**A bit more on Frequency-domain EEG**

...and then...

**The Event-related Brain Potential (Part 1)**

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**Time and Space**

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

- **POS**
- **NEG**
- **COMBINED**

\[
\text{r}^2 = .42! \\
(1\%)
\]

Allen & Cohen, 2010

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**Conventional Frontal EEG Alpha Asymmetry by MDD status**

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

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**Peri-burst Frontal EEG Alpha Power Asymmetry by MDD status**

Allen & Cohen, 2010
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

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

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.

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; Kaiser et al., 2015)
  - 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

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

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

Allen, Hewig, Mittner, Hecht, & Schnyer, in preparation
Dorsal ACC Seed

Within Subjects’ Moderation of RSfMRI Connectivity

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

Working Hypothesis:

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

Synchronization and Desynchronization

- Supposition that alpha blocking meant that the EEG had become desynchronized
  - Yet the activity is still highly synchronized -- not at 8-13 Hz
  - May involve fewer neuronal ensembles in synchrony
If Alpha Desynchs, what Synchs?

Ahern et al., (1994) Electroencephalography and clinical Neurophysiology

**Event-related Synchronization and Desynchronization**

- Pfurtscheller (1992) -- Two types of ERS
- Secondary (follows ERD)

**Alpha Power time course over left central region during voluntary movements with right and left thumb**

**Alpha Power time course over parietal and occipital leads during right finger movement. ERD is seen over central electrodes, with earlier onset over hemisphere contralateral to movement.**

**Alpha power time course during reading (upper) and voluntary finger movements (lower). Primary ERS is seen over electrodes overlying cortical areas not involved in the task.**

**Primary ERS seen over parietal and occipital leads during right finger movement. ERD is seen over central electrodes, with earlier onset over hemisphere contralateral to movement.**
40 Hz Activity

- First reports of important 40 Hz activity
- Sheer & Grandstaff (1969) review
  - pronounced rhythmic electrical bursting
- Daniel Sheer’s subsequent work until his death renewed interest in “40 Hz” phenomena

Sheer work with Cats

- Learning paradigm
- Cat must learn
  - press to $S_\text{D}$ (7cps light flicker)
  - not $S-$ (3 cps light flicker)
- the hypothesis is that the synchronized 40 Hz activity represents the focused activation of specific cortical areas necessary for performance of a task

Human Studies

- Hypothesis is that 40 Hz activity correlates with the behavioral state of focused arousal (Sheer, 1976) or cortical activation
  - a "circumscribed state of cortical excitability" (Sheer, 1975)
- Bird et al (1978)
  - biofeedback paradigm
  - increased 40 Hz activity is associated with high arousal and mental concentration
- Ford et al, (1980)
  - subjects once trained to voluntarily suppress 40 Hz EEG are unable to maintain that suppression while simultaneously solving problems
  - concluded that problem solving and absence of 40 Hz are incompatible

Lateralized Task Effects

- right-handed students
- analogies task
- spatial Task
- Results transformed into laterality ratios:
  - $(L-R)/(L+R)$ 40 Hz
  - higher # => greater LH activity (P3-O1-T5 triangle vs P4-02-T6 triangle);
- Results
  - greatest variability during baseline
  - smallest variability and greatest LH activation during verbal
  - no laterality effects in the 40Hz EMG bands
Laterality of 40 Hz

Controlling for EMG contributions

- Spydell & Sheer (1982)
  - used similar tasks and found similar results
  - using conservative controls for muscle artifact

Individual Differences

- Spydell & Sheer (1983), Alzheimers
  - controls showed task related changes in EEG with appropriate lateralization
  - Alz did not

- Schnyer & Allen (1995)
  - Most highly hypnotizable subjects showed enhanced 40 hz activity

So this is exciting, why didn’t this work take off immediately?

- The EMG concern
  - The concern is likely over-rated (recall Table 3)

Sheer died

But not all is lost, as there is renewed interest…
recorded single unit activity and local field potentials in auditory cortex of two neurosurgical patients and compared them with the fMRI signals of 11 healthy subjects during presentation of an identical movie segment. The predicted fMRI signals derived from single units and the measured fMRI signals from auditory cortex showed a highly significant correlation.

