Introduction to EEG and Event Related Potentials

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Outline of Talk

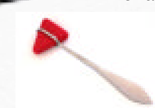
- Basic definitions and neurophysiology
- Principles of EEG recording
- Types of EEG studies
  - Clinical EEG
  - qEEG/spectral analysis
  - Event related potentials
- Designing and implementing an ERP study

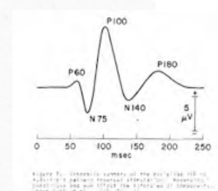
Key points

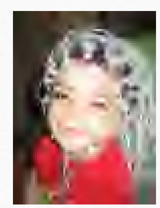
- EEG and ERP methodology promising in developmental populations
- Excellent temporal resolution
- Spatial resolution limited, requires inferences
- While post-acquisition data processing can be manipulated, rigorous study design critical in acquiring high quality data

My path to EEG

Child Neurology Residency (2007)
Behavioral Child Neurology Fellowship (2008)







Post-doctoral training in developmental cognitive neuroscience with Dr. Charles Nelson (CHB) (2009)

UCLA CART
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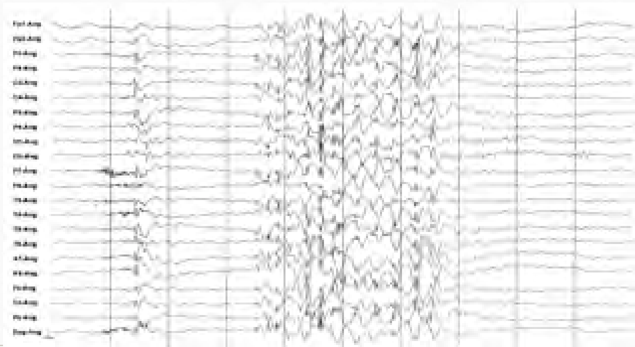
Moved to UCLA to establish an EEG program in the Center for Autism Research and Treatment (Jan 2010)

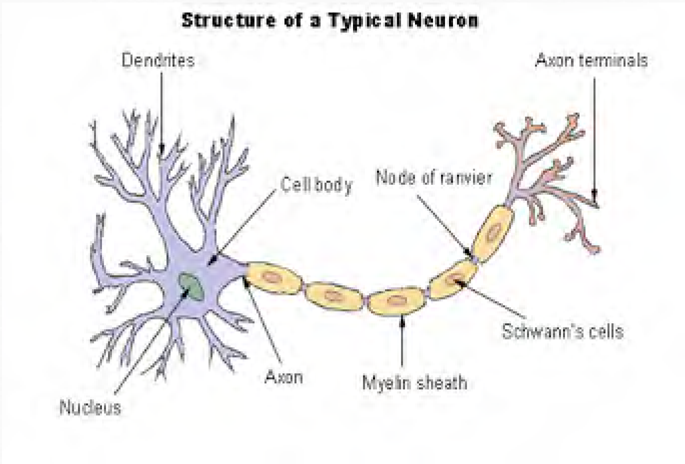
Electroencephalography

- The recording of the brain's electrical activity produced by firing of neurons

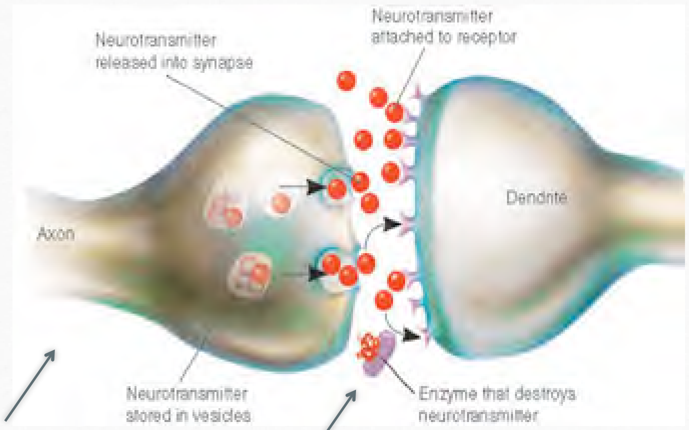


Electroencephalography

- Term *electroenkephalogram* first coined by Hans Berger in 1924
- First to formally study human subjects
- First to describe different brain rhythms such as alpha and to associate them to normal vs. abnormal function



