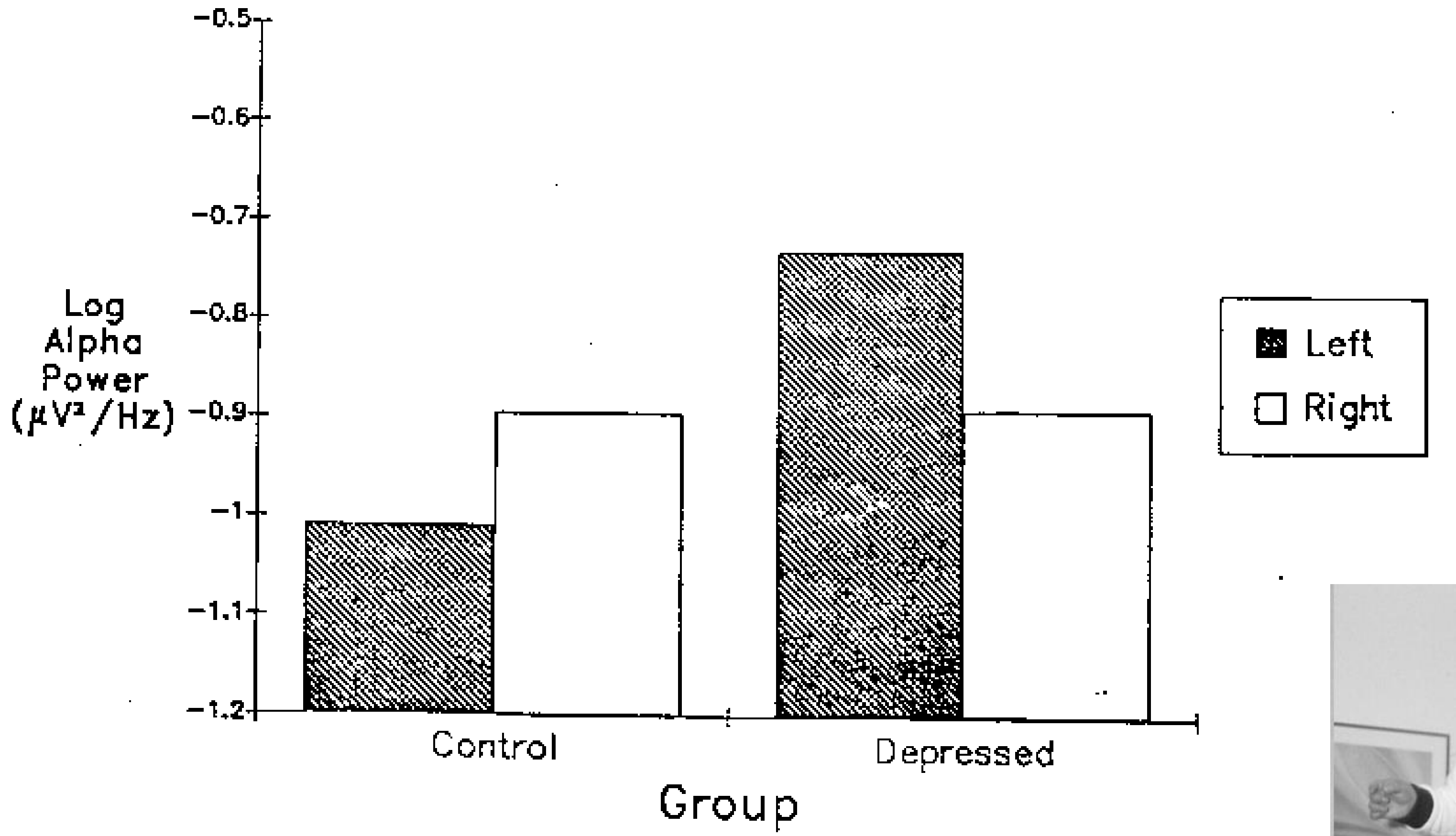
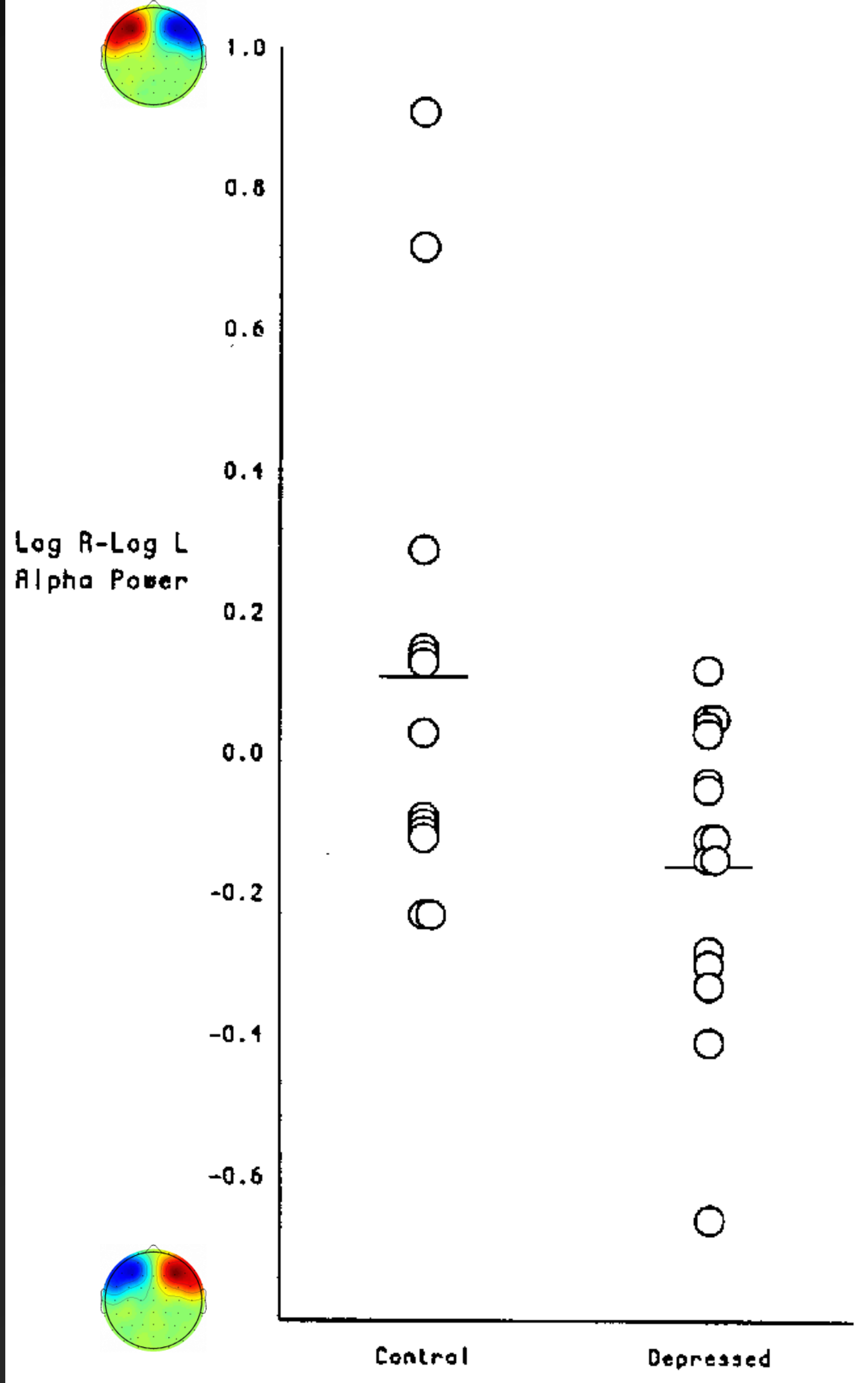


Figure 1. Mean log-transformed alpha (8–13 Hz) power (in $\mu V^2/Hz$) for Cz-referenced electroencephalograms (averaged across eyes-open and eyes-closed baselines), split by group and hemisphere, for the mid-frontal region. (Decreases in alpha power are indicative of increased activation.)

Henriques & Davidson (1991); see also, Allen et al. (1993), Gotlib et al. (1998); Henriques & Davidson (1990); Reid Duke and Allen (1998); Shaffer et al (1983)

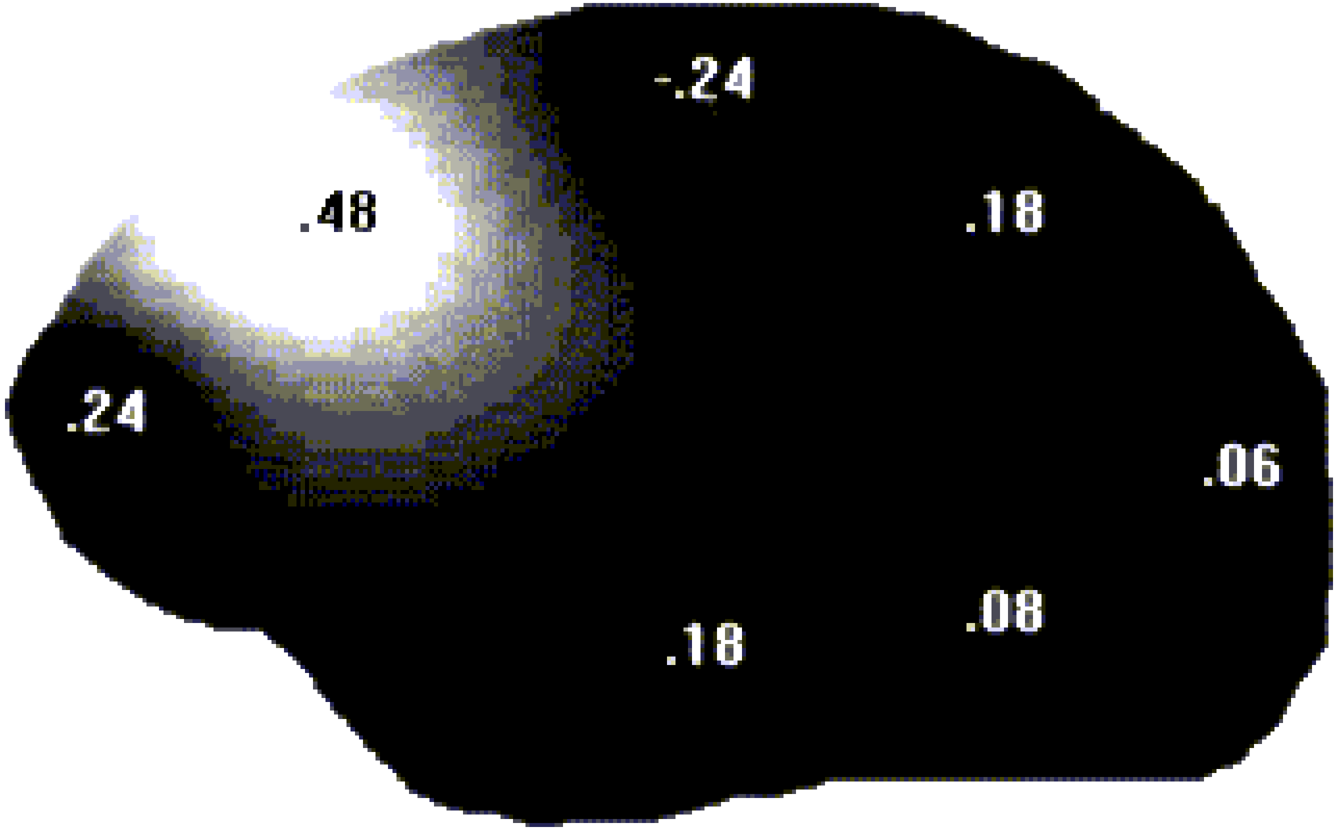
Individual Subjects' Data



Henriques & Davidson (1991)

Valence Vs Motivation

- Valence hypothesis
  - Left frontal is positive
  - Right frontal is negative
- Motivation hypothesis
  - Left frontal is Approach
  - Right frontal is Withdrawal
- Hypotheses are confounded
  - With possible exception of Anger



Correlation with alpha asymmetry (ln[right]-ln[left]) and trait anger. Positive correlations reflect greater left activity (less left alpha) is related to greater anger.

After Harmon-Jones and Allen (1998).

State Anger and Frontal Asymmetry

- Would situationally-induced anger relate to relative left frontal activity?

Harmon-Jones & Sigelman, *JPSP*, 2001

Method

- Cover story: two perception tasks – person perception & taste perception
- Person perception task – participant writes essay on important social issue; another ostensible participant gives written feedback on essay
- Feedback is neutral or insulting
  - negative ratings + “I can’t believe an educated person would think like this. I hope this person learns something while at UW.”

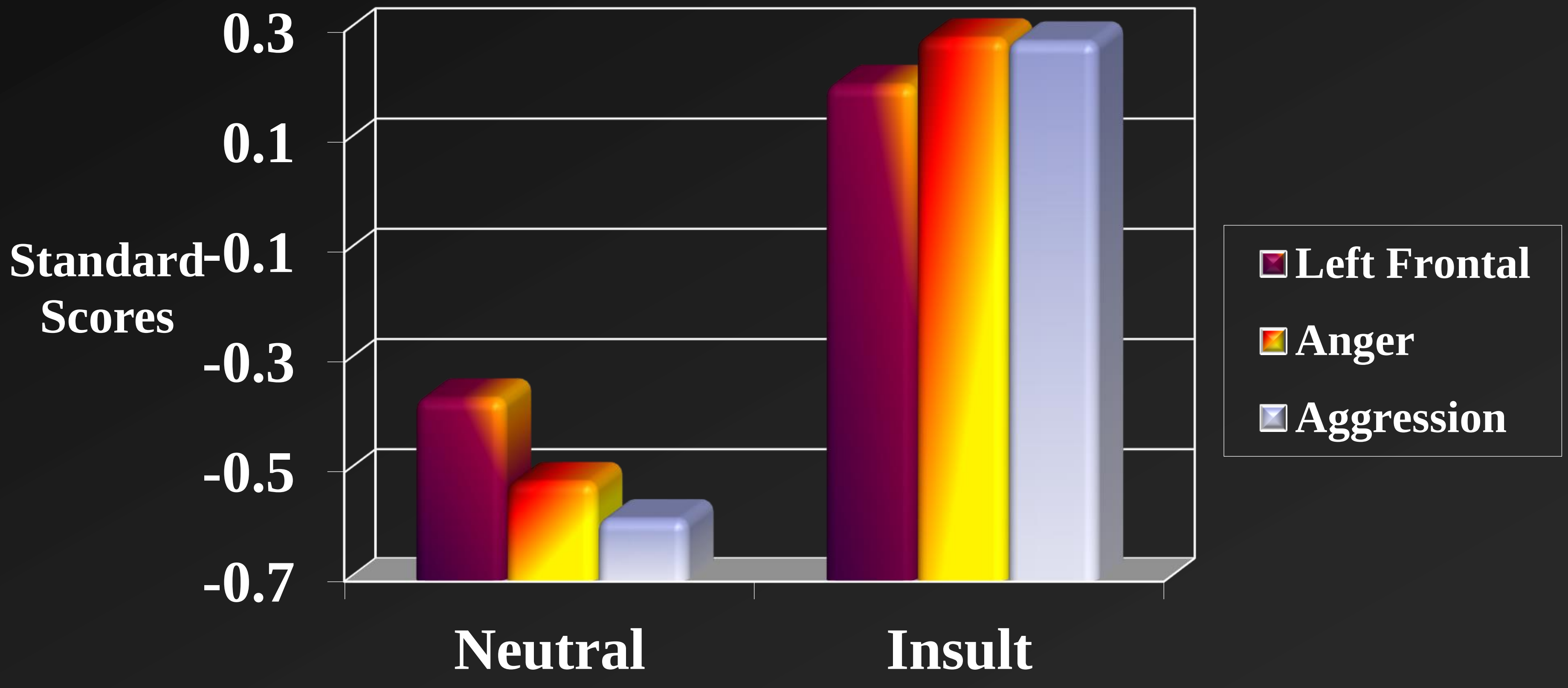
Harmon-Jones & Sigelman, *JPSP*, 2001

- Record EEG immediately after feedback
- Then, taste perception task, where participant selects beverage for other participant, “so that experimenter can remain blind to type of beverage.”
- 6 beverages; range from pleasant-tasting (sweetened water) to unpleasant-tasting (water with hot sauce)
  - Aggression measure

Harmon-Jones & Sigelman, *JPSP*, 2001

Harmon-Jones & Sigelman, *JPSP*, 2001

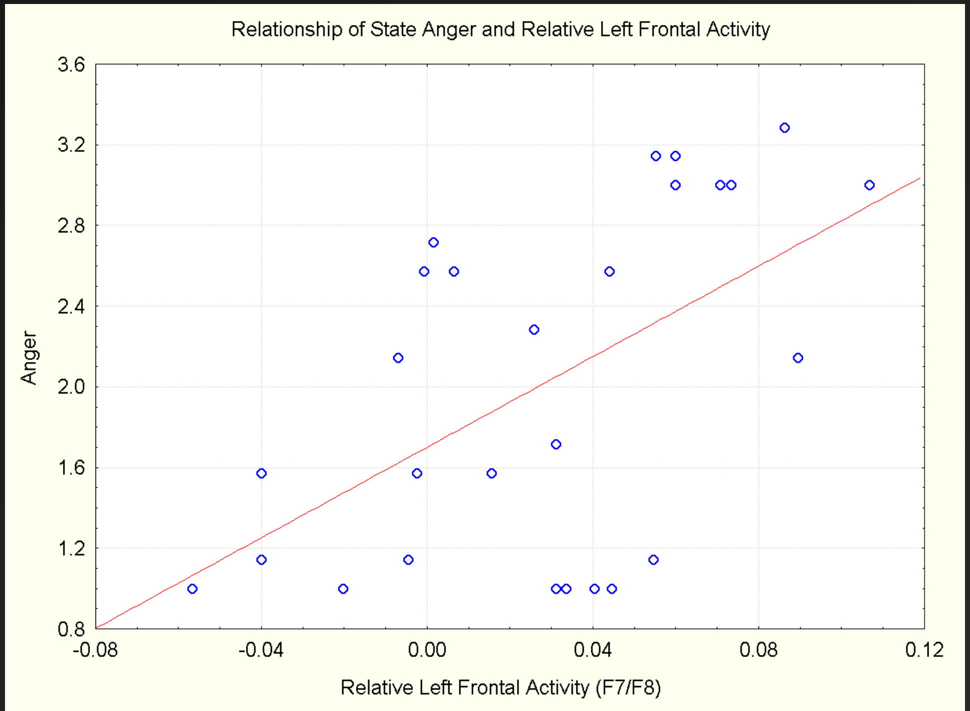
Relative Left Frontal, Anger, & Aggression as a Function of Condition



Harmon-Jones & Sigelman, *JPSP*, 2001

Frontal EEG asymmetry predicts Anger and Agression

- Not in Neutral condition … no relationship
- Strongly in Insult condition
  - r = .57 for anger
  - r = .60 for aggression
  - Note: partial r adjusting for baseline indiv diffs in asymmetry and affect



Harmon-Jones & Sigelman, *JPSP*, 2001

Manipulation of EEG

Peterson, Shackman, Harmon-Jones (2008)

- Hand contractions to activate contralateral premotor cortex
- Insult about essay (similar to Harmon-Jones & Sigelman, *JPSP*, 2001) followed by chance to give aversive noise blasts to the person who insulted them
- Hand contractions:
  - altered frontal asymmetry as predicted
  - Altered subsequent aggression (noise blasts)
- Asymmetry during hand contractions predicted aggression

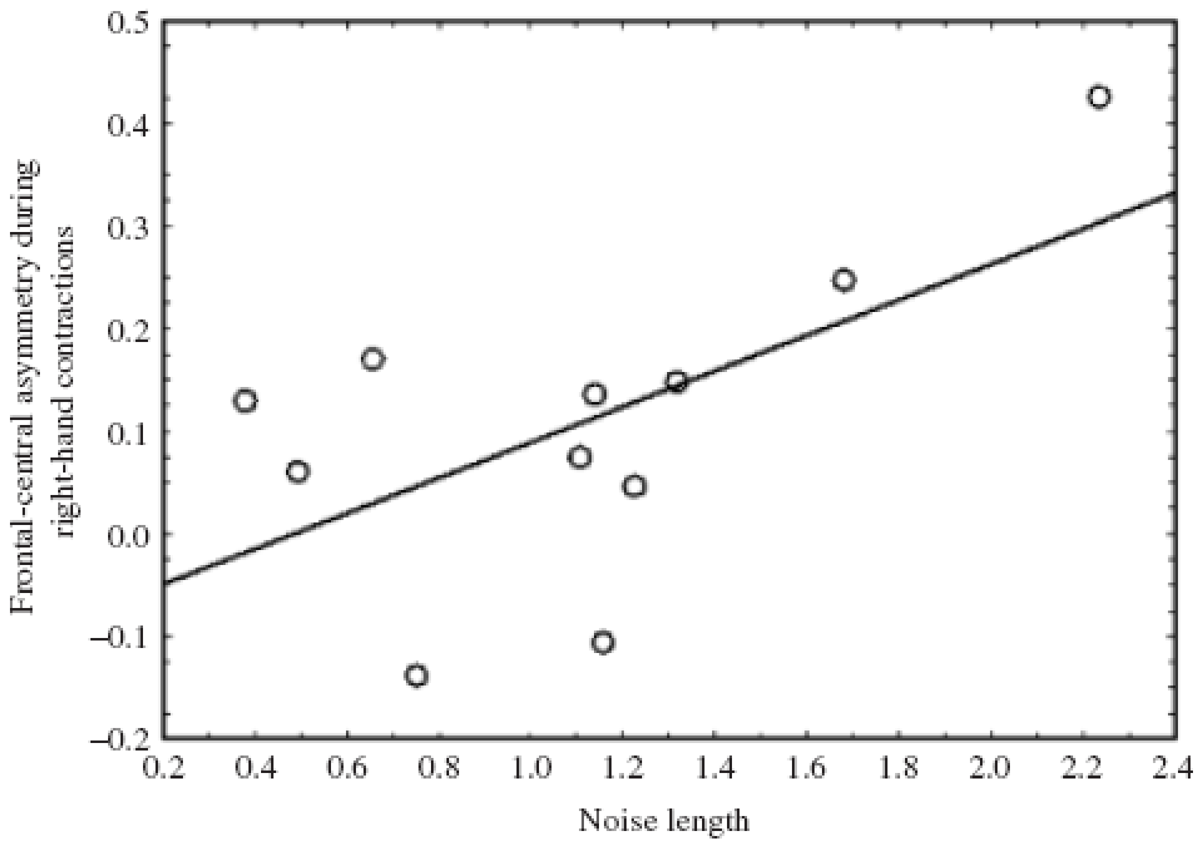


Figure 1. Relation between noise length and frontal-central asymmetry during right-hand contractions. Higher asymmetry scores indicate greater relative left than right activation.

Peterson, Shackman, Harmon-Jones (2008)

The BAS/BFS/Approach System

- **sensitive to signals of**
  - **conditioned reward**
  - **nonpunishment**
  - **escape from punishment**
- **Results in:**
  - **driven pursuit of appetitive stimuli**
  - **appetitive or incentive motivation**
  - **Decreased propensity for depression (Depue & Iacono, 1989; Fowles 1988)**

Motivational Styles and Depression

Behavioral Activation Scale

- Reward Responsiveness

  When I see an opportunity for something I like, I get excited right away.

- Drive

  I go out of my way to get things I want.

- Fun Seeking

  I'm always willing to try something new if think it will be fun.