Singer (1993)

- Revitalized interest in the field

The Binding Problem

- Potentially infinite number of things and ideas that we may attempt to represent within the CNS
- Cells code for limited sets of features
- These must somehow be integrated
- -- the so-called binding problem
- If there exists a cell for a unique contribution of attributes, then convergent information from many cells could converge on such a cell
- But there are a finite # of cells and interconnections
- And even the billions and billions of cells we have cannot conceivably handle the diversity of representations

The Functional Perspective

-- as yet merely a theory

- There is no site of integration
- Integration is achieved through simultaneous activation of an assembly of neurons distributed across a wide variety of cortical areas
- Neurons in such assemblies must be able to adaptively identify with other neurons within the assembly while remaining distinct from other neurons in other assemblies
- This association with other neurons is through a temporal code of firing (Synchronicity)
- This even allows for the possibility that a single neuron could be part of two active assemblies (via a multitasking procedure)

Implications

- Also allows for the possibility that there exists no direct neuronal connection between neurons within an assembly
  - merely the fact that they are simultaneously activated that makes the unified experience of the object possible
- Yet what can synchronize these oscillations?

Implications – Alpha as a synchronization mechanism

Jensen et al., TICS, 2012
Functional Role of Gamma Synchronization

- Feedforward coincidence detection
  - To summate effectively, signals must arrive at postsynaptic neuron from multiple sources within msec of each other (else decay)
  - Gamma-band synchronization can lead to temporal focusing of inputs from multiple and distributed presynaptic neurons
- Rhythmic Input Gain Modulation
  - Excitatory input is most effective when it arrives out of phase with inhibitory input and vice versa
  - Allows for precision and efficiency of signal transmission (or inhibition)

Fries, 2009

Implications

- This view is a dynamic view
- depends on experience
- can change with experience
- Synchronously activated units more likely to become enhanced and part of an assembly that will subsequently become synchronously activated
- Singer concludes:
  - Points out the problem of looking for synchronous activation on the micro level, suggesting that a return to the EEG literature looking for task-dependent synchronization in the gamma (aka 40 Hz) band!
  - “Forty-Hz” activity is alive and well
  - “Forty" = 40 ± some range
  - Gamma! (Stay tuned during advanced topics)

Overview

Event-related potentials are patterned voltage changes embedded in the ongoing EEG that reflect a process in response to a particular event: e.g., a visual or auditory stimulus, a response, an internal event
Time-locked activity and extraction by averaging

**The Classic View:**

Time-locked activity and extraction by signal averaging

- Ongoing activity reflects "noise"
- Activity that reflects processing of a given stimulus "signal"
- The signal-related activity can be extracted because it is **time-locked** to the presentation of the stimulus
- Signal Averaging is most common method of extracting the signal
  - Sample EEG for ~1 second after each stimulus presentation & average together across like stimuli
  - Time-locked signal emerges; noise averages to zero
  - Signal to noise ratio increases as a function of the square root of the number of trials in the average

**What does the ERP reflect?**

- May reflect sensory, motor, **and/or** cognitive events in the brain
- Reflect the synchronous and phase-locked activities of large neuronal populations engaged in information processing

**Component is a "bump" or "trough"**

**Nomenclature & Quantifying**

- Most commonly label peaks and troughs by polarity (P or N) and latency at active recording site
- Quantifying
  - Amplitude
  - Latency
  - Area
  - “String” measure
  - Fancy stuff to be discussed in “advanced” topics
**Component is a "bump" or "trough"**

![Image of an ERP waveform](image-url)

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**Early Components**

- Waves I-VI represent evoked activity in auditory pathways and nuclei of the brainstem
- Early components <60-100 msec
- Occur in **obligatory** fashion
- Are called **Exogenous** = determined "outside" organism
- Even subtle deviations in appearance may be indicative of pathology

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**Later ERP components**

- Highly sensitive to changes in
  - State of organism
  - Meaning of stimulus (NOT physical characteristics)
  - Information processing demands of task
- Therefore termed **Endogenous** = determined "within" organism

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**Defining Components:** 

*aka* how do I know one when I see one?