Neuronal transmission

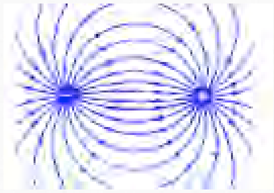


Action potential

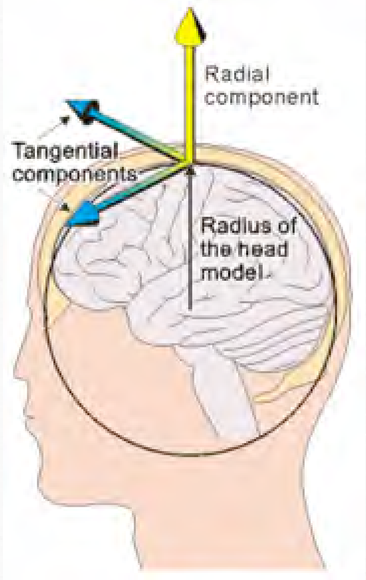
Post-synaptic potentials

Generation of EEG signal

- Electrical potentials generated by a single neuron are too small to be detected by EEG
- Duration (<10 msec) and orientation of action potential difficult to detect at scalp
- Post-synaptic potentials 100 msec and are able to summate
- EEG recording is the summation of postsynaptic potentials of pyramidal cells in cerebral cortex and hippocampus
- Parallel networks are configured so that an electrical field summates to create a **dipolar field**



- Intracellular ions move through and out the neuron, creating a source of the opposite charge (dipole)
- EEG detects the charge of the end of the dipole that is closer to scalp
- Direction and orientation of the dipole is critical for recording
- Radial vs. Tangential dipoles produce different recordings



Volume Conduction

- Dipole conducted through a medium until it reaches the surface
- EEG signal spreads out laterally when it reaches high resistance of skull
- Hence scalp distribution can be distorted and does not accurately reflect exact location of neural sources

Source localization

- Constrained by dipole orientations and volume conduction
- **Inverse problem**: determination of positions and orientations of dipoles (cortical and subcortical) on basis of observed scalp voltage distribution
- For any scalp distribution there are infinite number of possible sets of dipoles that could produce the distribution

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- **Principles of EEG recording**
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Key steps in EEG recording

(1) Detection of scalp EEG

(2) Amplification of signal

(3) Filtration

(4) Digitization of signal (from analog)

Goal is to maximize Signal to Noise Ratio

Sources of Noise

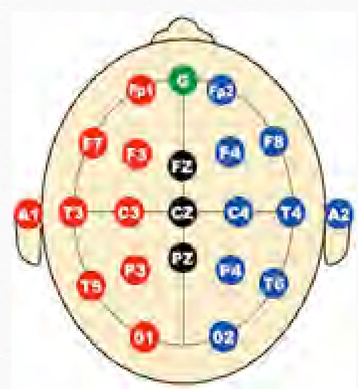
Subject dependent

- Scalp impedance
- Physical movement of electrodes
- Chewing
- Blinking

Environmental

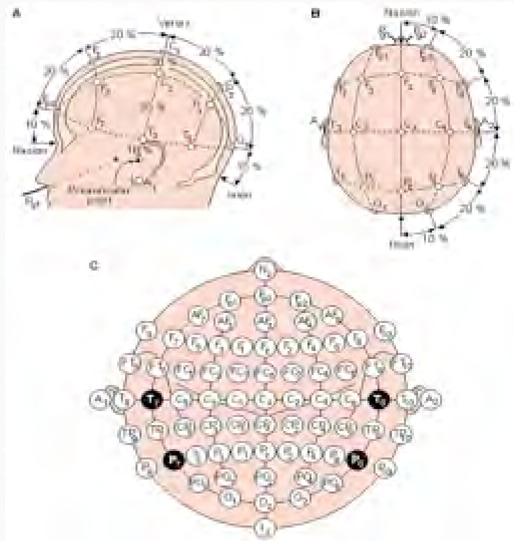
- AC line current
- Video monitors
- AC lights
- Pagers
- Cell phones etc etc