Carver & White, 1994

Motivational Styles and Depression

r = .45

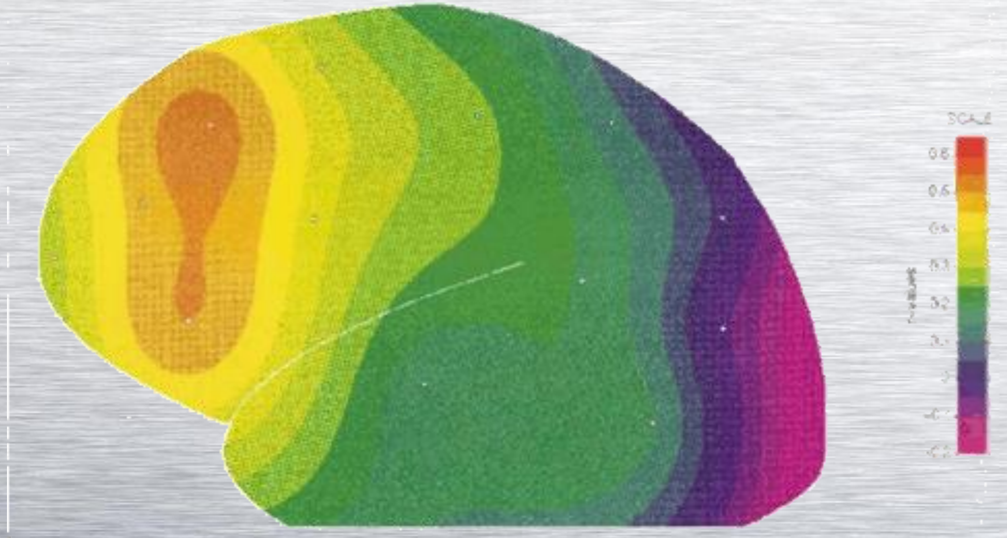
Mid-Frontal Asymmetry and BAS Scores

Mid-Frontal Asymmetry and PA Scores

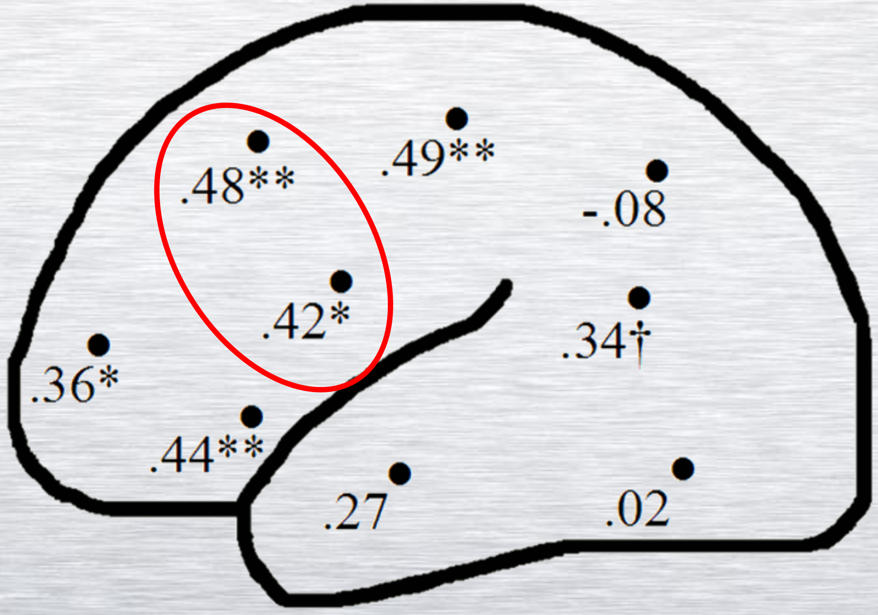
r = .00

Harmon-Jones & Allen, 1997

Motivational Styles and Depression
Replications



Sutton & Davidson, 1997



Coan & Allen, 2003

Correlations with alpha asymmetry (ln[right]-ln[left]) and self-reported BAS scores (right) or BAS-BIS (left).

Positive correlations reflect greater left activity (less left alpha) is related to greater BAS scores or greater BAS-BIS difference

L>R Activity (R>L Alpha) characterizes:

- an approach-related motivational style (e.g. Harmon-Jones & Allen, 1997; Sutton & Davidson, 1997)
- higher positive affect (e.g. Tomarken, Davidson, Wheeler, & Doss, 1992)
- higher trait anger (e.g. Harmon-Jones & Allen, 1998)
- lower shyness and greater sociability (e.g. Schmidt & Fox, 1994; Schmidt, Fox, Schulkin, & Gold, 1999)

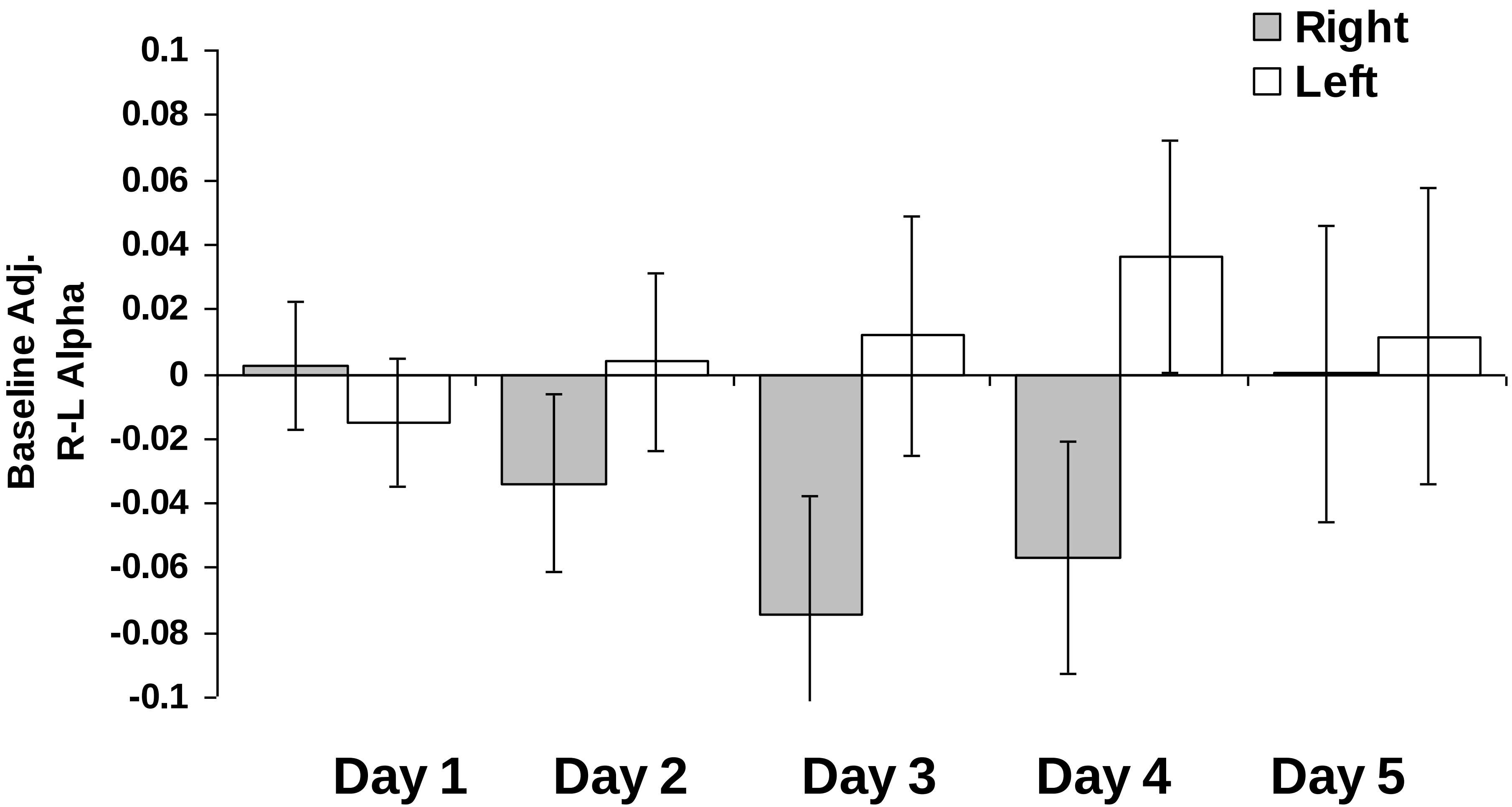
R>L Activity (L>R Alpha) characterizes:

- depressive disorders and risk for depression (e.g. Allen, Iacono, Depue, & Arbisi, 1993; Gotlib, Ranganath, & Rosenfeld, 1998; Henriques & Davidson, 1990; Henriques & Davidson, 1991 but see also Reid, Duke, & Allen, 1998
- certain anxiety disorders (e.g. Davidson, Marshall, Tomarken, & Henriques, 2000; Wiedemann et al., 1999)

Correlations ≠ Causality

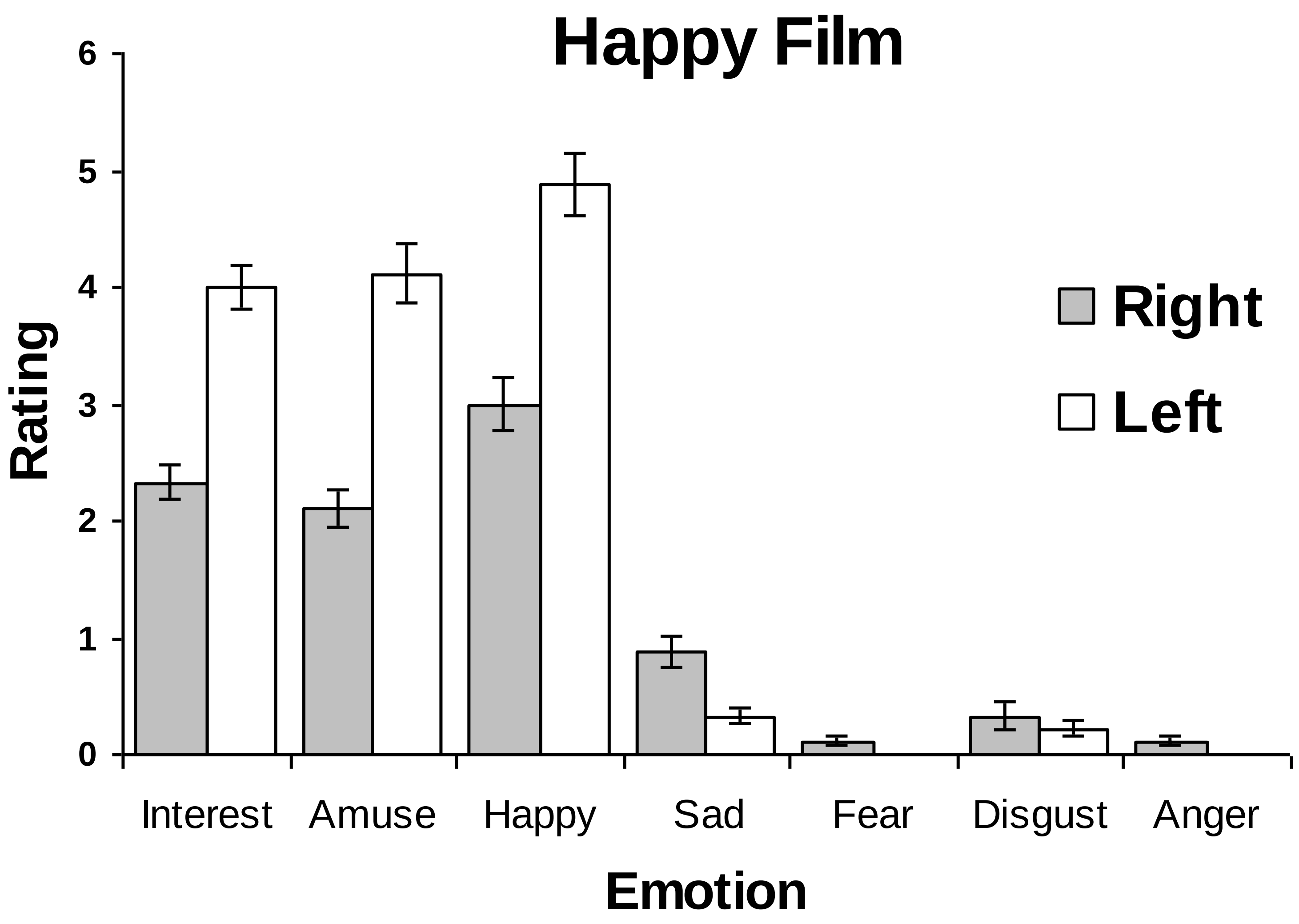
- Study to manipulate EEG Asymmetry
- Five consecutive days of biofeedback training (R vs L)
  - Nine subjects trained “Left”; Nine “Right”
  - Criterion titrated to keep reinforcement equal
- Tones presented when asymmetry exceeds a threshold, adjusted for recent performance
- Films before first training and after last training

Training Effects: Asymmetry Scores



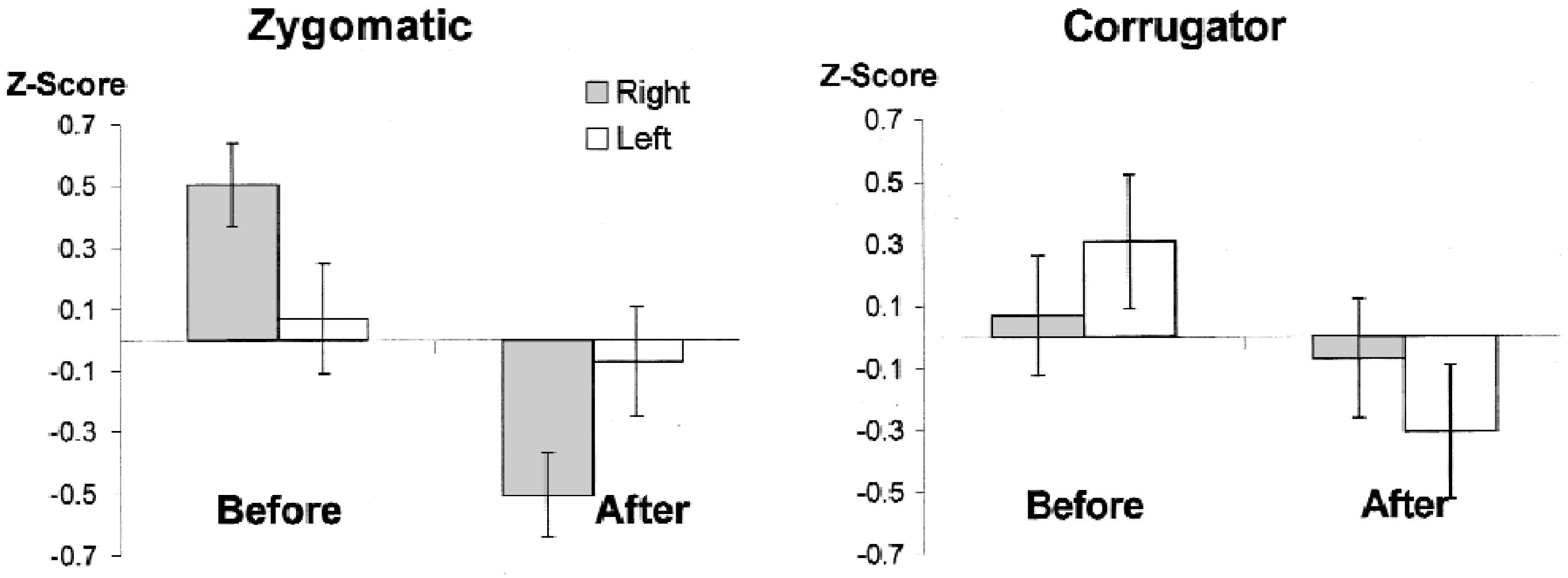
Manipulation of EEG asymmetry with biofeedback produced differential change across 5 days of training; Regression on Day 5

From Allen, Harmon-Jones, and Cavender (2001)



Despite no differences prior to training, following manipulation of EEG asymmetry with biofeedback subjects trained to increase left frontal activity report greater positive affect.

From Allen, Harmon-Jones, and Cavender (2001)

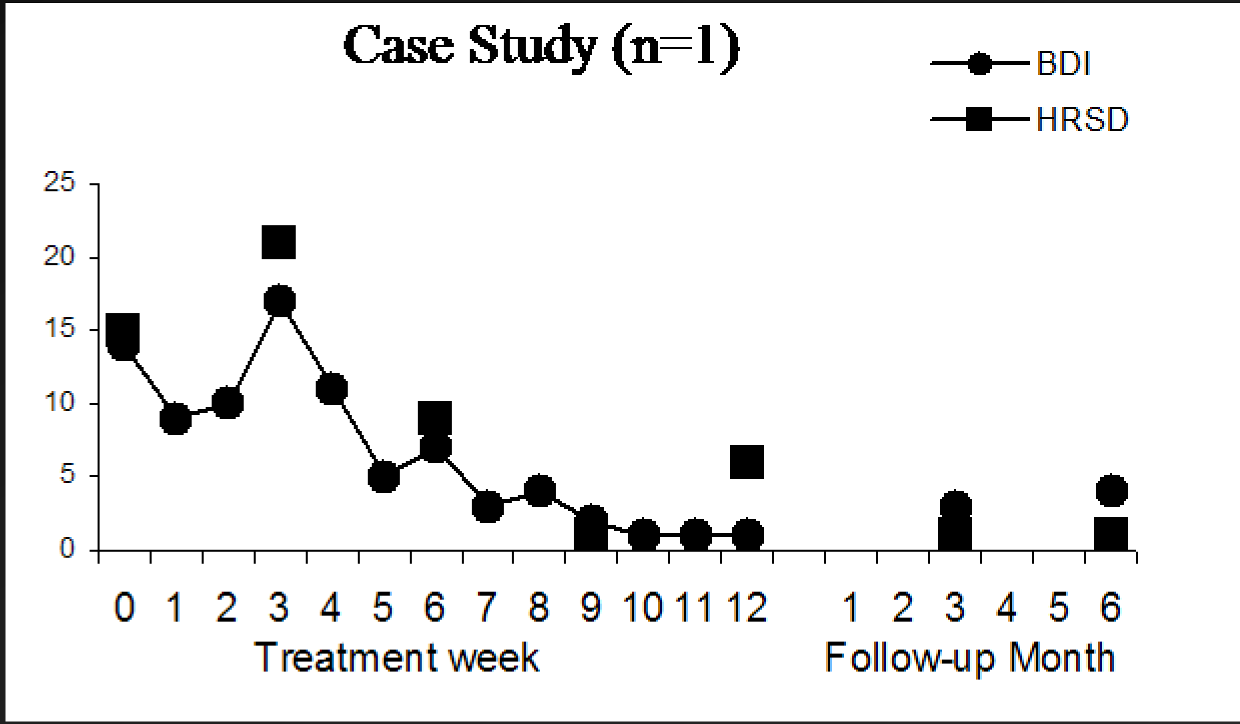


From Allen, Harmon-Jones, and Cavender (2001)

Manipulation of Asymmetry using Biofeedback

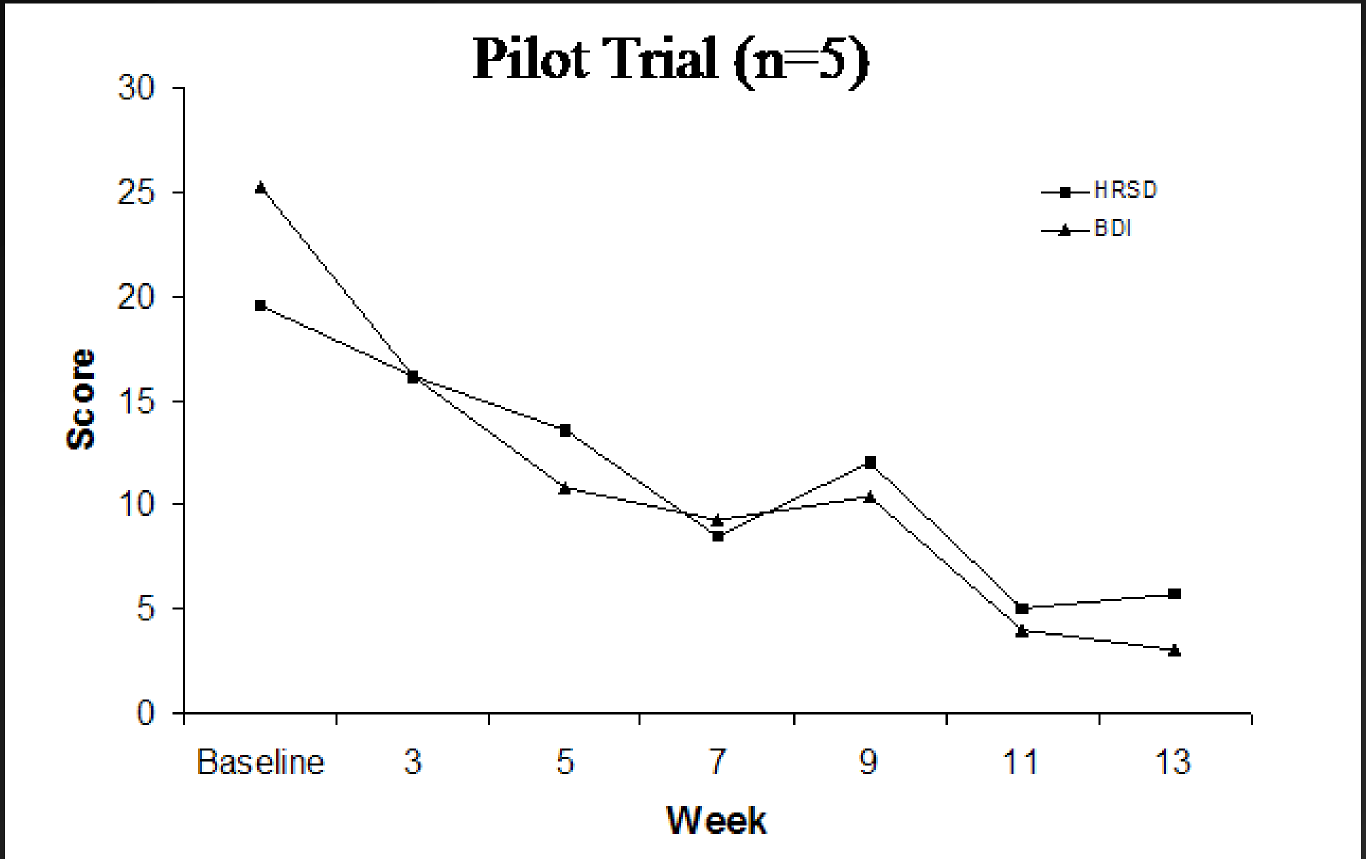
- Phase 1: Demonstrate that manipulation of EEG asymmetry is possible
- Phase 2: Determine whether EEG manipulation has emotion-relevant consequences
- Phase 3: Examine whether EEG manipulation produces clinically meaningful effects
- Phase 4: Conduct efficacy trial

Phase 3a



Biofeedback provided 3 times per week for 12 weeks

Phase 3b



"Open Label" pilot trial, with biofeedback provided 3 times per week for 12 weeks

Phase 4: Randomized Control Trial

- Depressed subjects ages 18-60 to be recruited through newspaper ads
- Ad offers treatment for depression but does not mention biofeedback
- Participants meet DSM-IV criteria for Major Depressive Episode (nonchronic)

Design

- Contingent-noncontingent yoked partial crossover design
- Participants randomly assigned to:
  - *Contingent Biofeedback*: tones presented in response to subject's EEG alpha asymmetry
  - *Noncontingent Yoked*: tones presented that another subject had heard, but tones not contingent upon subject's EEG alpha asymmetry
- Treatments 3 times per week for 6 weeks
- After 6 weeks, all subjects receive contingent biofeedback 3 times per week for another 6 weeks

Results

Dropout rate > 70%!