- By positive and negative peaks at various latencies and scalp locations
- By functional associations, covarying across subjects, conditions, or scalp locations in response to experimental manipulations
- By neuronal structures that plausibly give rise to them

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**Evoked Vs Emitted ERP’s**

- Evoked are most commonly studied: occur in response to a physical stimulus
- Emitted potentials occur in absence of a physical stimulus (e.g., omission of item in sequence)
- Evoked can have both exogenous and endogenous components; emitted usually have only endogenous

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After Fabiani, Gratton, Federmeier, 2007
Comparison to other "windows on the brain"

- Very precise temporal resolution

> At the surface, activity of many functional synaptic units recorded

> ERP's generated only by groups of cells that are synchronously activated in a geometrically organized manner
Comparison to other "windows on the brain"

- Very precise temporal resolution
- Spatial localization is more difficult
  - At the surface, activity of many functional synaptic units recorded
  - ERP's generated only by groups of cells that are synchronously activated in a geometrically organized manner
  - Synchronous activation may occur in one or more than one location
  - Monopolar recording technique most often used
  - Yet localization is not impossible in conjunction with other techniques

Caveat Emptor

- DO NOT interpret scalp distribution of ERP's as reflect cortical specialization
- Also, DO NOT interpret area of maximum amplitude to suggest that generator lies underneath

Correlate Vs substrate (AGAIN)

- Late ERP components should not be taken to indicate the existence of a neurological substrate of cognitive processing
- Rather should be considered a correlate
- Constructs in search of validation; Process of validation:
  - Determine antecedent conditions under which the ERP component appears and also magnitude and latency of ERP component
  - Develop hypotheses concerning functional significance of the "subroutine" underlying the ERP component
  - Predict consequences of subroutine—validate empirically

Paradigms and acquisition

- Precise temporal control over stimulus presentation necessary
- Requires discrete stimuli or responses
- Individual stimuli are presented numerous times; ERP's generally do not habituate, unlike peripheral measures
- Concurrent with each stimulus, a signal/pulse must be sent to the A/D converter to indicate time of stimulus onset
- Sampling epochs (legacy!) vs continuously
  - Considerations for sampling epochs
    - Pre-onset samples (to provide a baseline for comparison)
    - Epoch length
- Epochs for like stimuli averaged together to create ERP for that set of stimuli

Basic Signal Processing
Assumptions of Averaging methods

- Signal and noise (in each epoch) sum linearly together to produce the recorded waveform for each epoch (not some peculiar interaction)
- The evoked signal waveshape attributable solely to the stimulus is the same for each presentation
- The noise contributions can be considered to constitute statistically independent samples of a random process

Filtering and its influence on the ERP

- Despite many trials and averaging, some noise may remain in the averaged waveform
- If you are only interested in later & slower components, then a low-pass filter may be of interest
Applications of Early Components

- Neurological evaluation of sensory function; e.g. evaluation of hearing in infants
- Tones of various dB intensities presented and V wave in auditory brainstem ERP examined
- Figure 10, 4000 individual trials per average

Prediction of recovery from coma

Inter-Hemispheric Transfer Time (IHTT)

- Hypothesized that interhemispheric transfer of information may be abnormal in various disorders (e.g., dyslexia)
- Reaction Time measures contain too much variability not related to Transfer Time
- ERP early components appear promising as a measure of time required to transfer information between hemispheres

IHTT Study (Saron)

- Checkerboards subtending < 1 degree of visual angle presented 2.9 degrees from center
- ERPs recorded at O1 and O2
- Problem of lateralization and Paradoxical results possible: parafoveal regions on banks of calcarine fissure
- P100 wave latency examined; earlier latency in occiput contralateral to presentation
- Measured by peak picking procedure
- Also by cross-lagged correlation technique
- Both methods suggest ~15 millisecond IHTT; found to be in expected direction predicted by anatomy for over 90% of subjects
- Reaction time data from same task showed no reliable differences
**P1, N1, and Attention**

From Luck et al., *TICS*, 2000

**More than Spatial Directed Attention**

Taylor, *Clinical Neurophys* 2002

"These combined PET/ERP data therefore provide strong evidence that sustained visual spatial attention results in a preset, top-down biasing of the early sensory input channels in a retinotopically organized way."