Step 1: Electrodes



- Small metal plates (Sn, Ag)
- Conductive gel
- Recordings are based on differences in voltage between the electrode of interest and a reference
- 10-20 system (Jasper, 1958)
- Montages:
  - Average reference
  - Bipolar
  - Referential

10-20 system



High-density electrode nets

- 64, 128, 256 leads
- Fast application
- Electrodes inside soft sponge
- High impedance
- Bridging between electrodes

Step 1: Minimizing Noise

- Sources of impedance:
  - Hair
  - Hair products
  - Sweat and other scalp debris
- To minimize impedance:
  - Scalp abrasion
  - Application of conductive material such as salt

Step 1: Minimizing noise

- Acoustically and electrically shielded
- Faraday cage
- Minimize environmental noise

Step 2: Amplification

- Voltage fluctuations in scalp are tiny (1/100,000th of a volt)
- EEG must be amplified by factor of 10-50,000
- **Gain**: Amplification factor
- **Calibration**: Ensures that the gain in each electrode is the same (pass voltage of known size through system and measure output, then generate scaling factor for each channel)

Step 3: Filtration

Filter settings based on the data of interest

High pass: attenuates low frequencies (0.01-0.1 hz)

Low pass: attenuates high frequencies (30-100 hz)

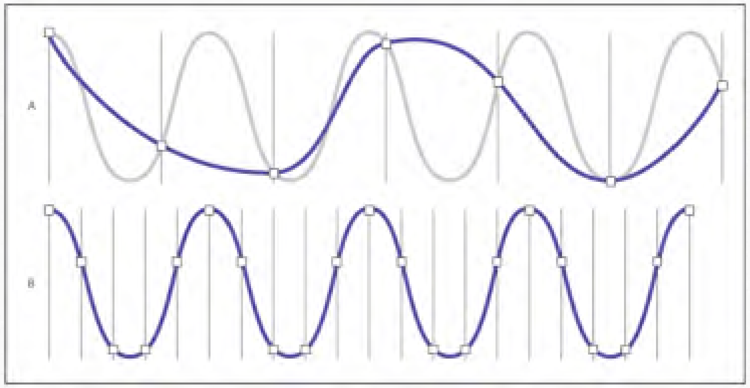
Bandpass: passes only intermediate frequencies

Notch: attenuates a narrow band (60 hz)

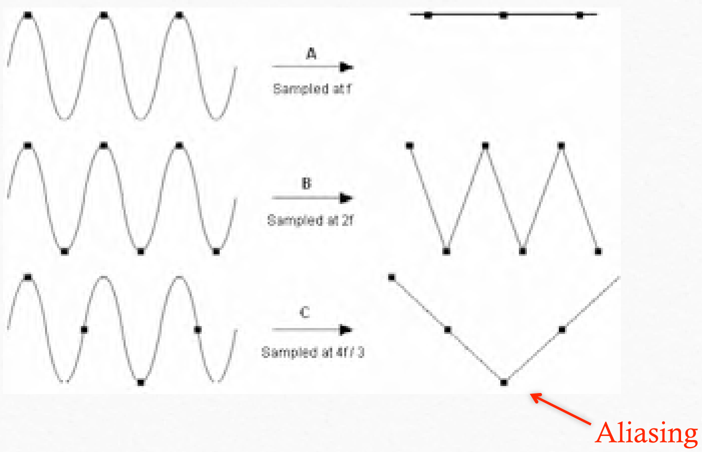
Step 4: Digitization

- Analog-to-Digital Converter (ADC) converts EEG voltage fluctuations into numbers
- Most EEG systems have ADC resolution of 12 bits
  - Can code 2^12 (4096) voltage values
- Set gain on amplifier to not exceed ADC range

<u>Sampling Rate</u>= # samples per second



Nyquist Theorem (SR must be ≥2x highest frequency)