State Changes

- Infants
  - Stanger/Mother paradigm (Fox & Davidson, 1986)
  - Sucrose Vs water (Fox & Davidson, 1988)
  - Films of facial expressions (Jones & Fox, 1992; Davidson & Fox, 1982)
- Primates
  - Benzodiazepines increases LF (Davidson et al., 1992)

State Changes

- Adults
  - Spontaneous facial expressions (Ekman & Davidson, 1993; Ekman et al., 1990; Davidson et al., 1990)
  - Directed facial actions (Coan, Allen, & Harmon-Jones, 2001)

EEG responds to directed facial actions

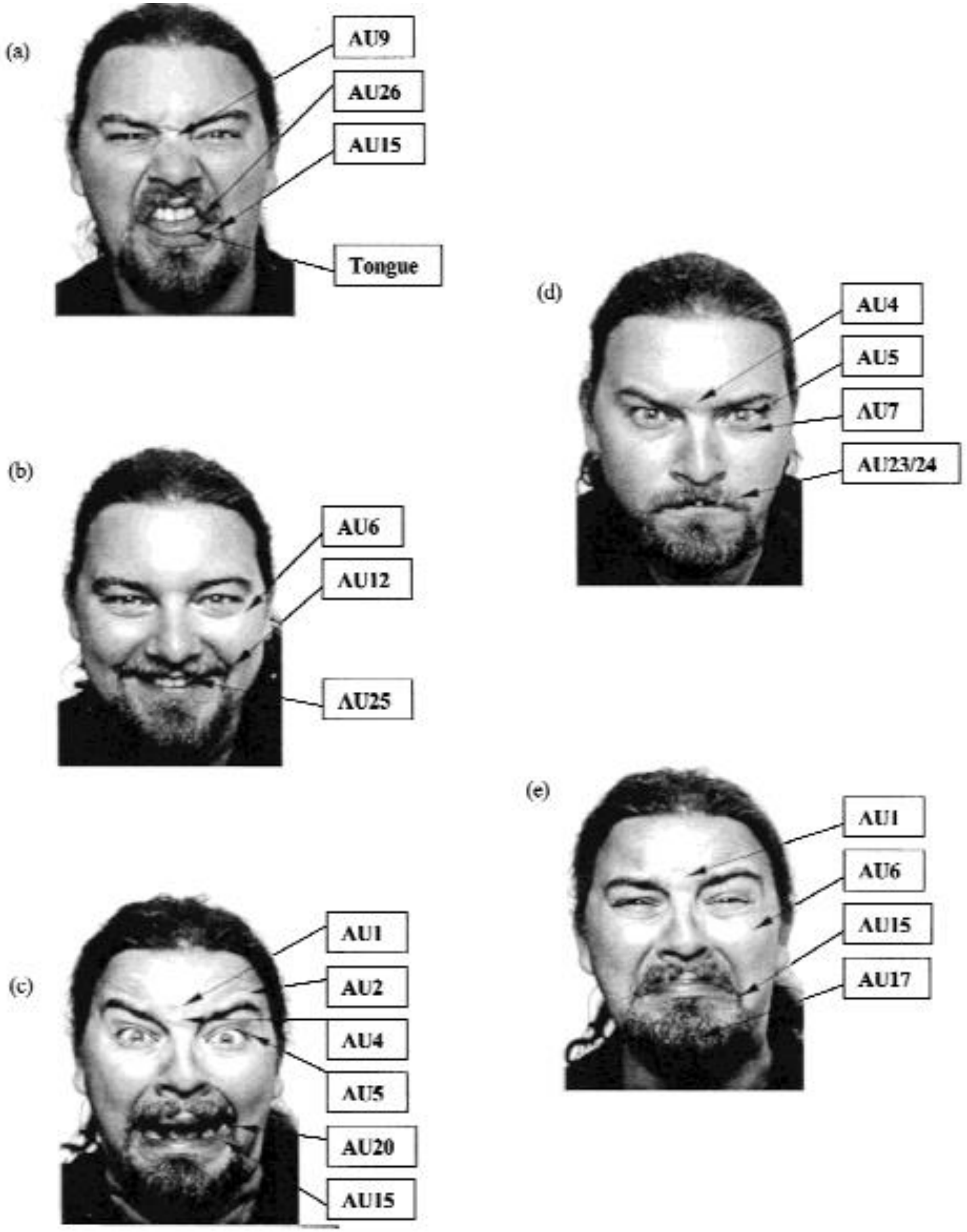
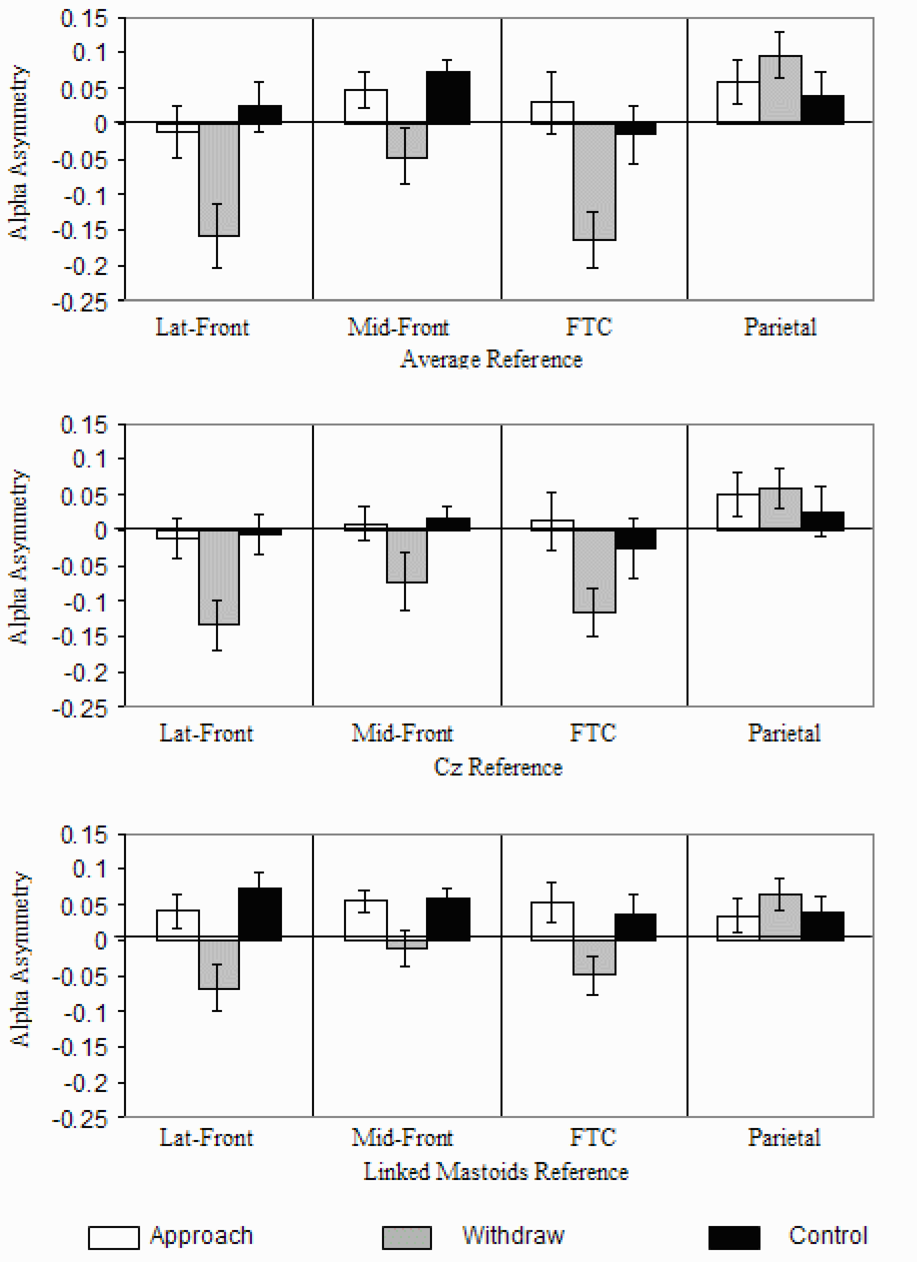


Figure 1. Muscle movements in the full face conditions: (a) disgust, activating AUs 9 (nose wrinkler), 15 (lip corner depressor), 26 (jaw drop), and the "tongue show;" (b) joy, activating AUs 6 (cheek raiser), 12 (lip corner puller), and 25 (lips part); (c) fear, activating AUs 1 (inner brow raiser), 2 (outer brow raiser), 4 (brow lowerer), 5 (upper lid raiser), 15 (lip corner depressor), and 20 (lip stretch); (d) anger, activating AUs 4 (brow lowerer), 5 (upper lid raiser), 7 (lid tightener), 23 (lip tightener), and/or 24 (lip pressor); (e) sadness, activating AUs 1 (inner brow raiser), 6 (cheek raiser), 15 (lip corner depressor), and 17 (chin raiser).

From Coan, Allen, and Harmon-Jones (2001)

EEG responds to directed facial actions



From Coan, Allen, and Harmon-Jones (2001)

States – how short can they be?

Psychophysiology, *46* (2009), 132–142. Wiley Periodicals, Inc. Printed in the USA.

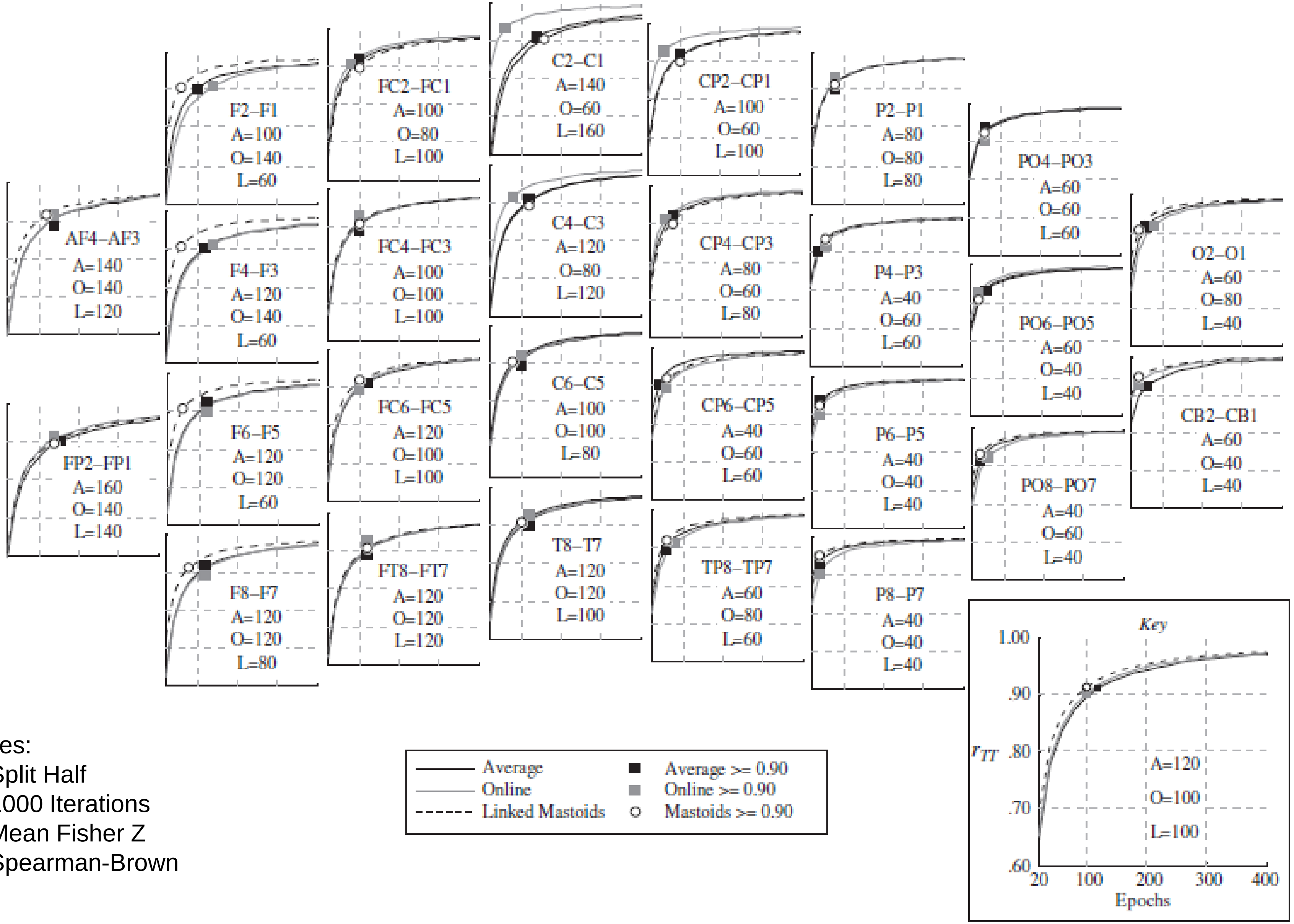
DOI: 10.1111/j.1469-8986.2008.00759.x

A better estimate of the internal consistency reliability of frontal EEG asymmetry scores

DAVID N. TOWERS AND JOHN J.B. ALLEN
Department of Psychology, University of Arizona, Tucson, Arizona, USA

Abstract

Frontal alpha asymmetry is typically computed using alpha power averaged across many overlapping epochs. Previous reports have estimated the internal consistency reliability of asymmetry by dividing resting EEG sessions into segments of equal duration (e.g., 1 min) and treating asymmetry scores for each segment as "items" to estimate internal consistency reliability using Cronbach's alpha. Cronbach's alpha partly depends on the number of items, such that this approach may underestimate reliability by using less than the number of distinct items available. Reliability estimates for resting EEG data in the present study (204 subjects, 8 sessions) were obtained using mean split-half correlations with epoch alpha power as treated as separate items. Estimates at all scalp sites and reference schemes approached .90 with as few as 100 epochs, suggesting the internal consistency of frontal asymmetry is greater than that previously reported.



Notes:
- Split Half
- 1000 Iterations
- Mean Fisher Z
- Spearman-Brown

Figure 1. Estimated internal consistency reliability (r_{TT}) of asymmetry scores for epoch set sizes n ranging from 20 to 400, across average (black), online (gray), and linked-mastoids (dashed) reference derivations and all homologous electrode pairs. Graph markers and table insets indicate the epoch set size n at which the estimated internal consistency reliability coefficient for each reference derivation was greater than or equal to .90.

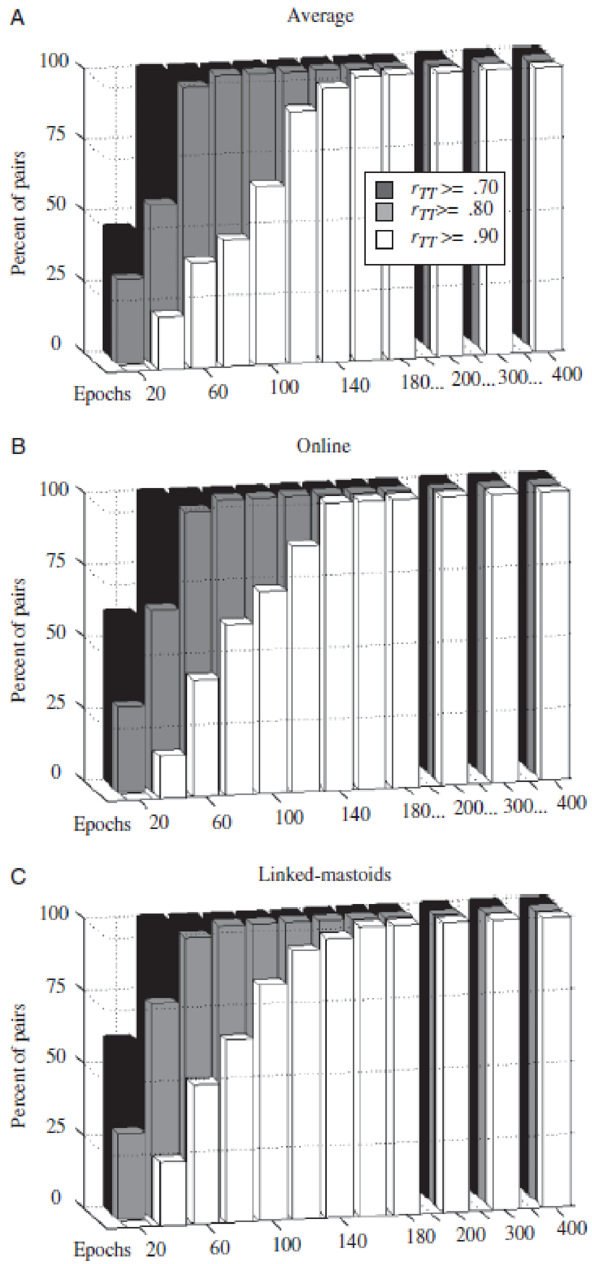


Figure 2. Percentage of homologous electrode pairs in which estimates of internal consistency reliability (r_{TT}) of asymmetry scores were greater than or equal to .70 (white), .80 (light gray), and .90 (dark gray) as a function of epoch set size n and reference derivation.

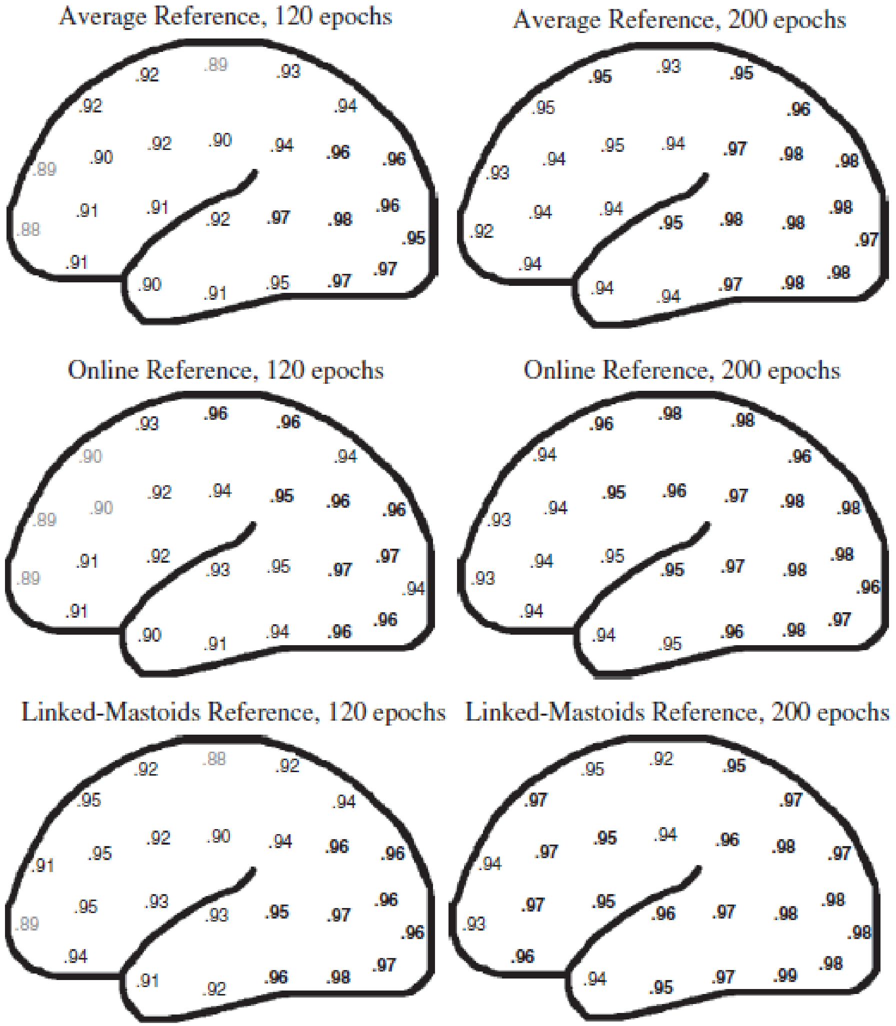


Figure 3. Estimated internal consistency reliability (r_{TT}) of asymmetry scores for epoch set sizes of 120 and 200, with light gray numbers indicating $.85 \leq r_{TT} < .90$ and bold numbers indicating $r_{TT} \geq .95$ (the pair CB2–CB1 was omitted).

State EEG in CIT!

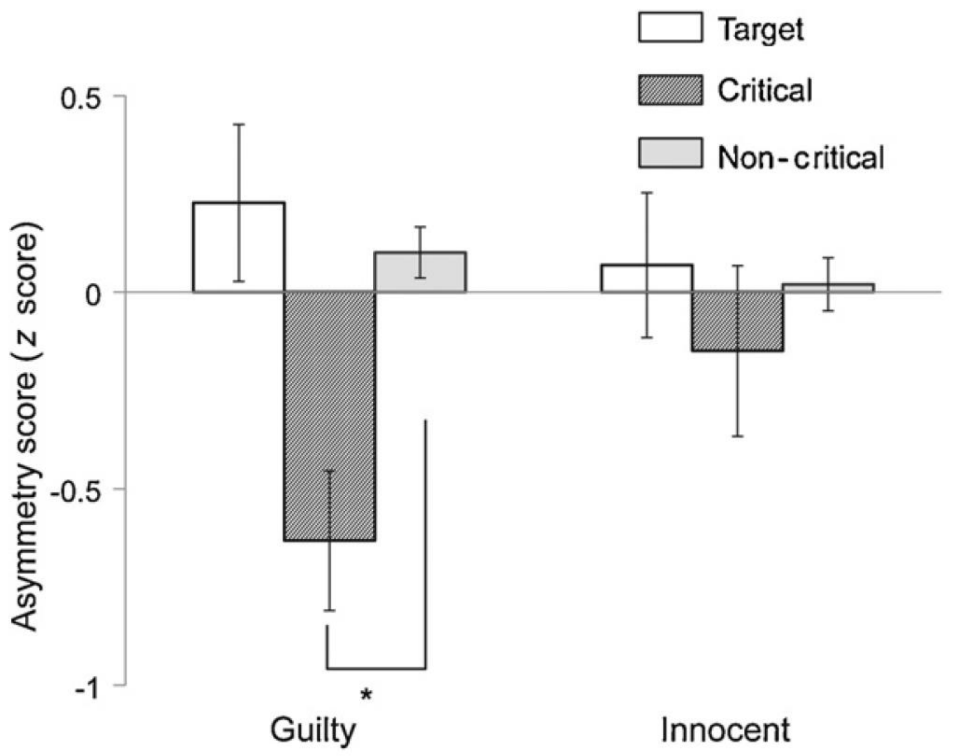


Fig. 2. Grand average frontal EEG asymmetry scores for target, critical, and non-critical items in the guilty and innocent condition. Asymmetry score = ln[F4 alpha power] – ln[F3 alpha power]. Bars depict standard errors. *$p < .05$.

Matsuda, Nittono, & Allen, *Neurosci Letters,* 2013

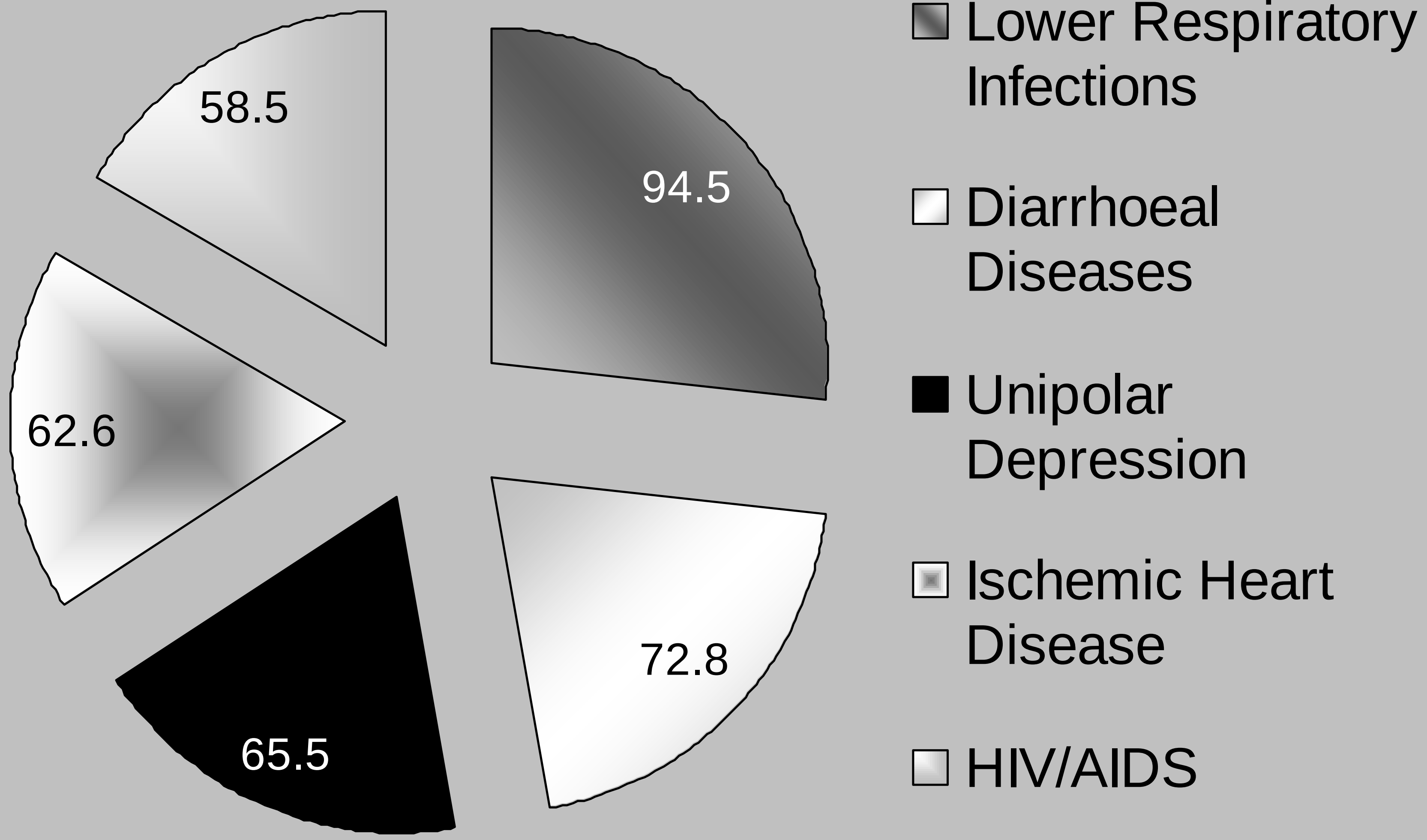
Resting brain asymmetry as an endophenotype for depression

Endophenotypes

- Intermediate-level measure of characteristics related to risk for disorder
- Less complex phenotype for genetic association
- Can include, biochemical and imaging measures, among others
- Desiderata
  - Specificity
  - Heritability
  - State-independence
  - Familial Association
  - Co-segregation within families
  - Predicts development of disorder