Woldorff et al., *Human Brain Mapping*, 1997

**Prelude to Advance Topic: Source Localization**

Taylor, *Clinical Neurophys* 2002

**P1 and Sleep**

Note P1 disappears in Stage 2 sleep, but reemerges in REM sleep
Construct Validity of P300 (P3, P3b)

- First observed by Sutton, Braren, Zubin, & John (1965)
- P300 Amplitude; Johnson's model is
  \[ P300 \text{ Amplitude} = \sqrt{P \times (1/P + M)} \]
  where
  - \( P \) = probability of occurrence,
  - \( M \) = Stimulus meaning, &
  - \( T \) = amount of information transmitted

Aspects of the Model

- Rarity
  - The P300 is observed in variants of the "oddball paradigm"
  - The rare stimulus almost invariably elicits a P300: largest at parietal, then central, and then frontal sites
- Subjective probability
- Stimulus meaning
  - Actually composed of three dimensions
    - task complexity
    - stimulus complexity
- Information Transmission (proportion 0 to 1; example)

Information Transmission

Fig. 2. Grand averaged visual ERP at Pz electrode for the 3 array sizes, showing the shorter latencies, larger P5s for array size 17, but longer latency P3 (dark arrows) than for array sizes 5 and 9 (gray arrows). These are averaged across color, orientation, and conjunction conditions, as this ERP effect was seen regardless of whether it was a single feature or conjunction trial.

Taylor
Clinical Neurophys
2002
P3 Latency

- An index of processing time, independent of response requirements
- RT measures confounds the two
- McCarthy & Donchin (1981) experiment:
  - The words "RIGHT" or "LEFT" embedded in a matrix of letters of X's
  - Compatible condition: respond with hand indicated in matrix; Incompatible condition: respond with opposite hand (e.g., LEFT signals right hand response)
- Results:
  - P300 latency delayed when discriminability more difficult
  - Response compatibility had no effect on P300 latency
  - Note amplitude reduction as function of noise—information transmission

Construct Validity?

- What, then, does the P300 mean in very general terms?
- A stimulus (or class of stimuli) is "important"; denotes information that is necessary or useful to the task
- Stimulus is meaningful, important, noticeable
- Evaluated within context of working memory? (cf. Donchin & Coles, 1988; Verlager 1988; Polich, 2007; Verlager, 2008)
- The P3a (Squires, Squires, and Hillyard, 1975): P3-like component with a frontal maximum and occurs to improbable stimuli in the "to-be-ignored" class of stimuli; a novelty response.

How Many P3s?

- The Classic P3/P300
- Parietal Central Maximum
- Largest when stimuli rare and task-relevant
- The P3a (Squires et al., 1975) or Novelty P3 (Courchesne et al., 1975)
- More anterior scalp distribution
- Slightly earlier latency
- Responsive to rare, unexpected, unattended stimuli
Simons et al., 2001

- Squires Task was tones (two tones)
- Courchesne task was digitized speech (“me” “you” and collection of naturally occurring sounds)
- In all cases subjects merely counted Tones

**P3a – Can you see it?**

- Some inconsistencies in finding P3a following the initial Squires, Squires and Hilyard 1975 report
- Comerchero & Polich (1998) may have resolved the enigma
  - P3a highly dependent on foreground discrimination

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**Table 1**

<table>
<thead>
<tr>
<th>Material</th>
<th>Conditions</th>
<th>Task</th>
<th>Low P</th>
<th>High P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target O1O2</td>
<td>Low</td>
<td>200 Rz</td>
<td>200 Rz</td>
<td>0.20 cm²</td>
</tr>
<tr>
<td>Standard 01O2</td>
<td>Low</td>
<td>100 Rz</td>
<td>100 Rz</td>
<td>0.15 cm²</td>
</tr>
<tr>
<td>Target O1O2</td>
<td>High</td>
<td>70 dB</td>
<td>90 dB</td>
<td>0.20 cm²</td>
</tr>
</tbody>
</table>

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**Note:** Nontarget peak amplitude was earlier and larger at the frontal electrodes than those from the target stimuli, but especially when foreground discrimination is difficult.

**Synopsis**

“...the manipulation of target-standard stimulus discriminability produced a stimulus environment in which the infrequently occurring nontarget engaged focal attention in a manner similar to that observed previously for ‘novel’ stimuli.”

“However, all stimuli in the present study were employed because of their ‘typical’ characteristics, so that the results imply that an anterior P3a component can be produced without using ‘novel’ stimuli per se.”

“If stimulus context is defined primarily by a difficult target-standard discrimination, attentional redirection to the nontarget would occur because of the frontal lobe activation that generates P3a.”

Comerchero & Polich 1998, p. 47