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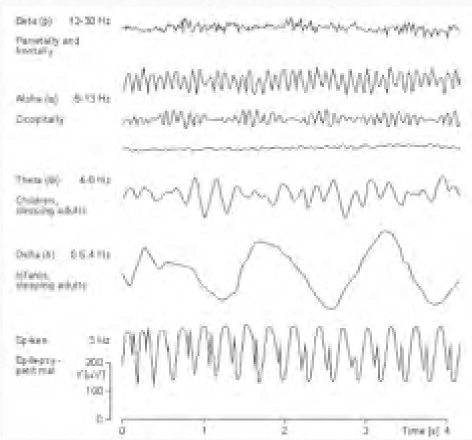
Oscillations



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Clinical EEG

- Diagnosis and management of epilepsy
- Characterization of sleep
- Evaluation of coma
- Confirmation of brain death

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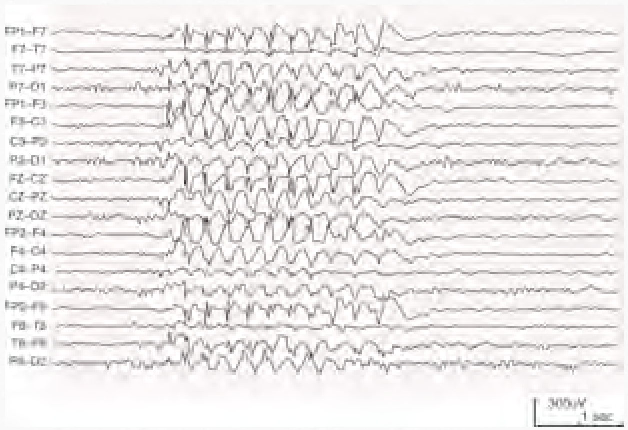
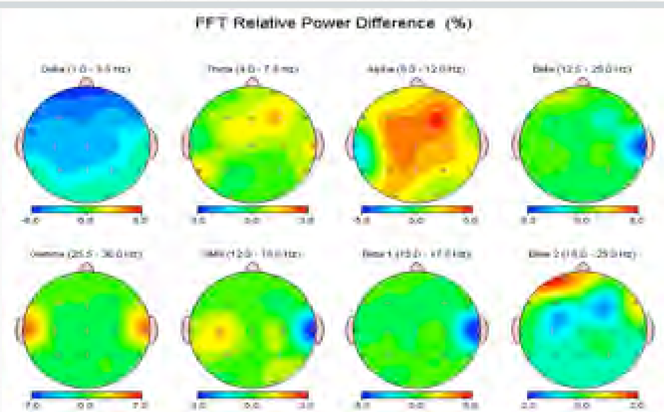
Clinical EEG



Quantitative EEG

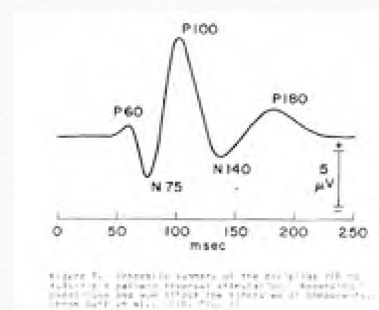
- Goal is to quantify spectral (frequency) components of EEG using Fast Fourier Transform (FFT) algorithm
- Adjust filtration based on frequencies of interest (ie to capture gamma, low pass filter ≥ 100 hz)
- Based on regions of interest, can cluster electrode placement
  - Example: prefrontal theta in depression

Quantitative EEG

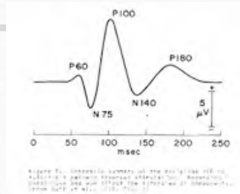


Event Related Potentials

- Embedded within the EEG
- Neural responses time locked to specific sensory, cognitive, or motor events
- Can extract these responses from EEG through processing techniques
- 3 Dimensions
  - Latency
  - Amplitude
  - Topography (Spatial Location)



ERP Components



- N for negative deflection
- P for positive deflection
- Number that follows is either
  - (1) Ordinal position in waveform (ie N1)
  - (2) Latency of component (ie N100)
- Early components (first 100 msec) are "endogenous" and reflect perception
- Late components (after 200 msec) are "exogenous" and reflect cognitive processing

Advantages of ERPs

- Non-invasive
- Motion artifact less of an issue
- Feasible in challenging populations
- Excellent temporal resolution
- Can tease apart perceptual and cognitive processes
- *Can assess processing without an overt (behavioral) response and before an overt response*