Gottesman & Shields, 1972; Gottesman & Gould, 2003; Iacono, 1998

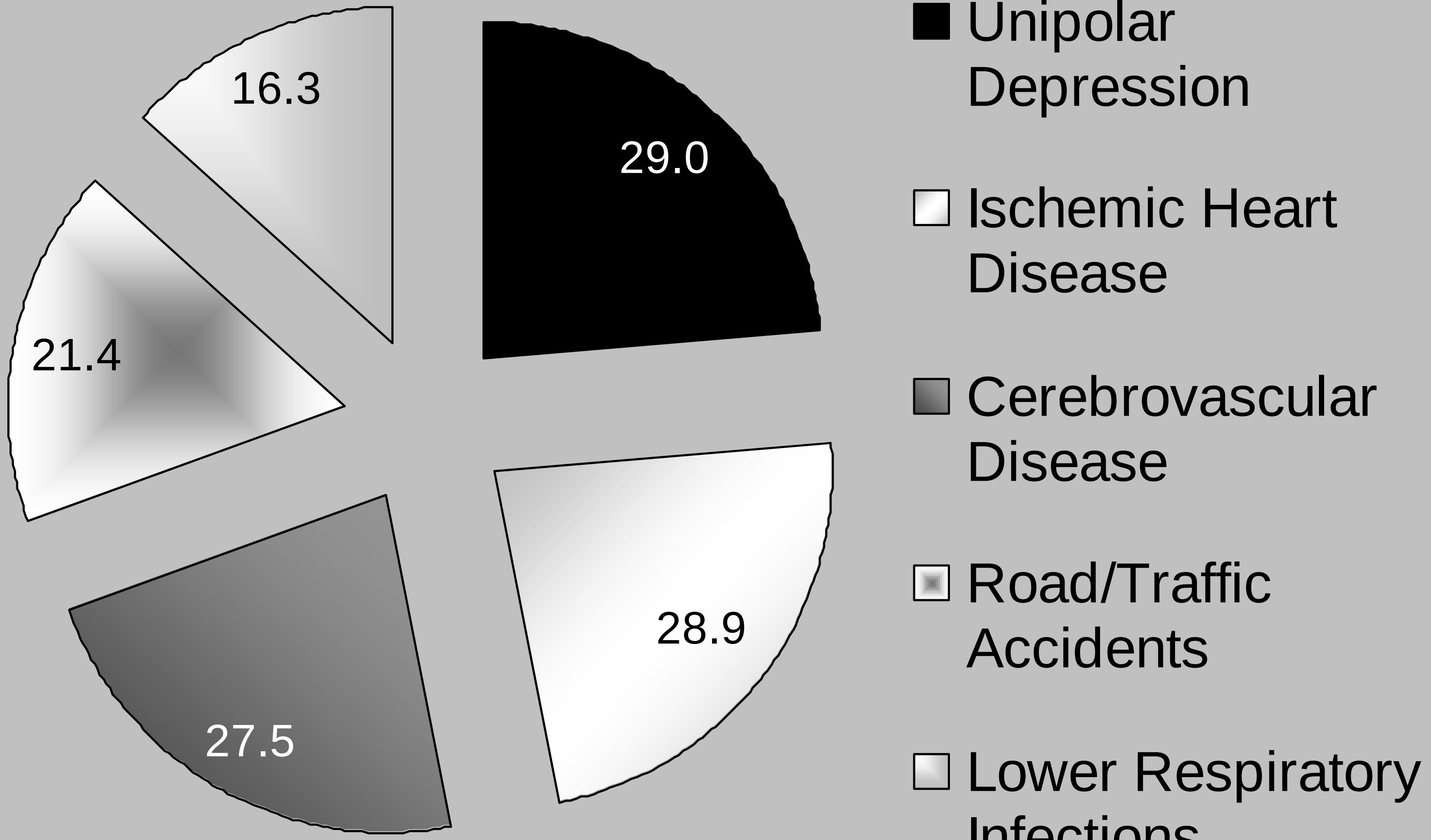
World Disability Adjusted Life Years (Millions)



World Health Organization, 2008

Middle Income Countries

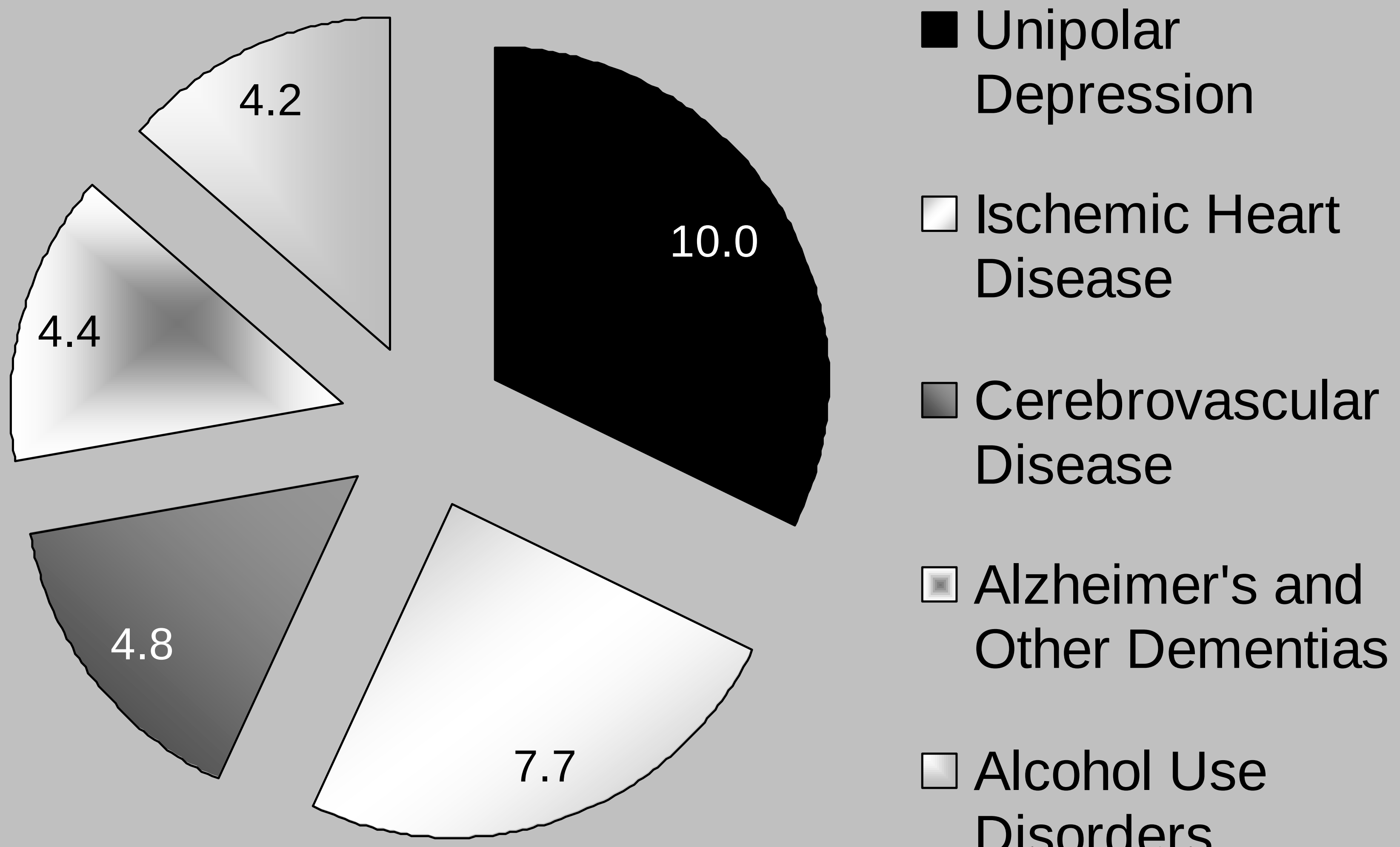
World Disability Adjusted Life Years (Millions)



World Health Organization, 2008

Upper Income Countries

World Disability Adjusted Life Years (Millions)



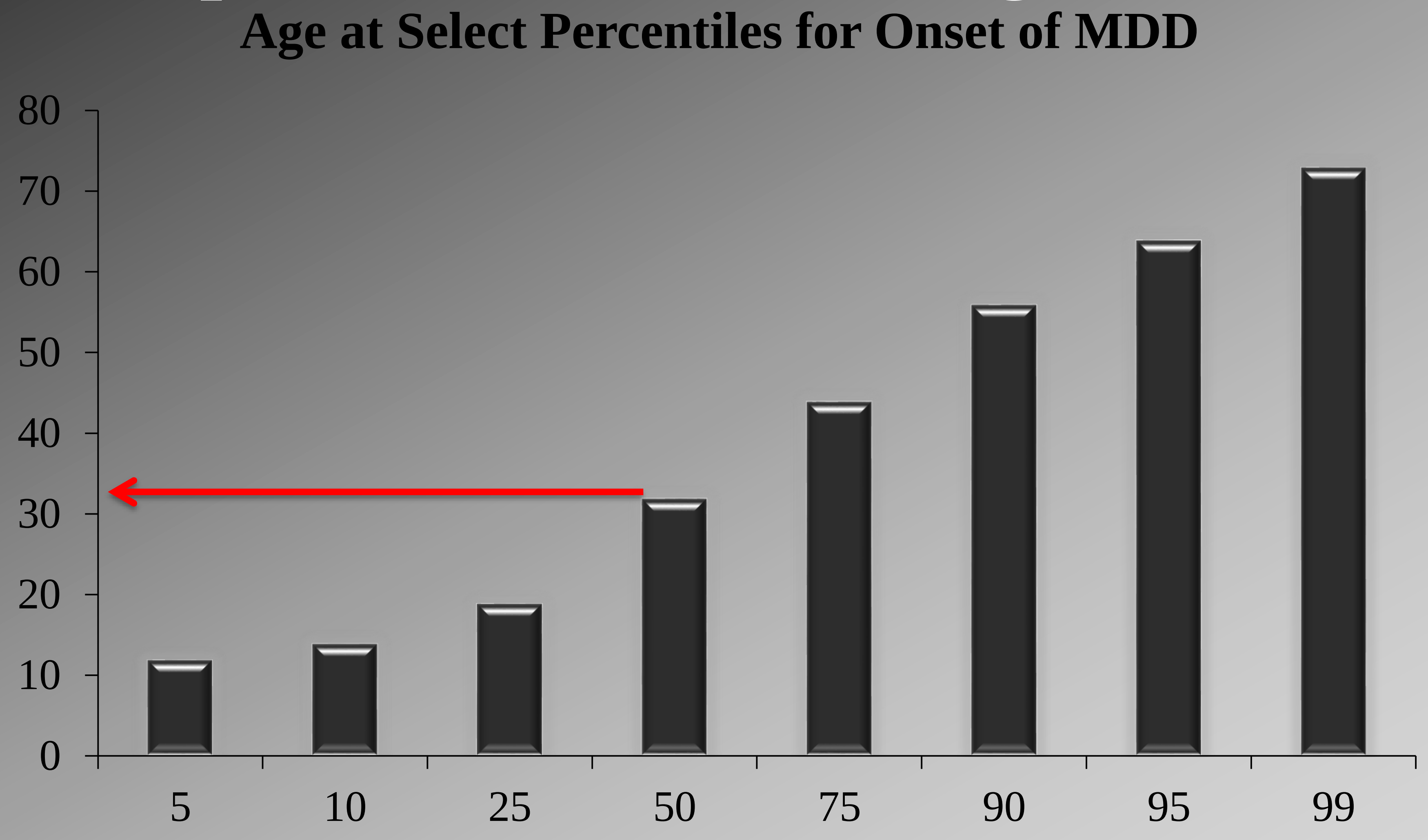
World Health Organization, 2008

Depression

Depression as a Heterogeneous Phenotype

- Variable Age of Onset
- Variable Symptom Presentation
- Variable Course
- Variable Response to Treatment

Depression: Variable Age Onset



Data from Kessler et al., Arch Gen Psychiatry, 2005, 62:593-602

Depression: Variable Age Onset

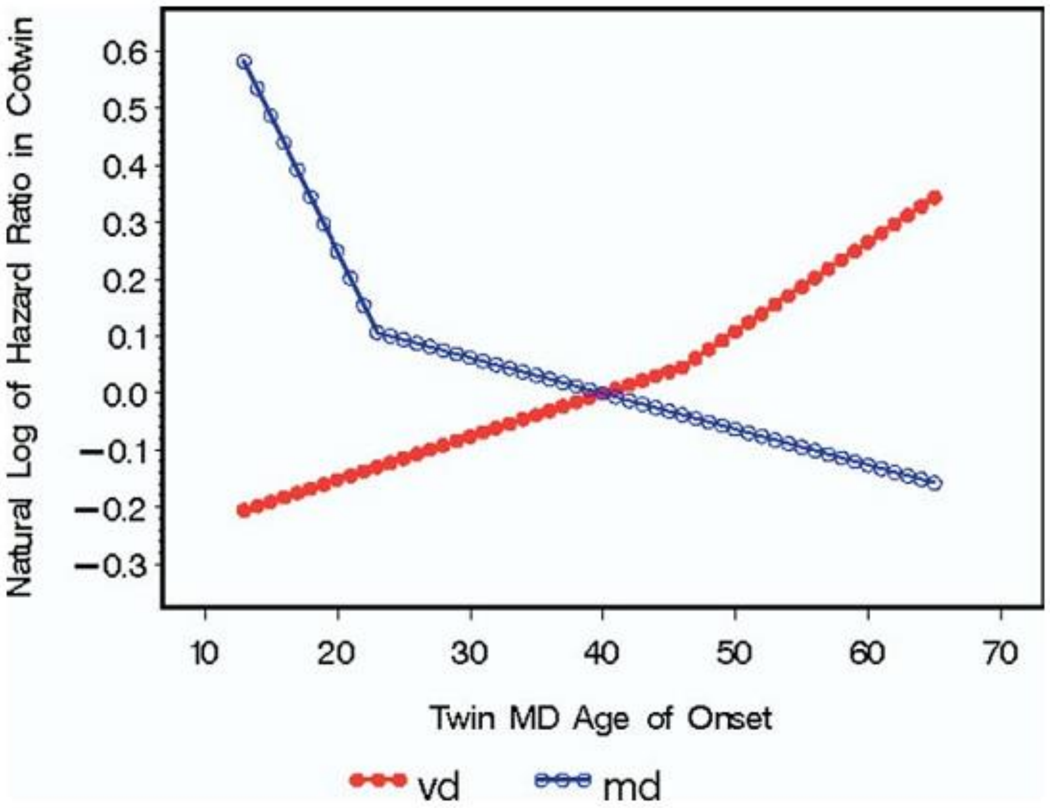
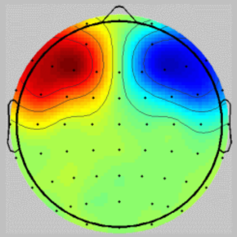


Figure 1. The relationship between the age at onset of major depression (MD) in an affected twin and the natural logarithm of the hazard ratio in the cotwin for MD (in open circles) and vascular disease (VD) (in filled-in circles). These results are obtained from a Cox proportional hazard model controlling for age, sex, and birth cohort. We fitted to these results piecewise models with a single inflection point using a grid search to find the single inflection point that maximized the model's −2 log likelihood.

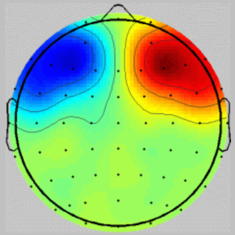
Kendler, Fiske, Gardner, & Gatz, 2009, *Biological Psychiatry*

Treating and Preventing Depression

- Identify those at risk
- Identify factors that place folks at risk
- Develop interventions to address those factors



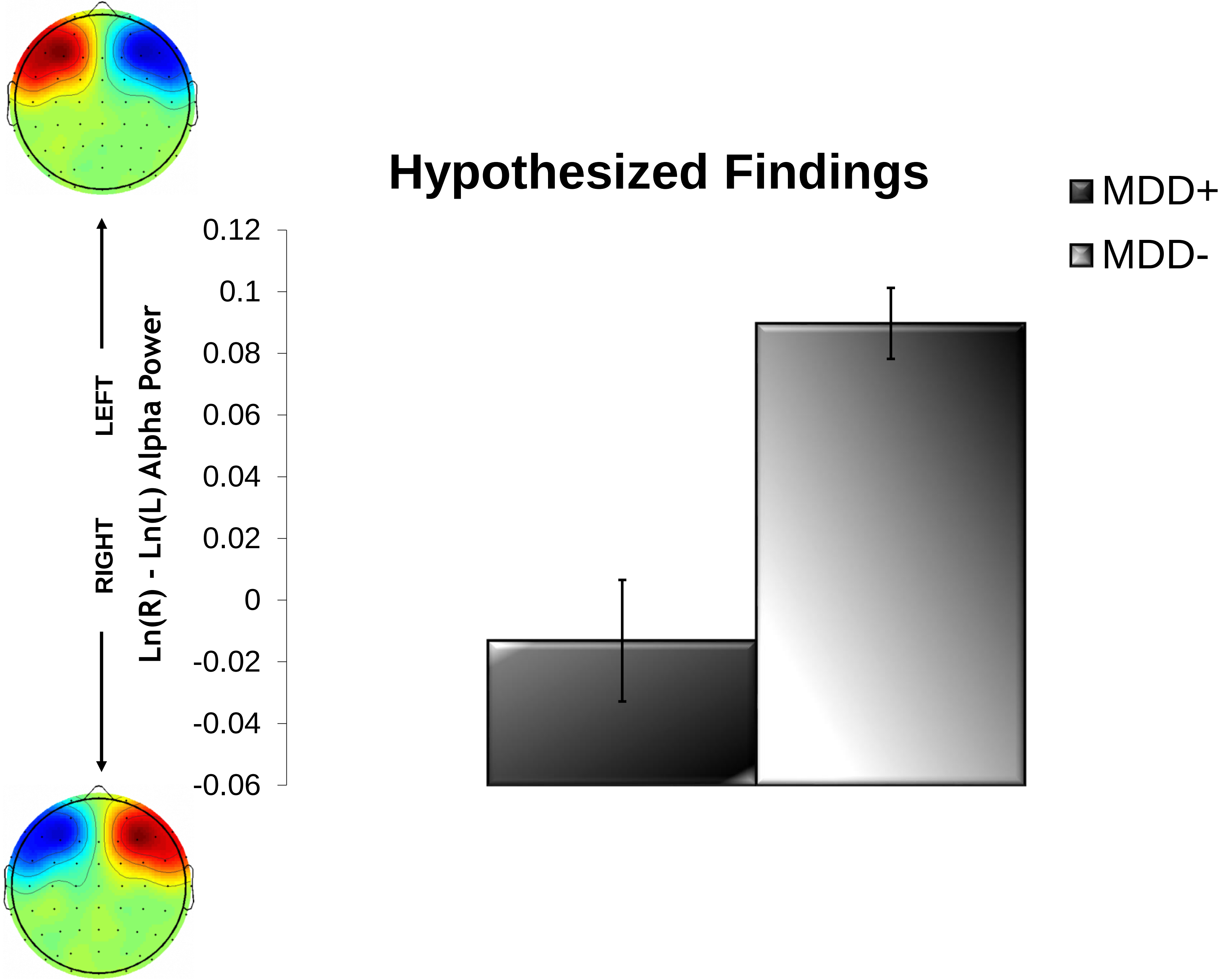
Ln(R)-Ln(L) Alpha



- Positive Affect and Mood
- Behavioral Engagement
- Approach Motivation (including Anger)
- High Behavioral Activation

- Negative Affect and Mood
- Behavioral Disengagement
- Withdrawal Motivation
- Low Behavioral Activation

Hypothesized Findings

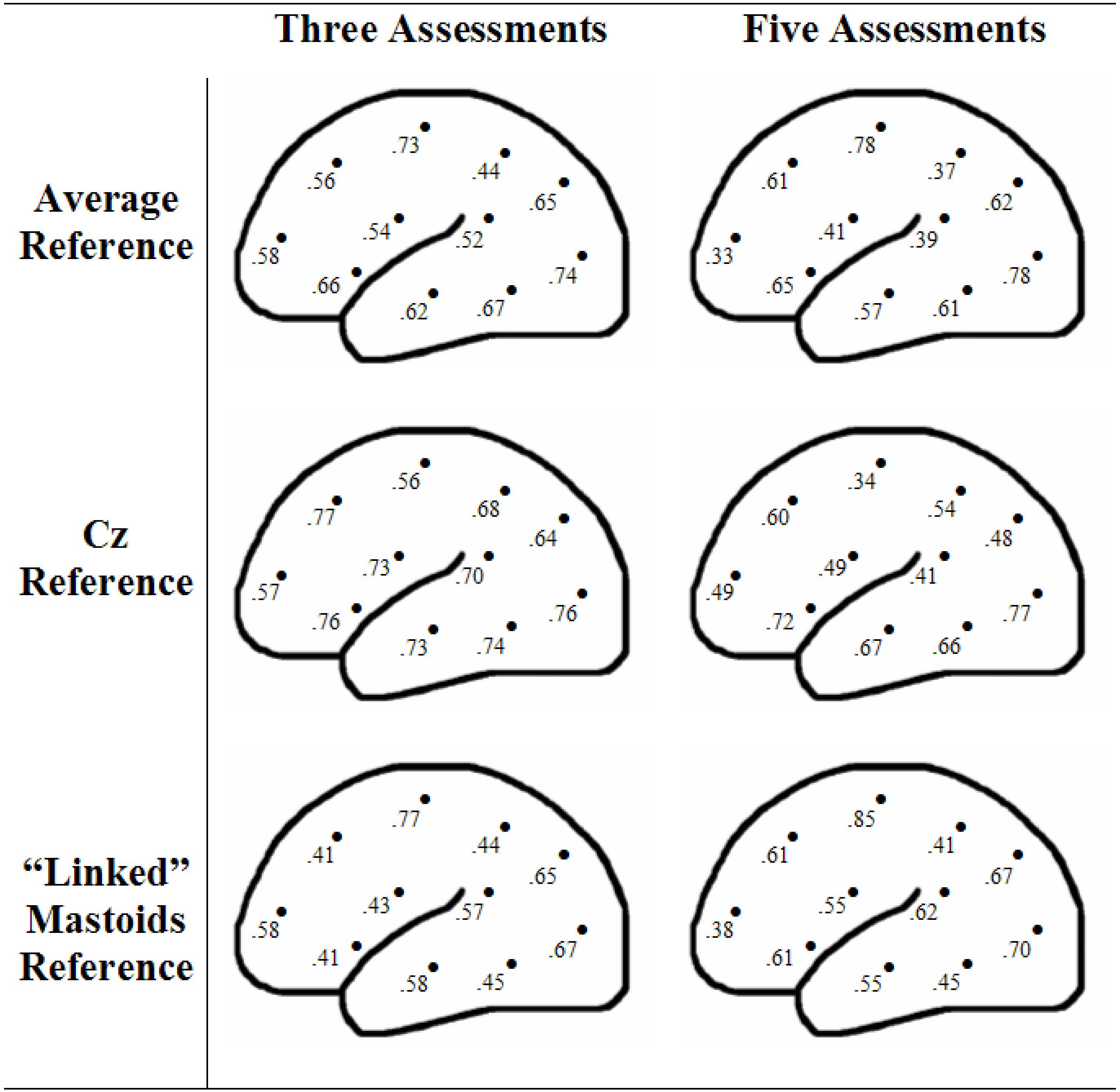


Frontal EEG asymmetry as risk marker for MDD

Several Desiderata…

Frontal EEG asymmetry as risk marker for MDD

- Resting EEG asymmetry is a stable trait
  - in clinical populations
    (Allen, Urry, et al., 2004; Jetha, Schmidt, & Goldberg, in press; Niemic & Lithgow, 2005; Vuga, et al., 2006)
  - and nonclinical populations
    (Hagemann, Naumann, Thayer, & Bartussek, 2002; Jones, Field, Davalos, & Pickens, 1997; Papousek & Schulter, 1998, 2002; Tomarken, Davidson, Wheeler, & Doss, 1992; Tomarken, Davidson, Wheeler, & Kinney, 1992)



Allen, Urry, Hitt, & Coan (2004), *Psychophysiology*

Frontal EEG asymmetry as risk marker for MDD

- Changes in clinical status are not associated with changes in resting EEG asymmetry
  (Allen, Urry, et al., 2004; Debener, et al., 2000; Vuga, et al., 2006).