Pitfalls of ERPs

- Electrode placement takes time
- Single application nets can be uncomfortable
- Poor spatial resolution
  - Source localization?
- Potential for "fishing" for findings if no *a priori* hypothesis
- Not as much foundation for cognitive paradigms in young and developmental populations (ie we don't have a lot of prior data to build upon)

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- **Designing an ERP study and ERP data processing**

Infants at Risk for ASD

- At 12 months, differences in:
  - Initiation/response to referencing behaviors
  - Requesting
  - Language production and comprehension
  - Response to changes in another person's emotional state
- At 18 months, differences in:
  - Functional play acts
  - Repeated non-functional play acts
- No behavioral predictors prior to age 12 months

Study Questions

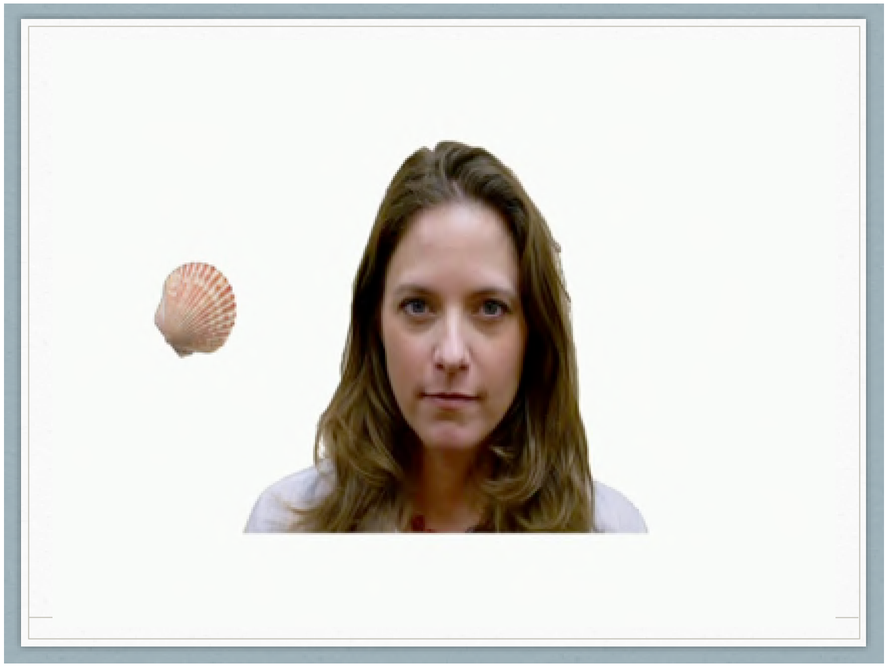
- Are there pre-behavioral markers of ASD in high risk infants?
- Are there signs of cognitive and perceptual dysfunction in early infancy that correlate to later phenotypes (not just ASD)?
  - Particular interest in language acquisition
- Domains of interest:
  - **Joint attention (and learning from social cues)**
  - Statistical language learning
  - Face processing

High density EEG system

- EGI system (Electrical Geodesic Inc)
- 128 channel HCGSN nets (Hydrocel Geodesic Sensor Nets)
- Stimuli presented in eprime 2.0
- Stimuli "tagged" into EEG file to facilitate segmentation of data
- Netstation 4.4 software and waveform tools for data processing

Joint Attention Paradigm

- Infants can distinguish direct from averted eye gaze
- Infants prefer to look at faces with directed eye contact
- By 4 months, infants will follow eye gaze and shift their attention to the direction of adult's eye gaze
- By 4 months infants learn best when taught in a joint attention format
- Are infants at high risk for ASD use social cues to learn?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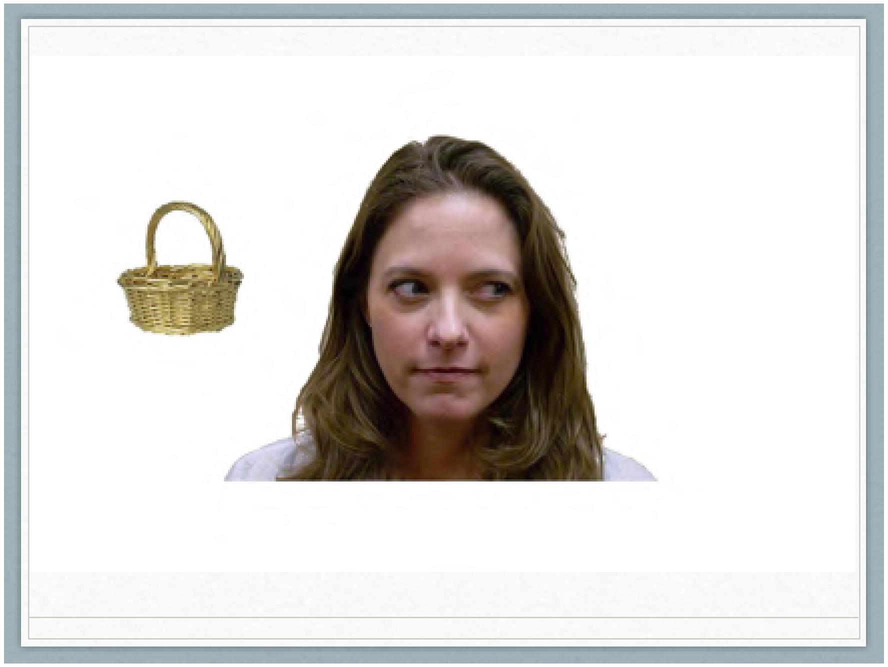
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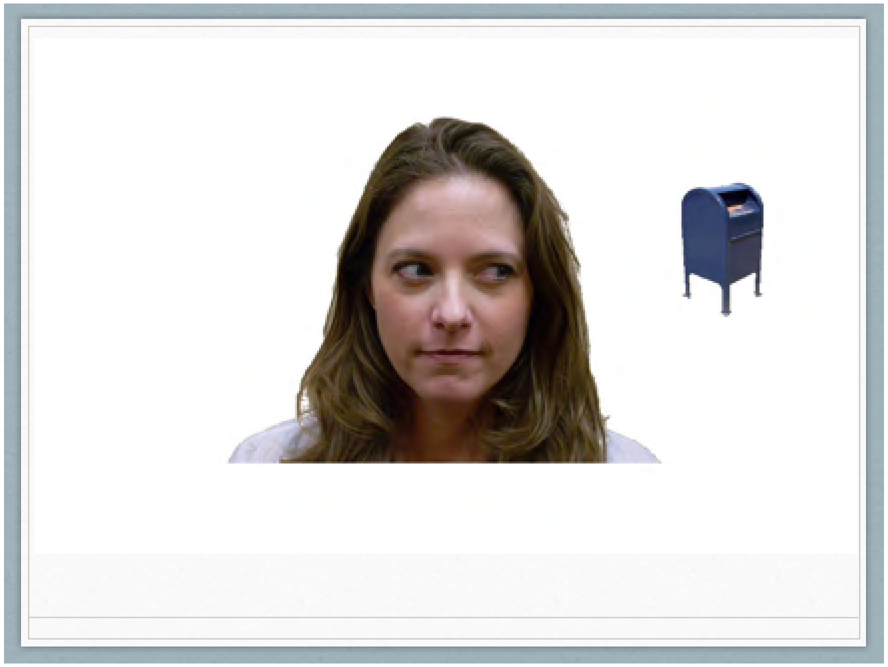
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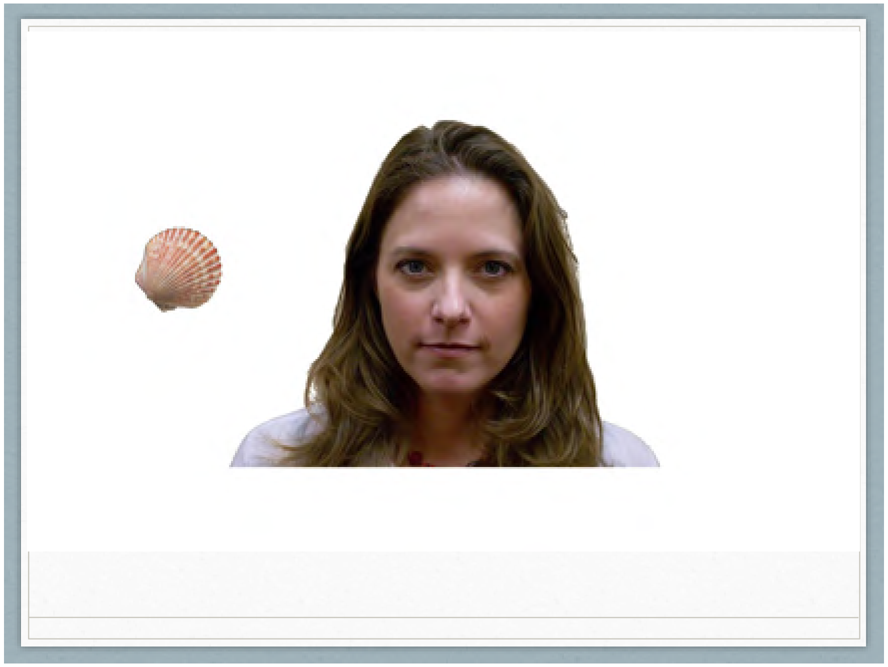
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Components of interest