Frontal EEG asymmetry as risk marker for MDD

- Resting EEG asymmetry is:
  - modestly heritable
    (Anokhin, Heath, & Myers, 2006; Coan, Allen, Malone, & Iacono, 2009; Smit, Posthuma, Boomsma, & De Geus, 2007)
  - related to serotonergic candidate genes such as HTR1A allele variations (Bismark, et al., 2010)

Frontal EEG asymmetry as risk marker for MDD

- Resting EEG asymmetry relates to internalizing disorders:
  - MDD and depressive symptoms (Allen, Urry, et al., 2004; Bruder, et al., 2005; Debener, et al., 2000; Diego, Field, & Hernandex-Reif, 2001; Diego, Field, & Hernandez-Reif, 2001; Fingelkurts, et al., 2006; Ian H. Gotlib, Ranganath, & Rosenfeld, 1998; J. B. Henriques & Davidson, 1990; Jeffrey B. Henriques & Davidson, 1991; Mathersul, Williams, Hopkinson, & Kemp, 2008; Miller, et al., 2002; Pössel, Lo, Fritz, & Seeman, 2008; Schaffer, Davidson, & Saron, 1983; Vuga, et al., 2006);

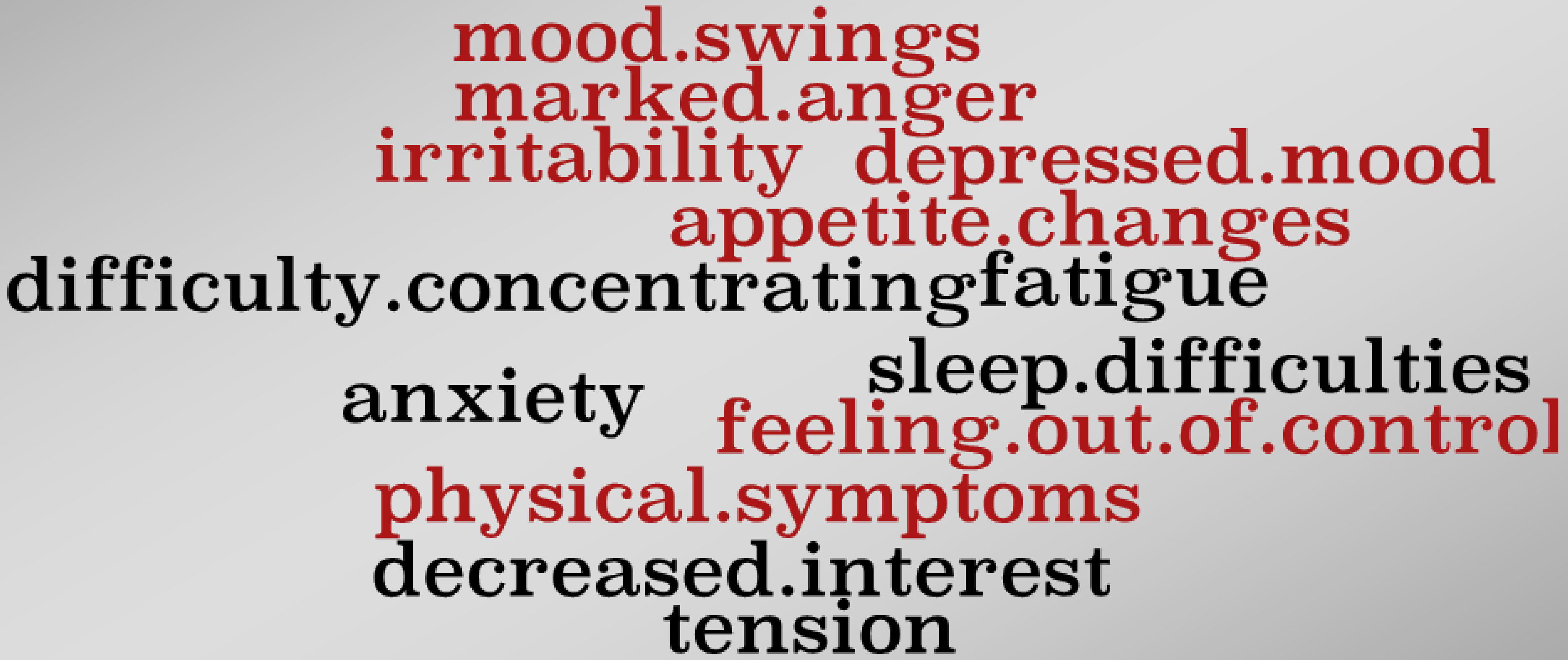
Frontal EEG asymmetry as risk marker for MDD

- Resting EEG asymmetry relates to internalizing disorders:
  - Anxious arousal/somatic anxiety (Mathersul, et al., 2008; Nitschke, Heller, Palmieri, & Miller, 1999; J.L. Stewart, Levin-Silton, Sass, Heller, & Miller, 2008);
  - Panic disorder (Wiedemann, et al., 1999);
  - Comorbid anxiety/depression (Bruder, et al., 1997);
  - Social phobia (R. J. Davidson, Marshall, Tomarken, & Henriques, 2000);

Frontal EEG asymmetry as risk marker for MDD

- Resting EEG asymmetry relates to internalizing disorders:
  - Premenstrual dysphoria (Accortt & Allen, 2006; Accortt, Stewart, Coan, Manber, & Allen, 2010);

PMDD



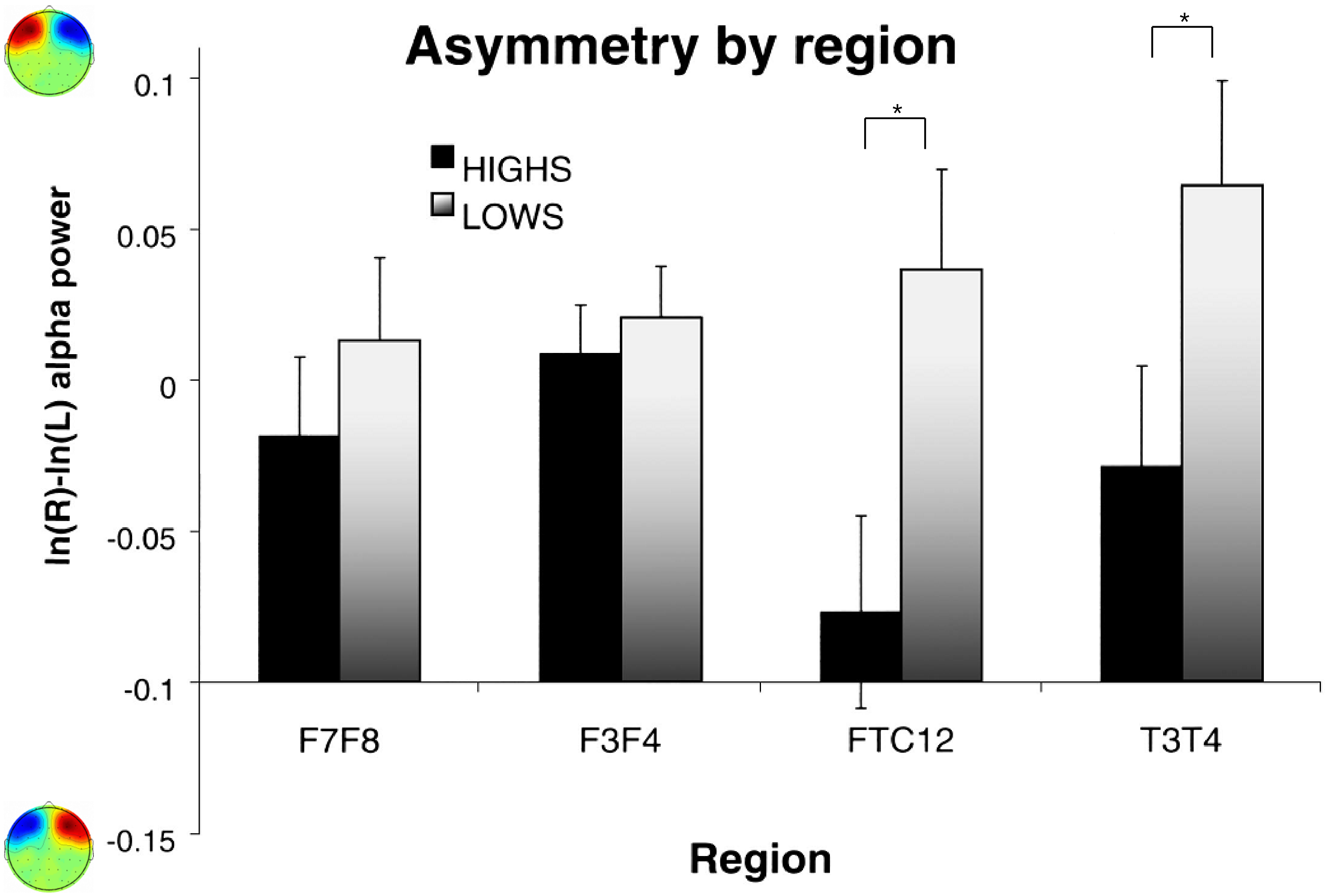
Accortt & Allen, 2006

PMDD

- Assessed at
  - Late-Luteal
  - Follicular

Accortt & Allen, 2006

Specificity or Spectrum: PMDD



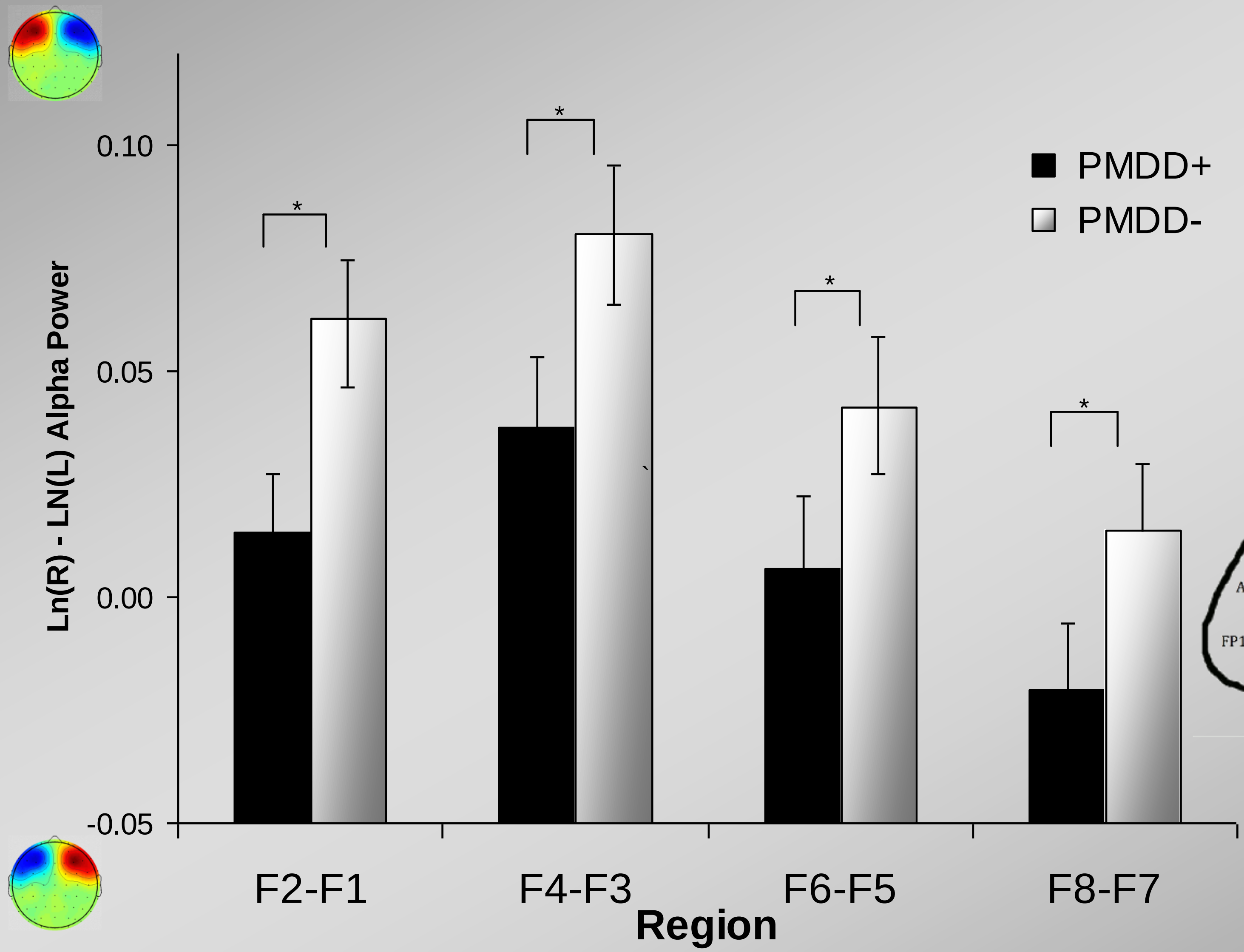
Accortt & Allen, 2006

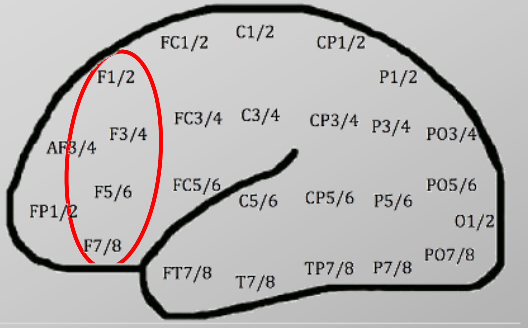
PMDD

- Larger Sample
- Diagnostic Interviews
- Matched for MDD

Accortt, Stewart, Coan, & Allen, 2010

PMDD





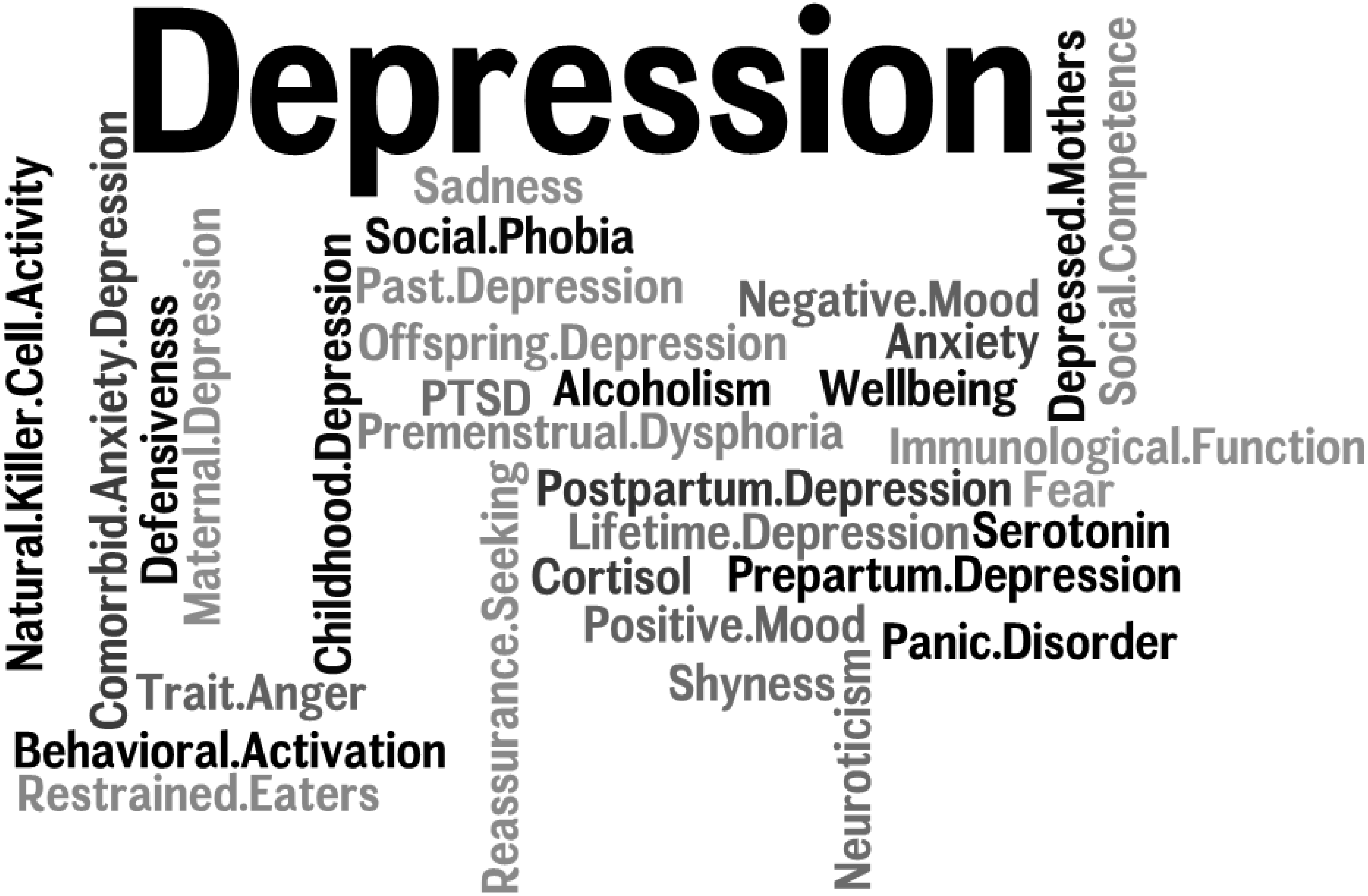
Accortt, Stewart, Coan, & Allen, 2010

Frontal EEG asymmetry as risk marker for MDD

- Resting EEG asymmetry relates to internalizing disorders:
  - Childhood/adolescent internalizing psychopathology (anxiety, sadness, disappointment, low empathy and sociability, higher stress cortisol, and avoidant-withdrawn behavior
    (Baving, Laucht, & Schmidt, 2002; Buss, et al., 2003; R.J. Davidson, 1991; Forbes, Fox, Cohn, Galles, & Kovacs, 2005; N.A. Fox, Henderson, Rubin, Calkins, & Schmidt, 2001; Henderson, Marshall, Fox, & K.H., 2004; Schmidt, Fox, Schulkin, & Gold, 1999).

Frontal EEG asymmetry as risk marker for MDD

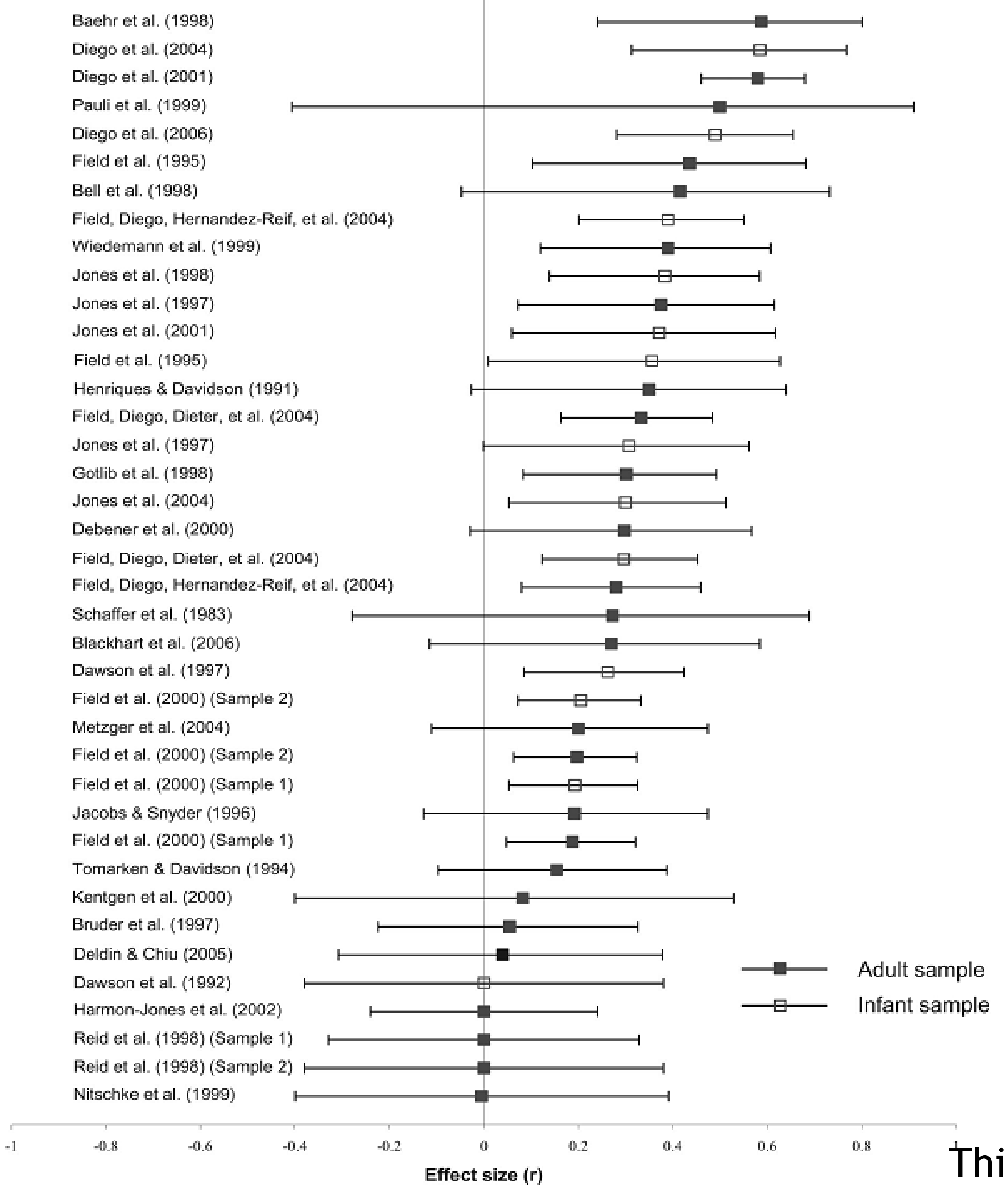
- Resting EEG asymmetry identifies *family members* of those with internalizing disorders
  - MDD (Dawson, Frey, Panagiotides, Osterling, & Hessl, 1997; Dawson, Frey, Panagiotides, et al., 1999; Dawson, Frey, Self, et al., 1999; Field, Diego, Hernandez-Reif, Schanberg, & Kuhn, 2002; Forbes, et al., 2007; Jones, Field, & Davalos, 2000; Jones, et al., 1997; Miller, et al., 2002; Tomarken, Dichter, Garber, & Simien, 2004).


Depression
Natural.Killer.Cell.Activity
Comorrbid.Anxiety.Depression
Defensivensss
Maternal.Depression
Childhood.Depression
Sadness
Social.Phobia
Past.Depression
Negative.Mood
Offspring.Depression
Anxiety
PTSD
Alcoholism
Wellbeing
Depressed.Mothers
Social.Competence
Premenstrual.Dysphoria
Immunological.Function
Reassurance.Seeking
Postpartum.Depression
Fear
Lifetime.Depression
Serotonin
Cortisol
Prepartum.Depression
Positive.Mood
Panic.Disorder
Shyness
Neuroticism
Trait.Anger
Behavioral.Activation
Restrained.Eaters

Meta-Analysis: Depression, Anxiety

- Studies of resting frontal alpha asymmetry
- Measures of depression or anxiety
- Both adult and infant samples
- Literature Sample:
  - 31 papers
  - 59 tests (studies, sites, reference)
  - Adult samples predominantly female

Thibodeau, Jorgensen, & Kim, 2006



Mean Effect Sizes

- Adults d=0.54
- Infants d=0.61

Moderators

- Reference
- Recording length
- Co-morbidity

Publication Bias

- ↑ Effect Size
- Can't account for full effects

Thibodeau, Jorgensen, & Kim, 2006

A "Definitive" Study

- Large (n=306), medication-free
  - Both men (n=95) and women (n=211)
  - Lifetime Depressed (n=143)
  - Never Depressed (n=163)
- Assessed for Family History
- No co-morbidity, medically healthy