- Nc: Marker of attention
  - Larger to unfamiliar than familiar stimuli
  - Negative component 350-650 msec after stimulus
  - Fronto-central
- PSW: updating of partially encoded information
  - Larger to less frequently presented stimuli
  - Positive component 700-1000 msec after stimulus
  - Fronto-central
- N290/P400 complex
  - Face processing
  - Modulated by gaze direction

Considerations in study design

(1) Timing of stimuli and ISI (jitter)

(2) Enough trials to maximize signal, minimize noise

(3) …while still keeping subject's attention

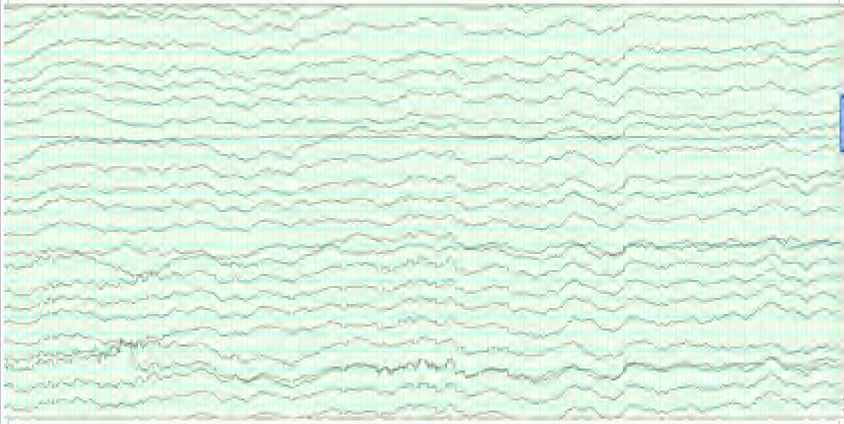
Need to know what you are looking for before designing experiment!!

Joint attention study design

- Exposure phase: Stimulus presentation 1000 msec
- Test phase:
  - Stimulus presentation 500 msec
  - ISI 1000-1250 msec
- 200 test trials, randomized in blocks of 50
- Goal is to have >10 good trials per condition
- Components of interest: N290/P400 during exposure, frontal Nc and PSW during test

Data processing: How to get an ERP from raw EEG?

- Filtering
- Segmentation
- Signal averaging
- Artifact detection and rejection



Filtering

Filter settings based on the data of interest

High pass: attenuates low frequencies (0.1 hz)

Low pass: attenuates high frequencies (30 hz)

Bandpass: passes only intermediate frequencies

Notch: attenuates a narrow band, passes everything else

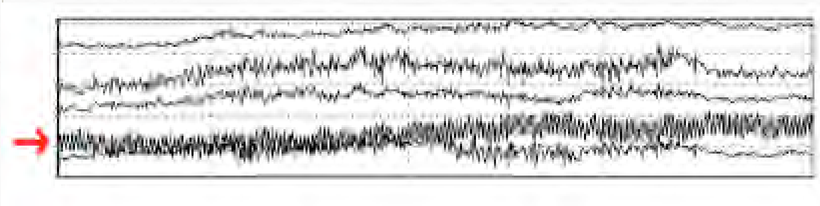
Segmentation

- Defining parameters for time-locked segment of interest
- 100-200 msec of baseline prior to segment
- Segment length depends on components of interest
- Study design depends on segmentation