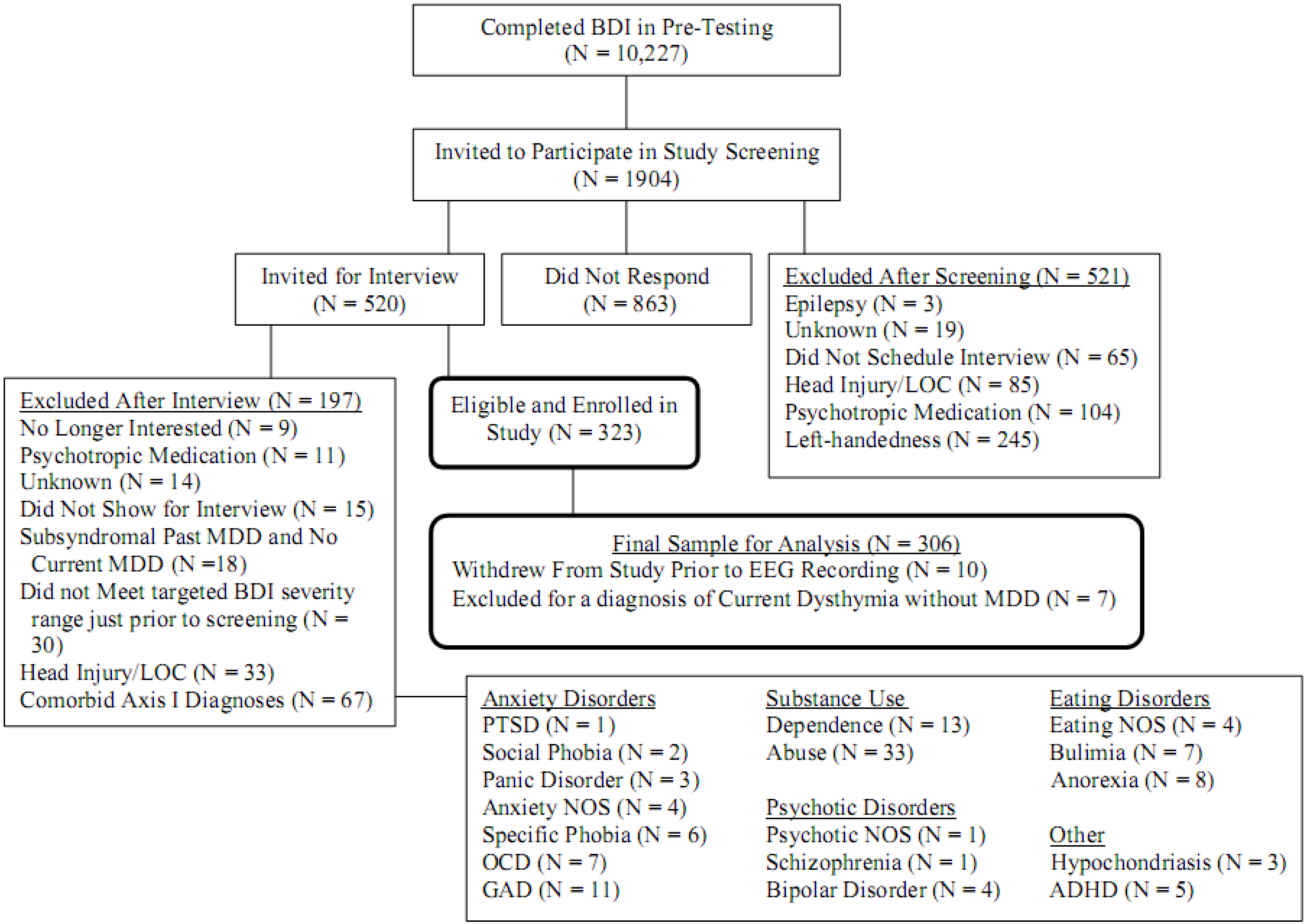



Stewart, Bismark, Towers, Coan, & Allen, 2010

A “Definitive” Study

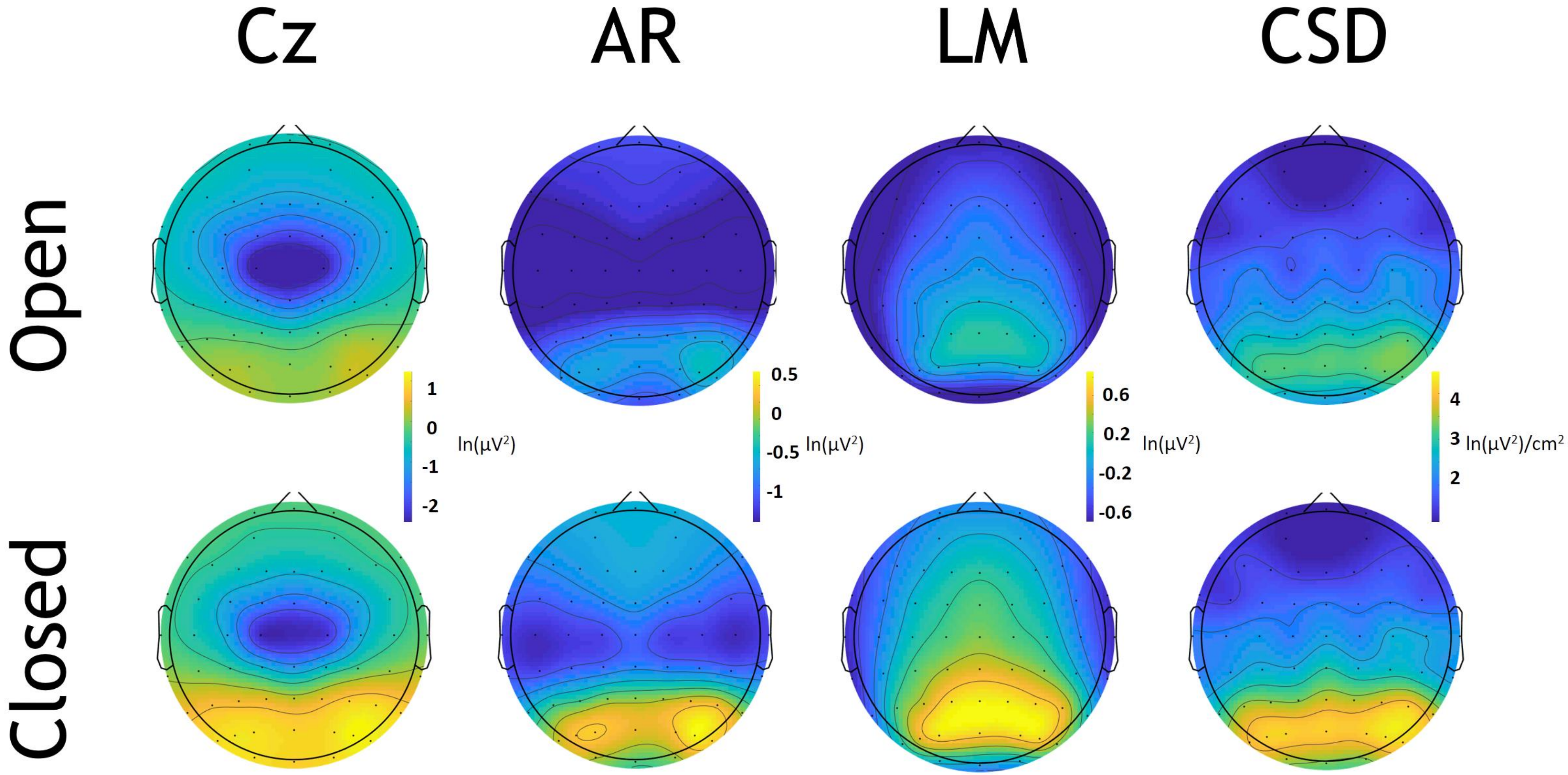
- Large (n=306), medication-free
- Assessed for Family History
- No co-morbidity, medically healthy
- Resting EEG
  - Two sessions per day
  - Four days
- Four Reference Montages
- Mixed Linear Models

Stewart, Bismark, Towers, Coan, & Allen, 2010



Stewart, Bismark, Towers, Coan, & Allen 2010, *J Abnormal Psychology*

Reference Effects



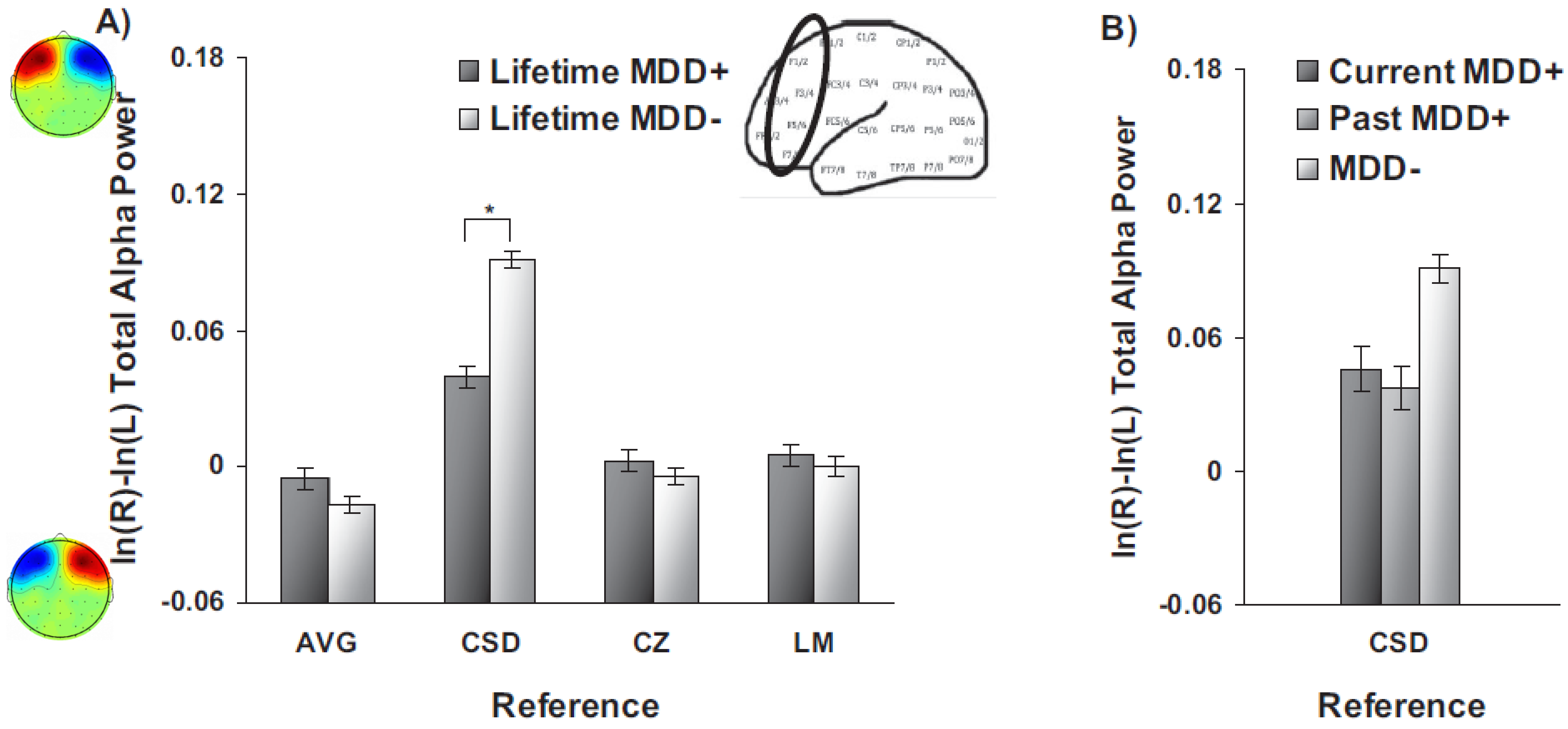


Figure 2. Panel A shows frontal alpha asymmetry scores (8–13 Hz at F2–F1, F4–F3, F6–F5, F8–F7) by lifetime MDD status for each reference montage across all four frontal regions depicted on the head insert. Error bars reflect standard error. Panel B shows results of a follow-up assessment indicating that the relationship of lifetime MDD status to CSD-referenced asymmetry is not solely accounted for by current MDD status. The *y*-axis is ln μV^2 for AVG, Cz, and LM references, and ln $\mu V^2/cm^2$ for CSD referenced data. MDD = major depressive disorder; AVG = average; CSD = current source density; CZ = Cz; LM = linked mastoid.

Stewart, Bismark, Towers, Coan, & Allen, 2010

STICK WITH CSD…

Interim Synopsis: Endophenotype Desiderata

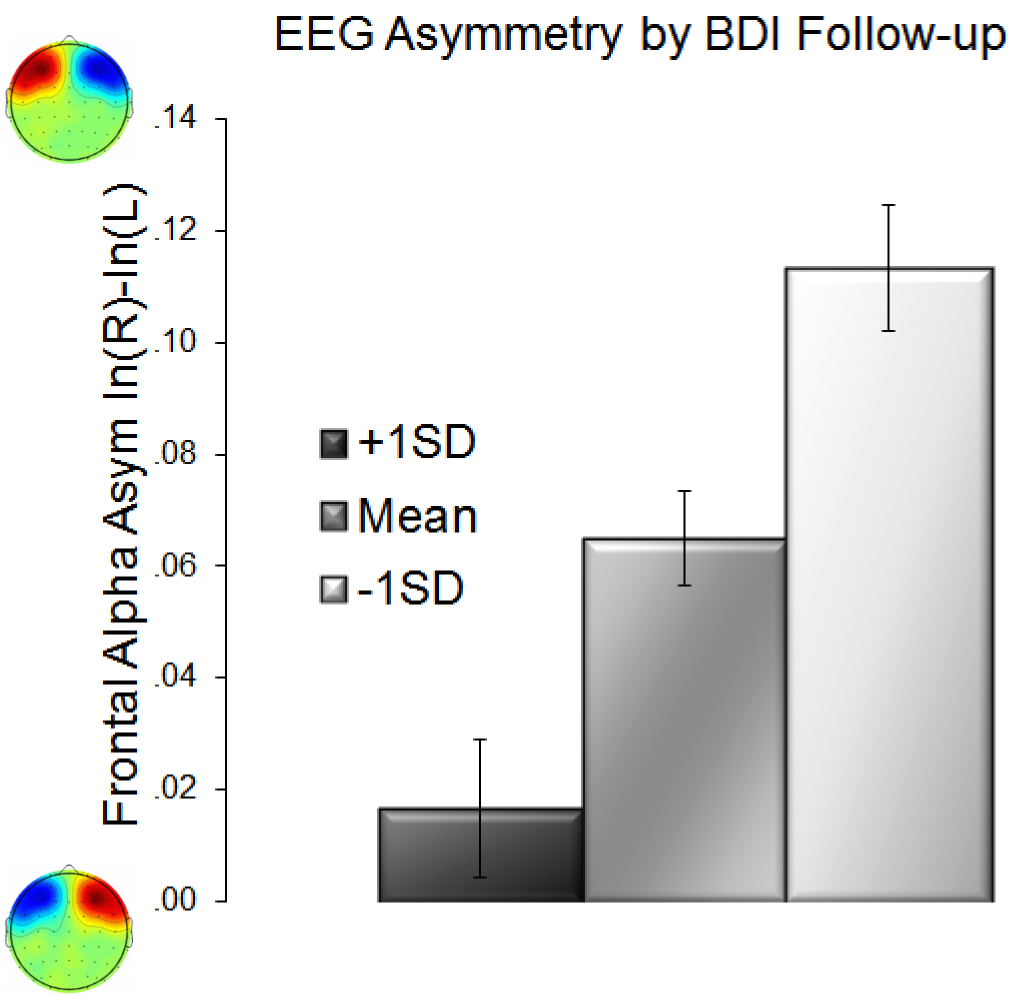
Gottesman & Shields, 1972; Gottesman & Gould, 2003; Iacono, 1998

- ☑ Specificity: Associated with disorder
- ☑ Heritability
- ☑ State-independence: Primarily trait
- ☑ Familial Association: Seen in unaffected family members at rates higher than general population
- Predictive Power: predicts future disorder in unaffected individuals

Prospective Pilot Data

- Assessed never depressed (MDD-) individuals ~1 year after EEG
- Obtained 54 of 163 (representative)
- Completed BDI based on “worst month”
- BDI worst month residualized on BDI at EEG assessment
- Can EEG predict this worst month BDI score?

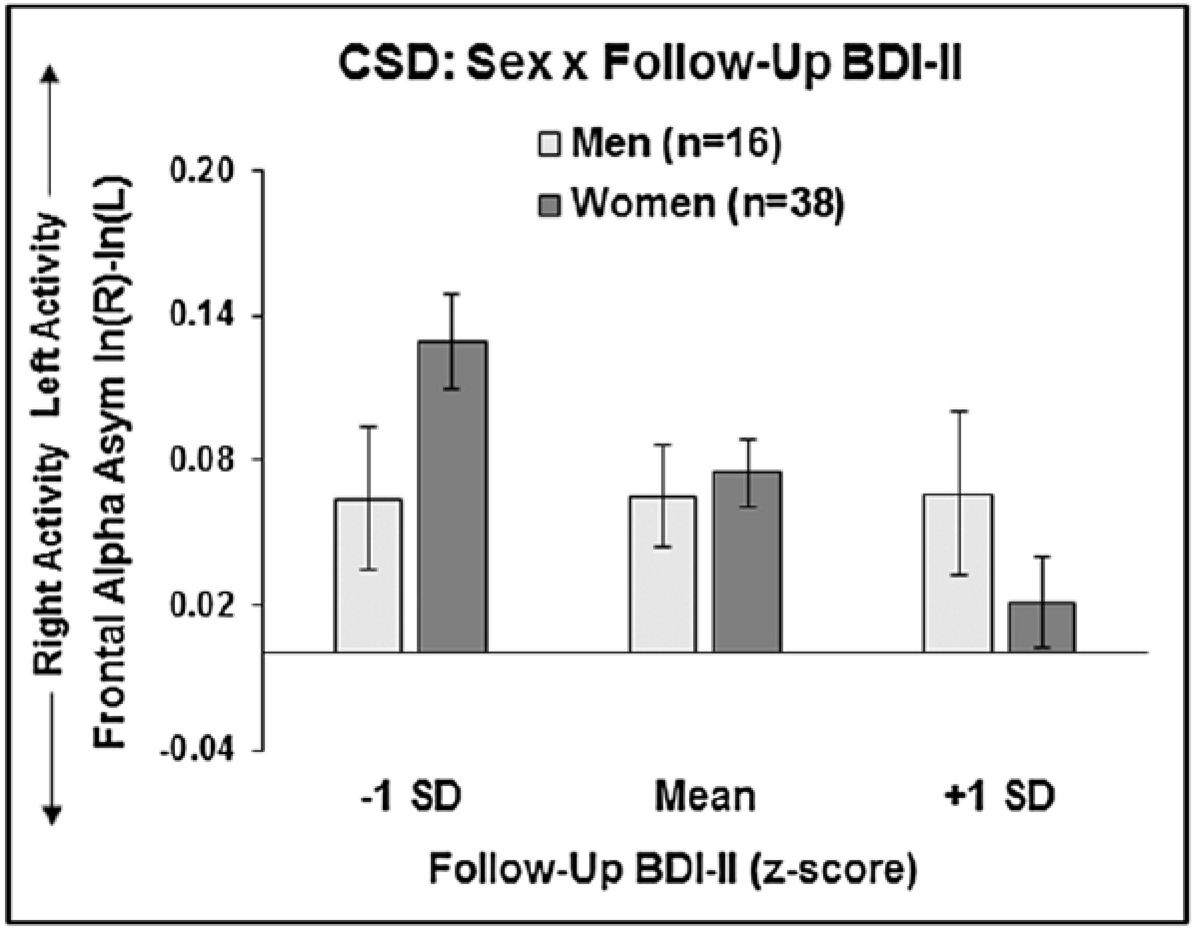
Prospective Pilot Data



See also Nusslock et al., *J Abnormal Psychology*, 2011

Stewart & Allen, *Bio Psychology* 2018

Prospective Pilot Data: a wrinkle



Stewart & Allen, *Bio Psychology* 2018

Thus

- Frontal EEG asymmetry has promise as a risk indicator for MDD and other internalizing disorders
- Need:
  - Large-scale prospective study
  - Links to underlying neural systems

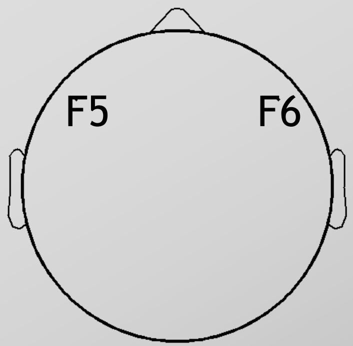
TIME AND SPACE

Deconstructing the “resting” state: Exploring the temporal dynamics of resting frontal brain asymmetry as an endophenotype for depression

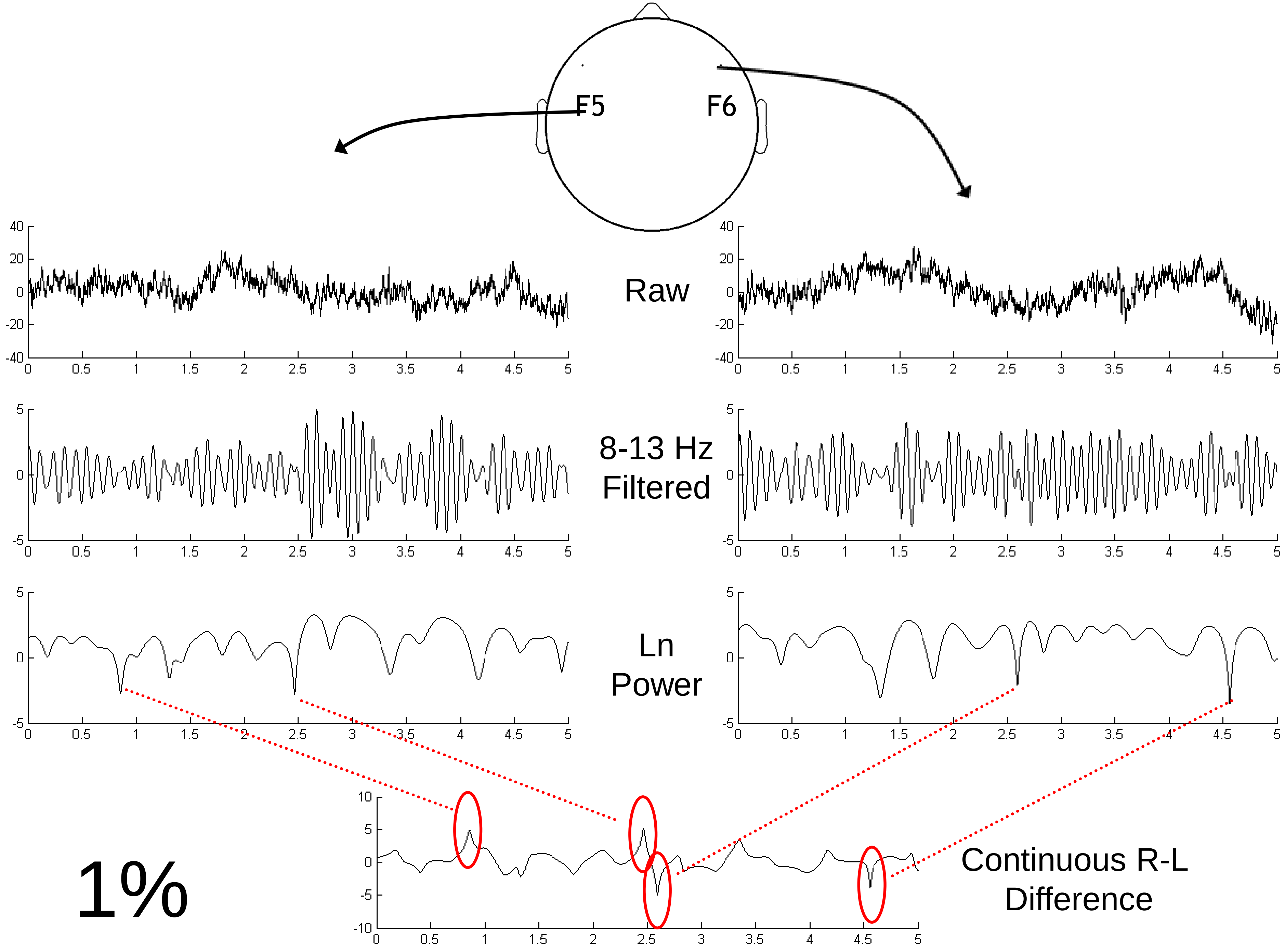
Allen & Cohen, 2010

The Conventional Approach

- One number to summarize several minutes of resting data
- Good reliability, but…
  - Lacks temporal specificity
  - Confuses "more" with "more often"



Asym = Ln(Right)-Ln(Left) Alpha Power



F5
F6
Raw
8-13 Hz
Filtered
Ln
Power
1%
Continuous R-L
Difference

Three Central Questions

- How do the novel peri-burst metrics of dynamic asymmetry compare to the conventional FFT-based metrics?
- Do the peri-burst metrics adequately differentiate depressed and non-depressed participants
- What EEG dynamics surround the asymmetry bursts that are captured by the novel peri-burst metrics?

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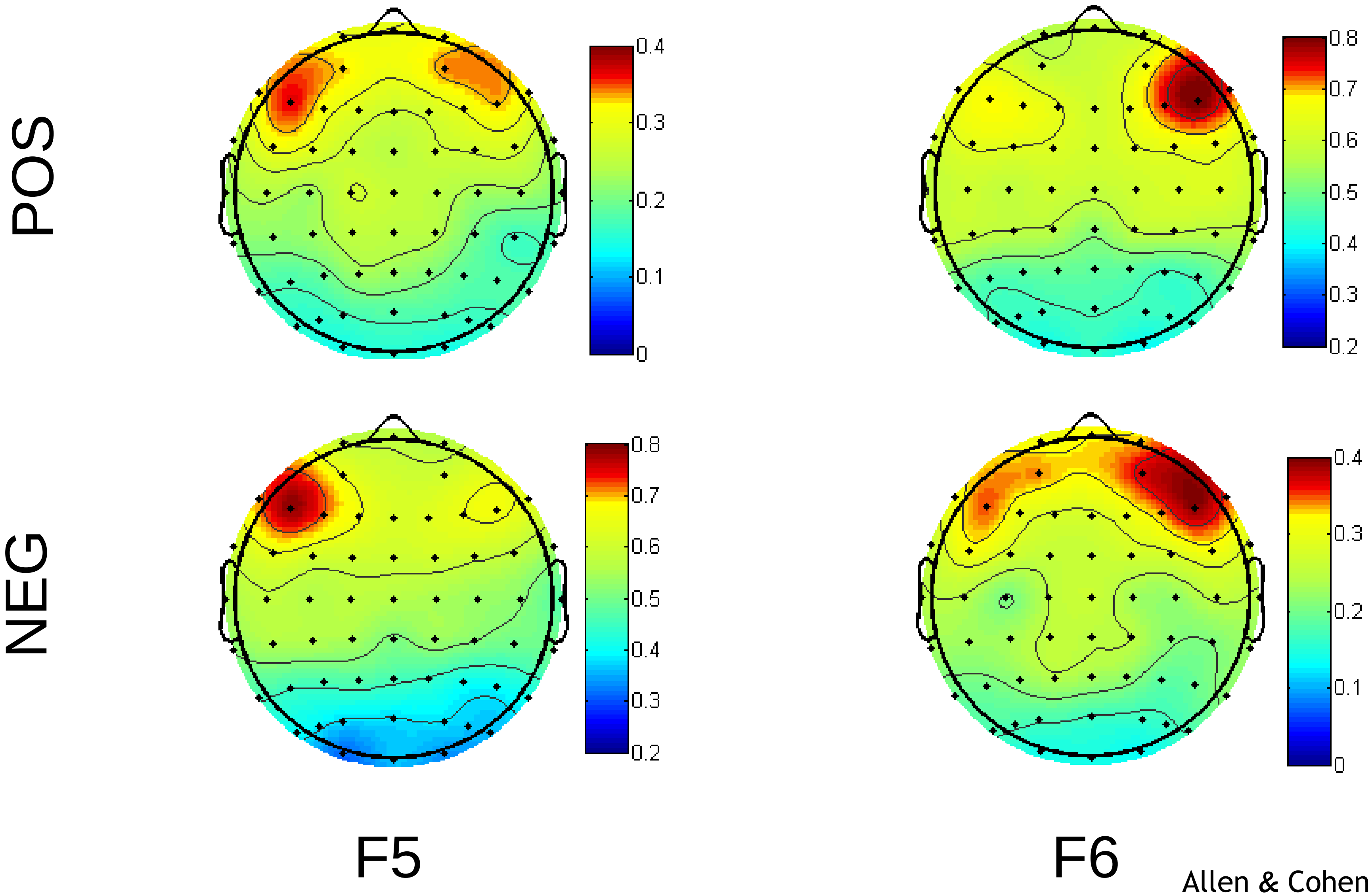
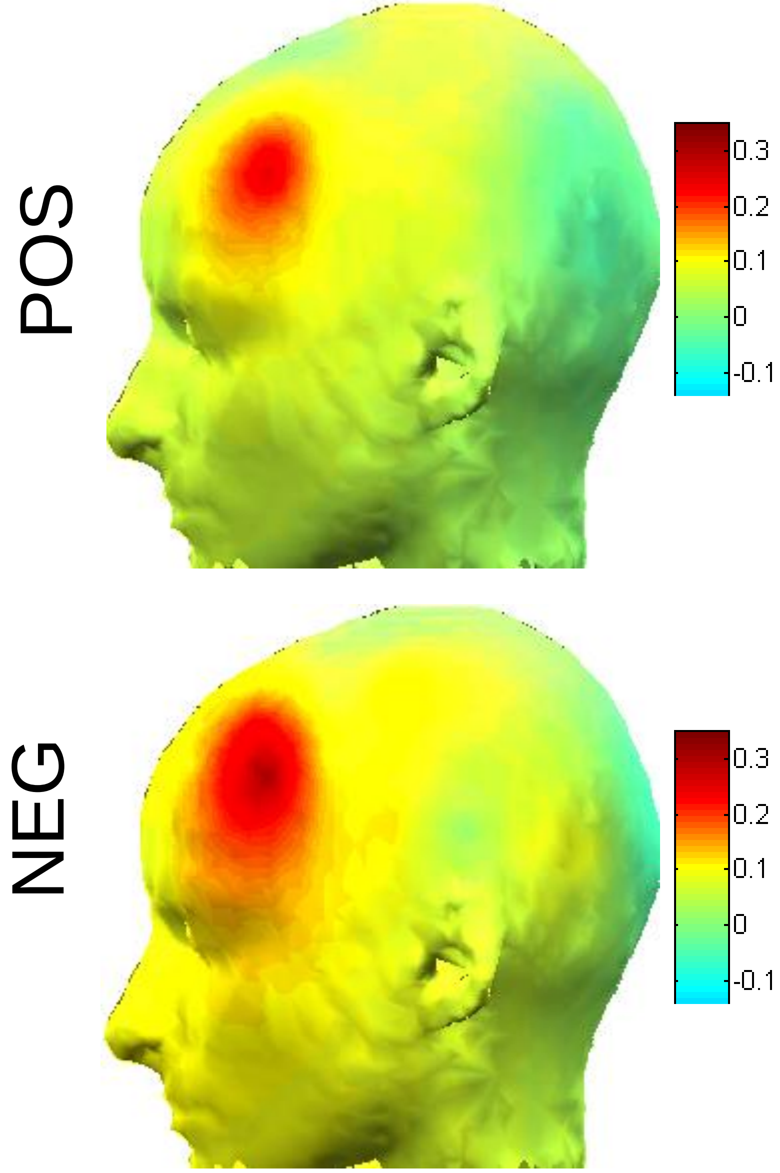
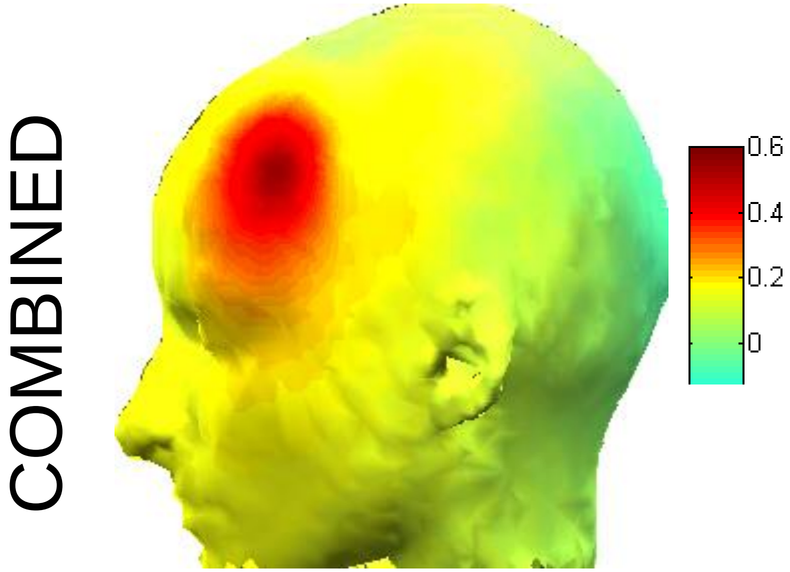
Relationship of Peri-Burst Alpha Power with Conventional FFT-Derived Power



Allen & Cohen, 2010

Relationship of Peri-Burst Alpha Asymmetry at F6-F5 with Conventional FFT-Derived Alpha Asymmetry across the scalp





r^2=.42 !

(1%)

Allen & Cohen, 2010

Three Central Questions

- How do the novel peri-burst metrics of dynamic asymmetry compare to the conventional FFT-based metrics?
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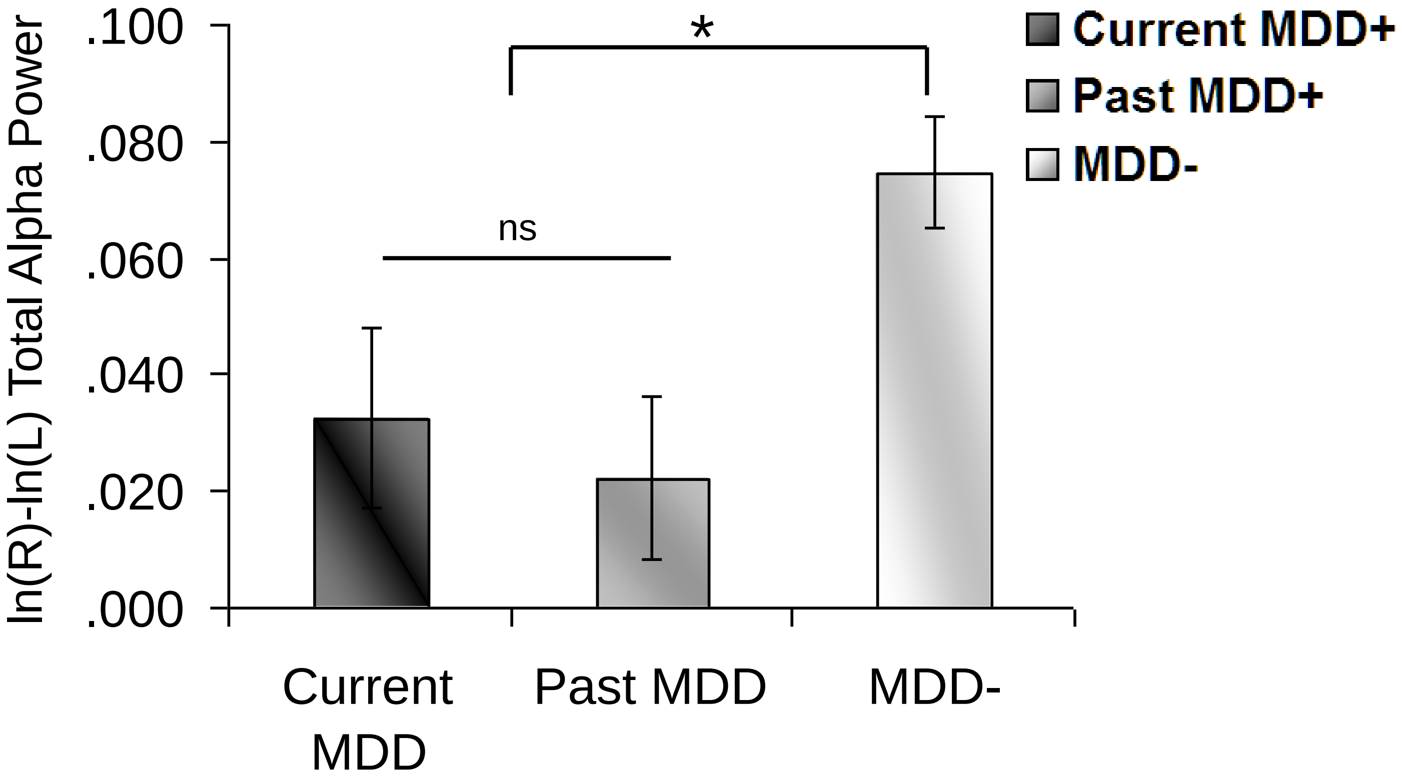
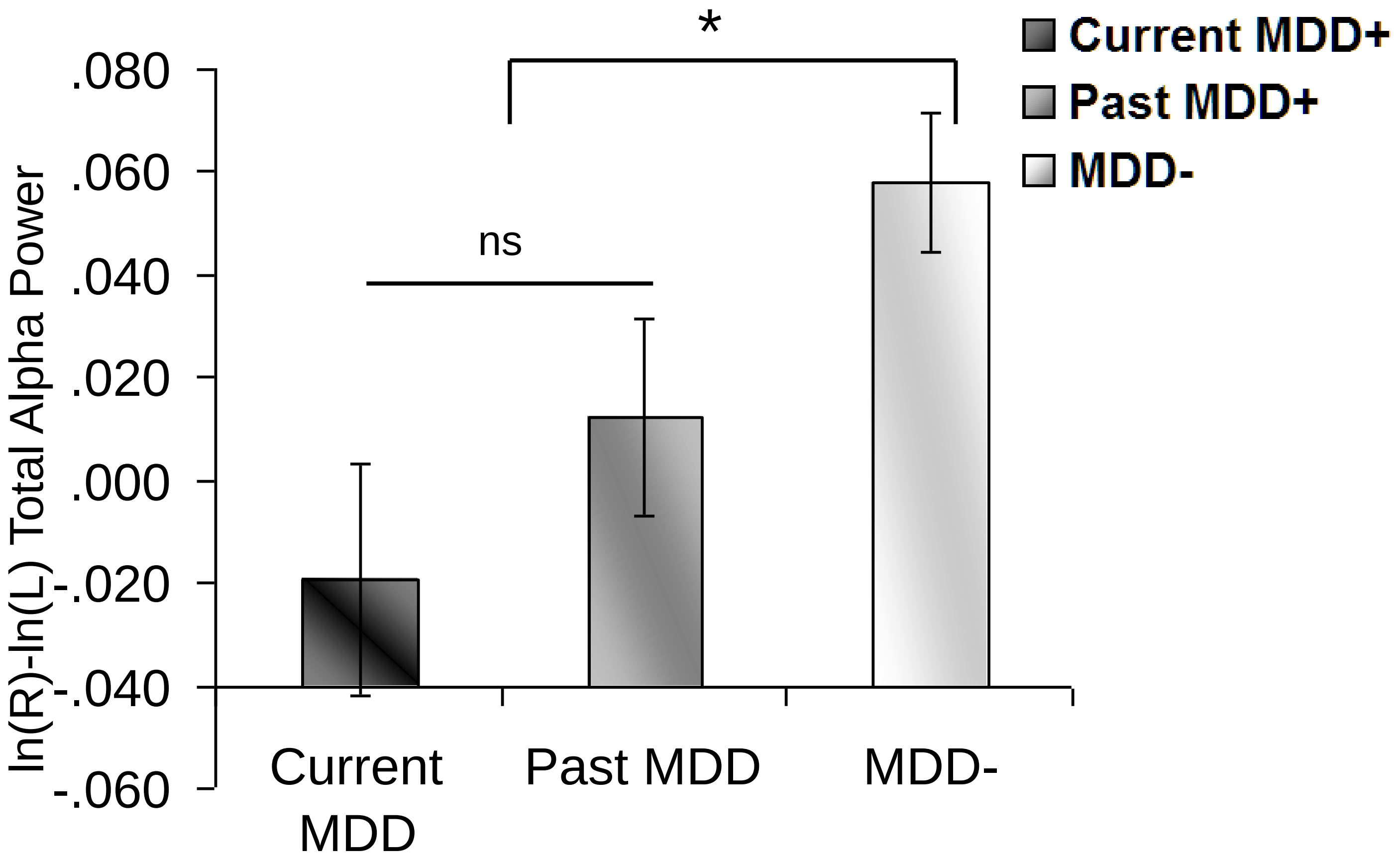
Conventional Frontal EEG Alpha Asymmetry by MDD status



Stewart, Bismark, Towers, Coan, & Allen 2010, *J Abnormal Psychology*

Peri-burst Frontal EEG Alpha Power Asymmetry by MDD status

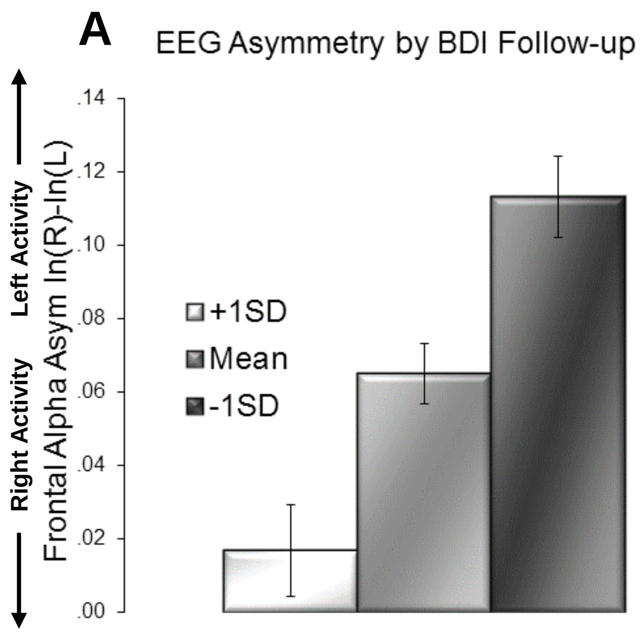


Allen & Cohen, 2010

Table 3. Effect sizes (Cohen's *d*) comparing depressed groups to never depressed controls.

Diagnosis	Conventional	Peri-burst
Lifetime MDD	.43	.38
Past MDD only	.43	.27
Current MDD (with or without Past MDD)	.35	.45

Prospective Pilot Data



Three Central Questions

- How do the novel peri-burst metrics of dynamic asymmetry compare to the conventional FFT-based metrics?
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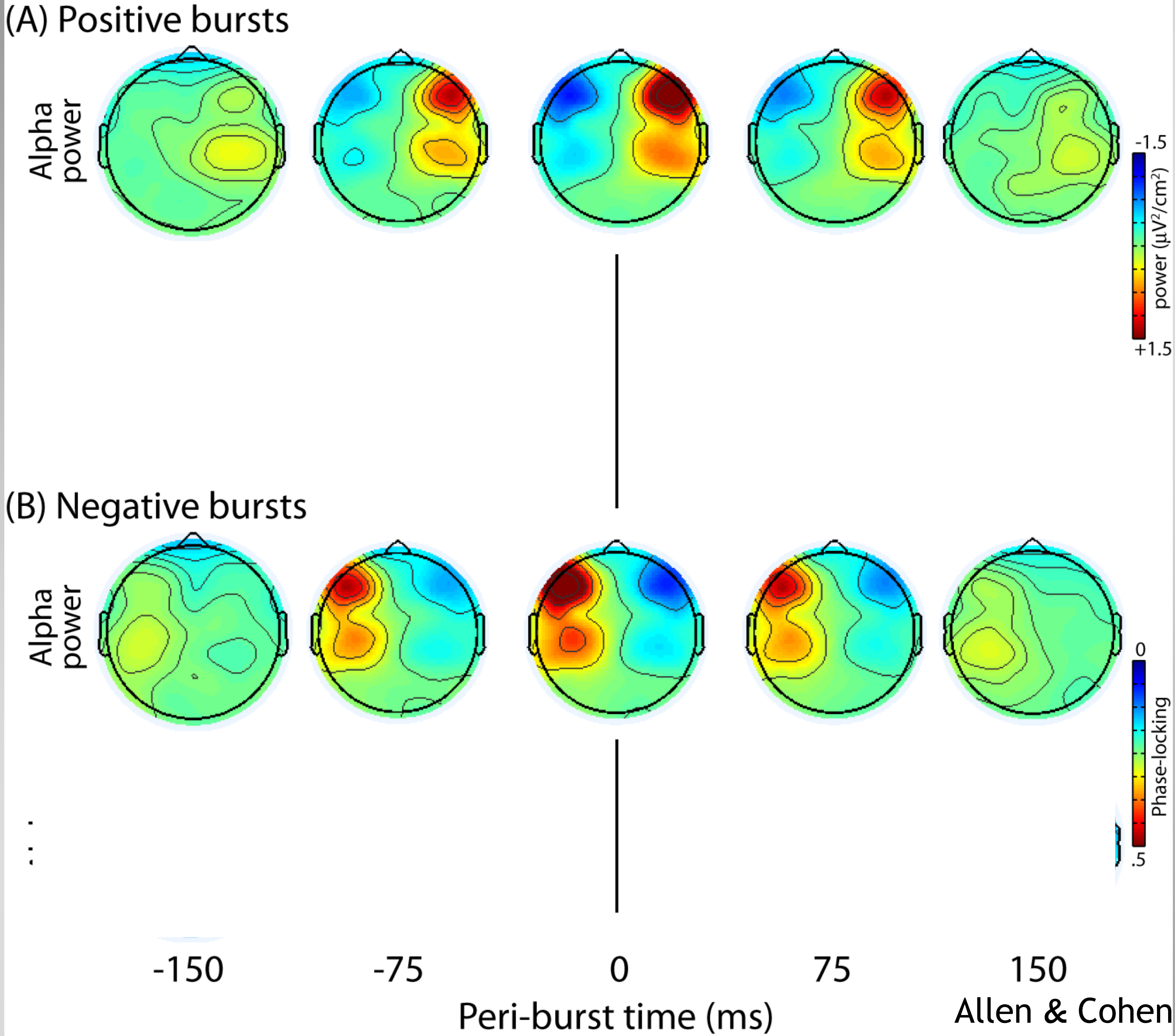


Allen & Cohen, 2010

So?

- Novel peri-burst metrics account for substantial variance in conventional metrics (despite being just 1%)
- Peri-burst metrics differentiate depressed and non-depressed participants, similar to conventional metrics

So?

- Bursts reflect …
  - Transient lateralized alpha suppression that shows a highly consistent phase relationship across bursts
  - Along with concurrent contralateral transient alpha enhancement that is less tightly phase-locked across bursts
- Analogous to ERD/ERS (Pfurtscheller, 1992)?

So?

- The fact that the alpha suppression is particularly tightly phase-locked across bursts raises the possibility that the lateralized alpha suppression may drive or regulate cortical processing
- Alpha has been shown to regulate gamma power (i.e., cross-frequency coupling, Cohen et al., 2009)

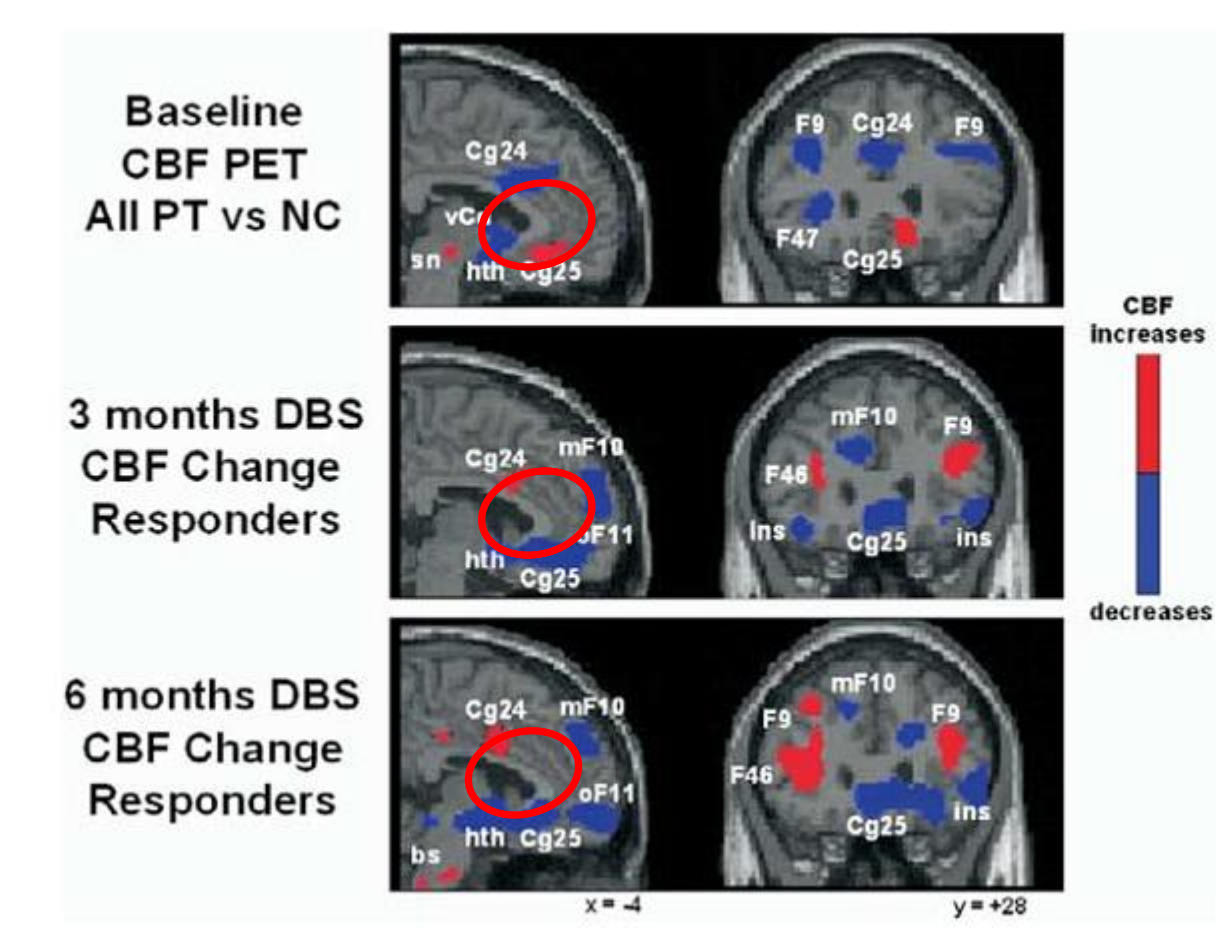
TIME AND SPACE

Multi-modal Imaging

- Tether EEG asymmetry to other measures neural systems known to be involved in MDD
- 23 subjects with simultaneous EEG and fMRI during resting state

Multi-modal Imaging

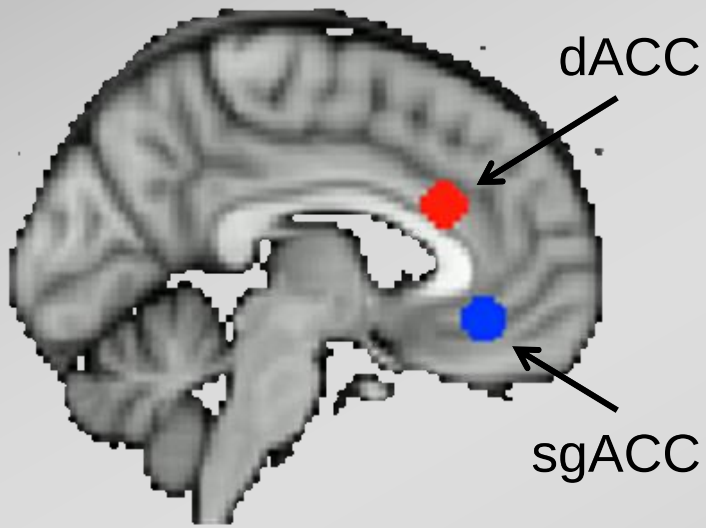
- Tether EEG asymmetry to other measures neural systems known to be involved in MDD

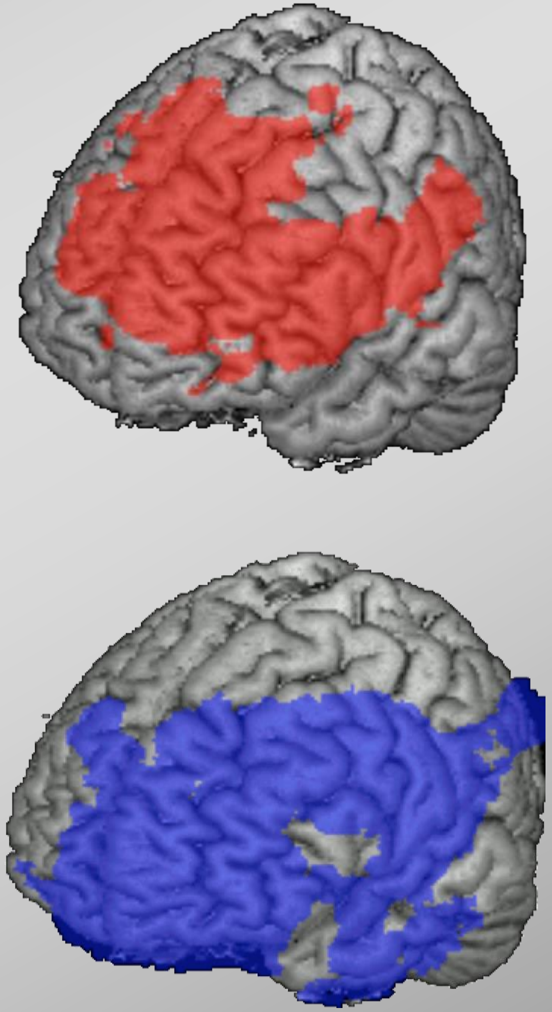


Mayberg et al., 2005

Multi-modal Imaging

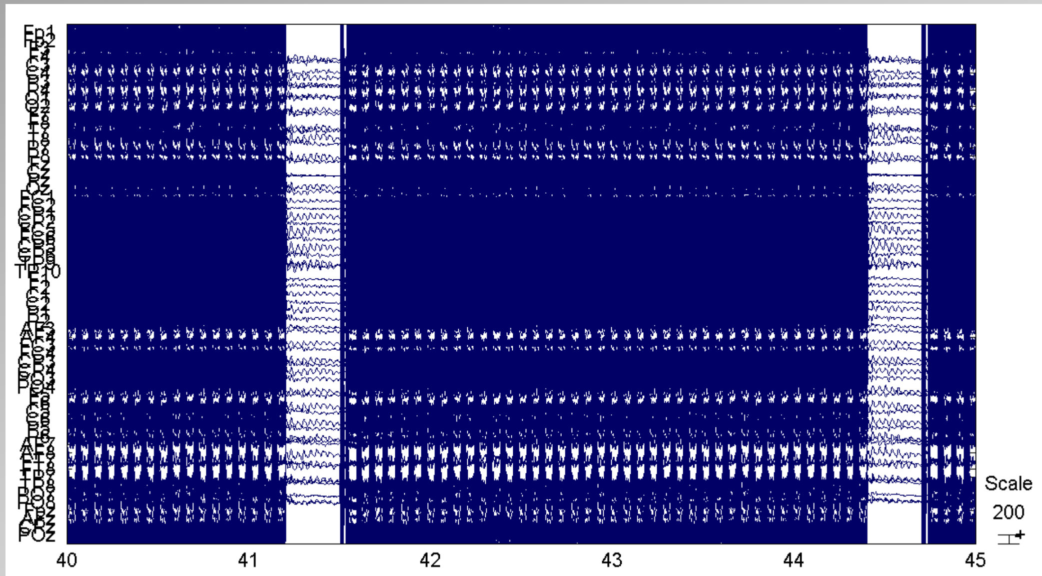
- Create RS-fMRI network with ACC seeds

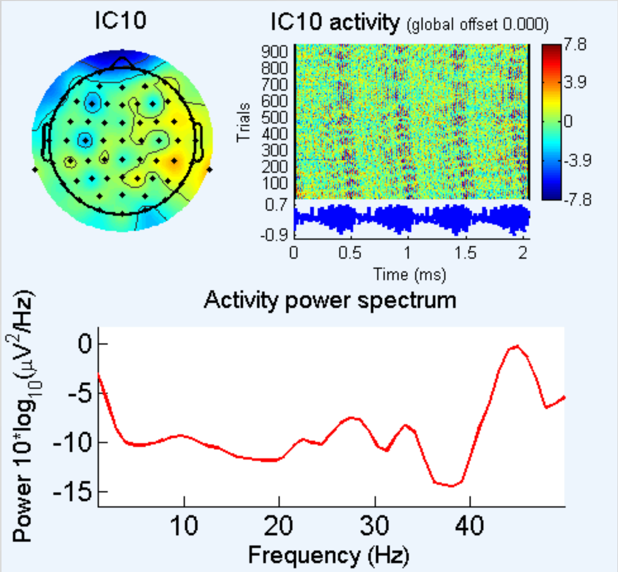


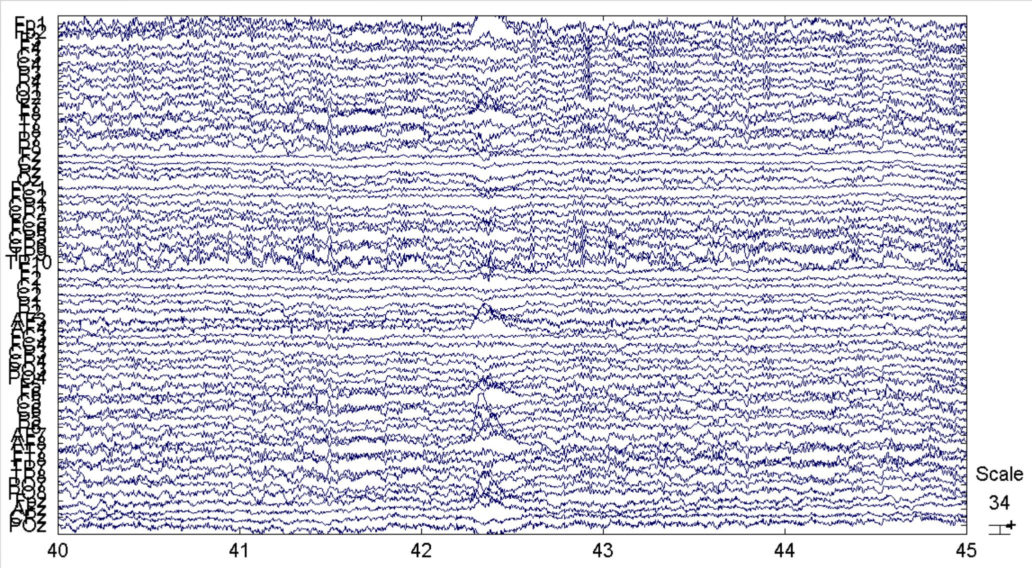


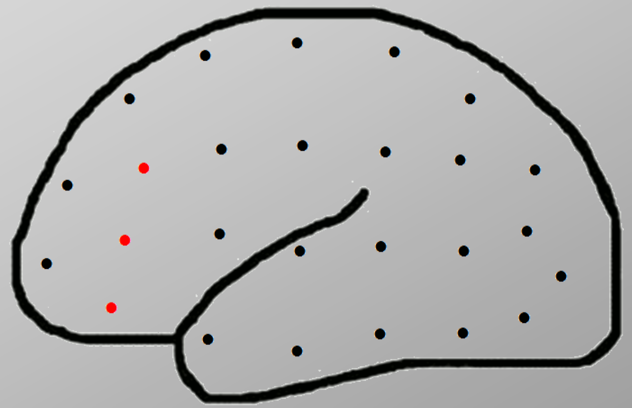
Allen, Hewig, Miltner, Hecht, & Schnyer, *in preparation*

Remove Artifacts from Resting EEG







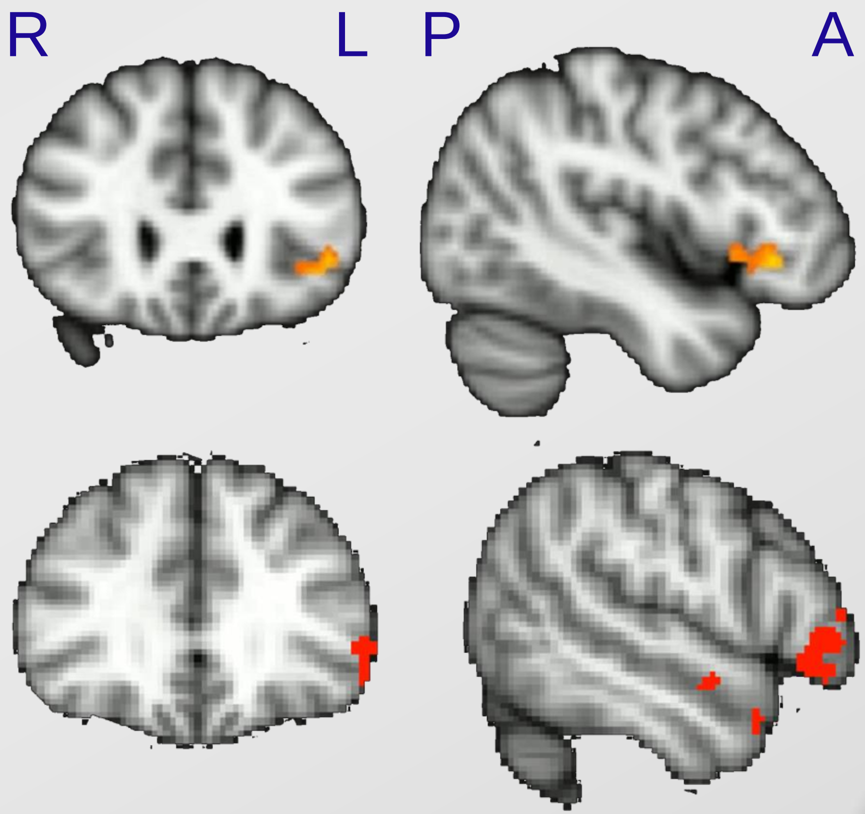


EEG Alpha Asymmetry is Negatively Correlated with IFG Connectivity in Two ACC-seeded Resting State Networks

Spatially-enhanced EEG asymmetry (using CSD transform) at sites F8-F7 is related to resting state connectivity between left inferior frontal gyrus and two ACC-seeded networks.

Dorsal ACC-seeded Network
Center of the depicted cluster is (x,y,z) -46, 28, -4 MNI coordinates.
Largest correlation: r = -0.69

Subgenual ACC-seeded Network
Center of the depicted cluster is (x,y,z) -54, 28, -4 MNI coordinates.
Largest correlation: r = -0.71



Allen, Hewig, Miltner, Hecht, & Schnyer, *in preparation*

EEG-fMRI Synopsis

- Less relative left frontal activity (indexed by EEG) is related to increased connectivity of left IFG to two ACC-seeded RS networks
- Consistent with:
  - Hyper-connectivity in RSfMRI emotion networks in MDD (e.g., Grecius et al., 2007; Sheline et al., 2010)
  - Frontal EEG asymmetry findings of less relative left frontal activity in risk for MDD.
- Alpha power may regulate network connectivity
  - Note: Between vs Within Subjects

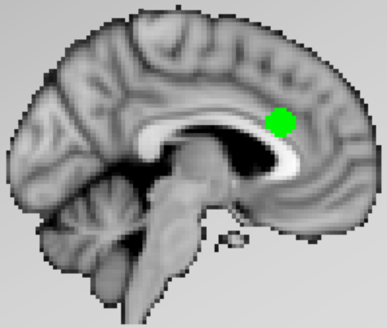
BETWEEN-SUBJECTS' DATA DOES NOT NECESSARILY SUPPORT A WITHIN-SUBJECTS' INTERPRETATION

Within Subjects' Moderation of RSfMRI Connectivity

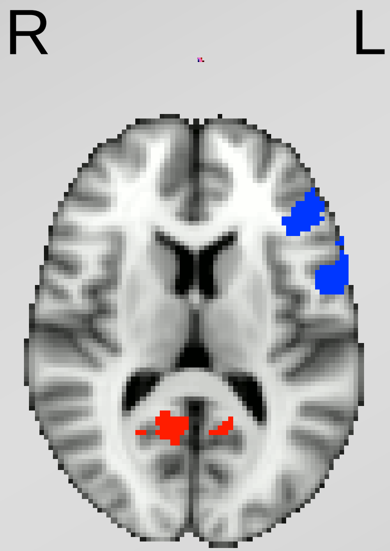
- Calculate F8-F7 alpha asymmetry for each TR
  - EEG leads TR by 4.096 seconds
- Median split into high (left) and low (right)
- Entered as moderator in PPI approach (cf. Friston et al., 1997)
  - Tests whether strength of connectivity to seed region varies as a function of the moderator

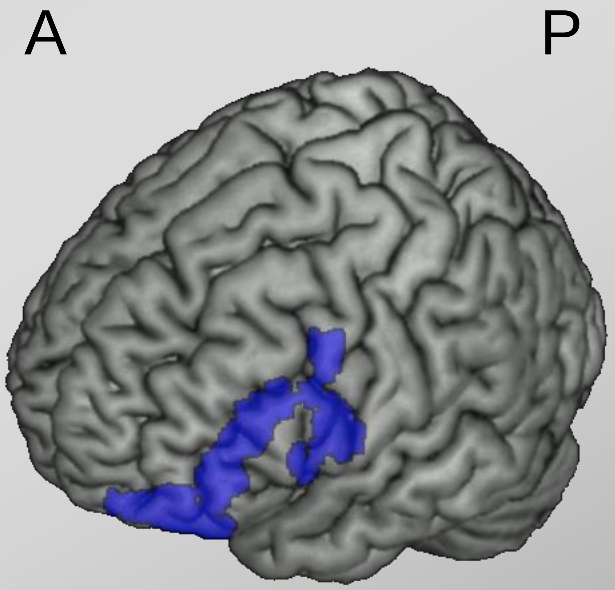
Allen, Hewig, Miltner, Hecht, & Schnyer, *in preparation*

Within Subjects' Moderation of RSfMRI Connectivity



Dorsal ACC Seed



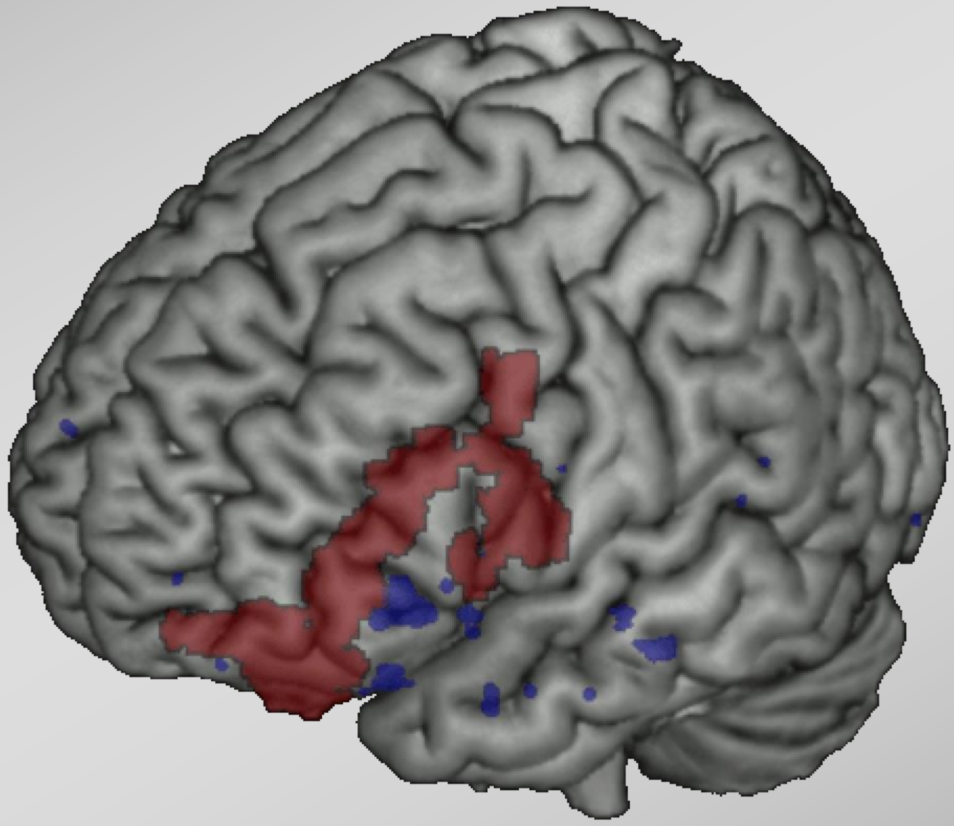


Greater Connectivity with
Less Left Frontal Alpha or
Greater Left Frontal Alpha

Allen, Hewig, Miltner, Hecht, & Schnyer, *in preparation*

Within (red) and Between (blue)

Within-subject effects more extensive

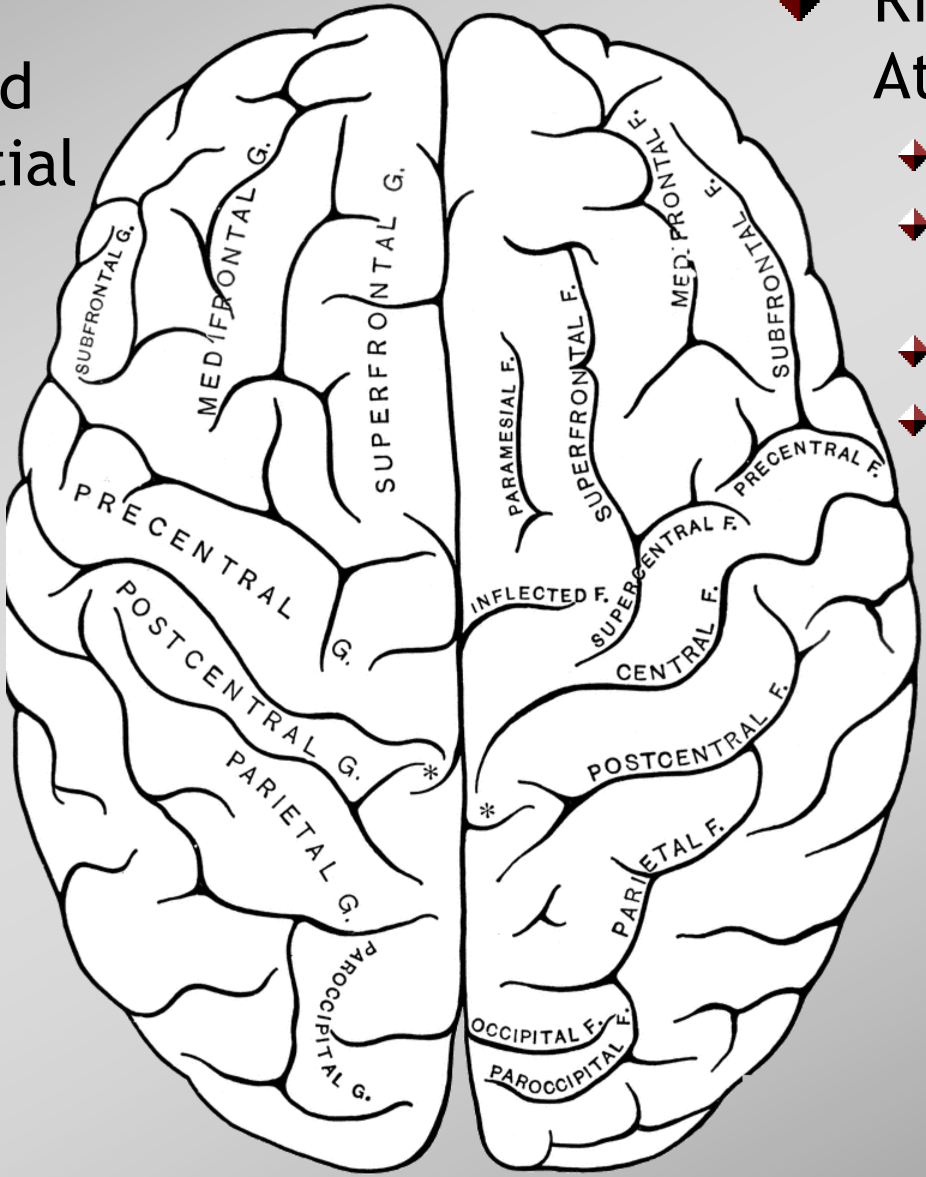


Cognitive Control over Emotion

- IFG has a key role in mediating the success of cognitive control over emotional stimuli

Cognitive Control over Emotion

- Left IFG: Language and self-referential processing



- Right IFG: Attentional control
  - behavioral inhibition
  - suppression of unwanted thoughts
  - attention shifting
  - efforts to reappraise emotional stimuli

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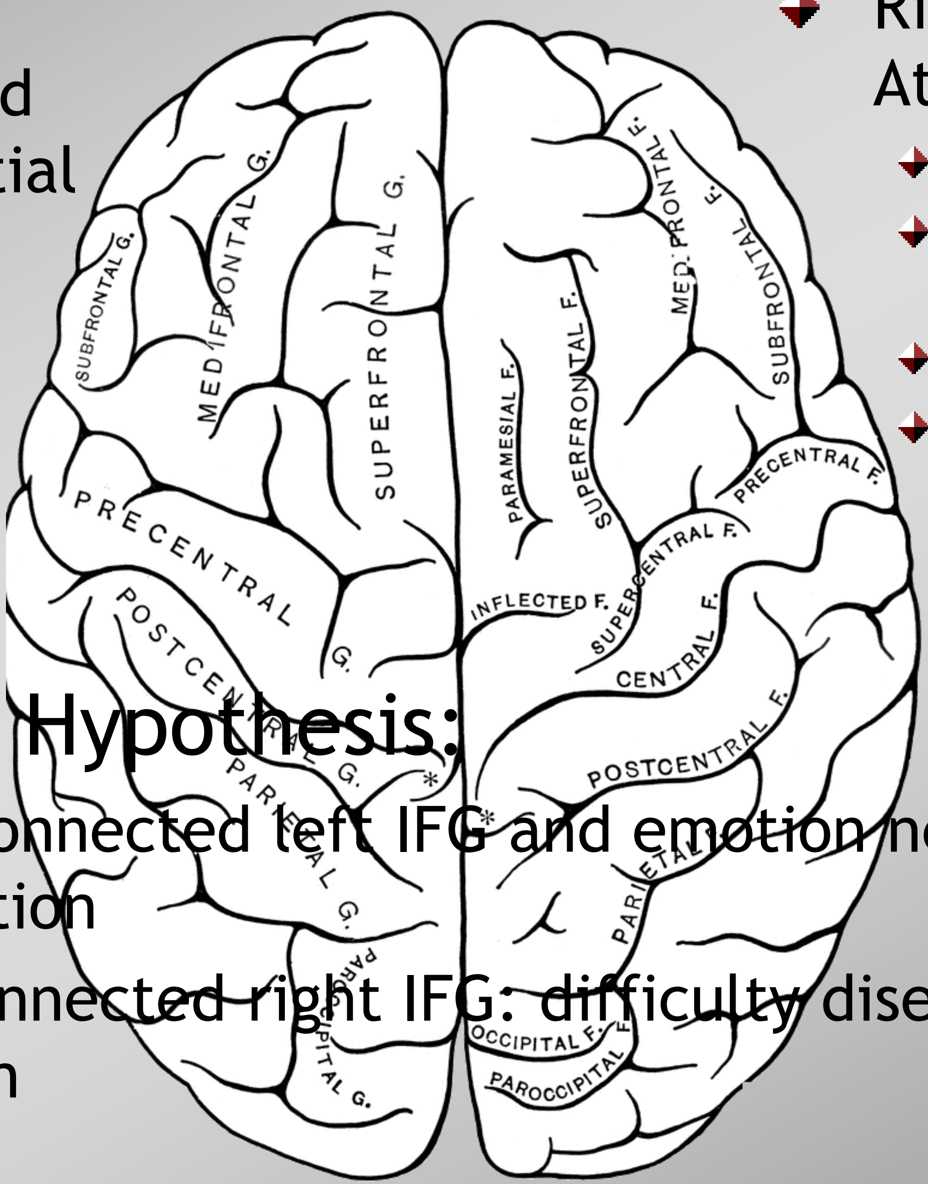

- Working Hypothesis:
  - Hyperconnected left IFG and emotion networks: rumination
  - Hypoconnected right IFG: difficulty disengaging from emotion