Artifact detection

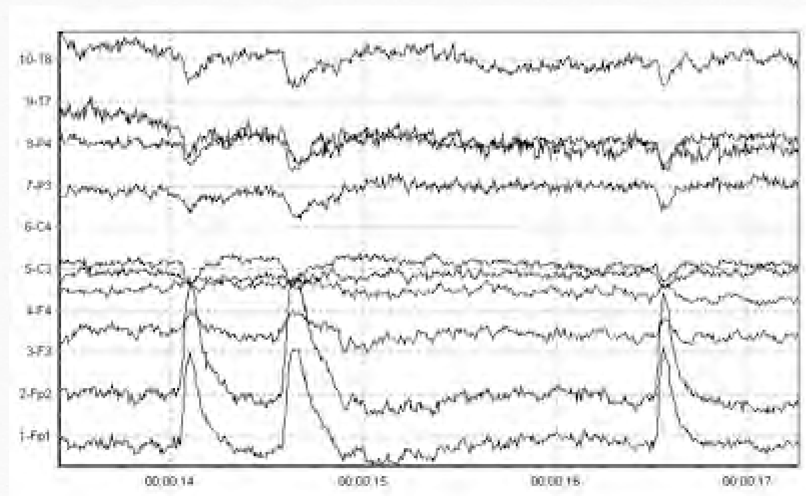
- Blinks, eye movements, muscle activity, skin potentials, electrical noise
  - Usually larger than the ERP, decrease S/N
  - Might be systematic rather than random, so may lead to wrong conclusions about data
- Automated artifact detection in adults (eye blinks, eye movements, bad channels)
- In child data, best to do manual artifact detection
  - But need to set an *a priori* threshold for rejection

High frequency electrical noise



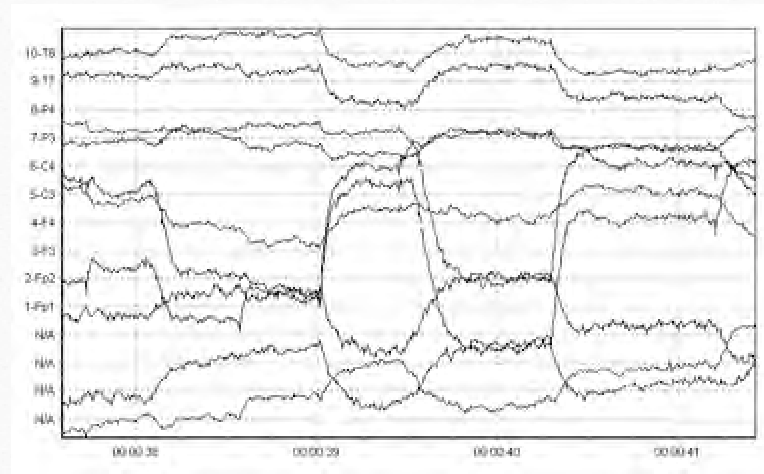
Blinks

- Electrical gradient in each eye
  - Positive in front, negative in back
- Blink causes monophasic deflection
- 50-100 uV, lasting 200-400 msec
- Opposite in polarity for sites above vs. below the eye
- How to reduce blinks:
  - Glasses over contacts
  - Short trials blocks
  - Give participant feedback during session



Eye movements

- Voltage gradient on scalp changes when eyes move, more positive in location where eyes look
- Also have to look for saccade induced ERP response
- Boxcar shaped because saccade in one direction followed by another to return to fixation point
- Video helps



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EMG and EKG

- Muscle and heart activity
- EMG
  - High frequency
  - Usually eliminated by low pass filter
  - In kids often see chewing / sucking artifact
- EKG
  - Distinctive shape
  - Picked up by mastoids
  - 1 hz during entire recording session
  - Not a big deal, just decreases S/N

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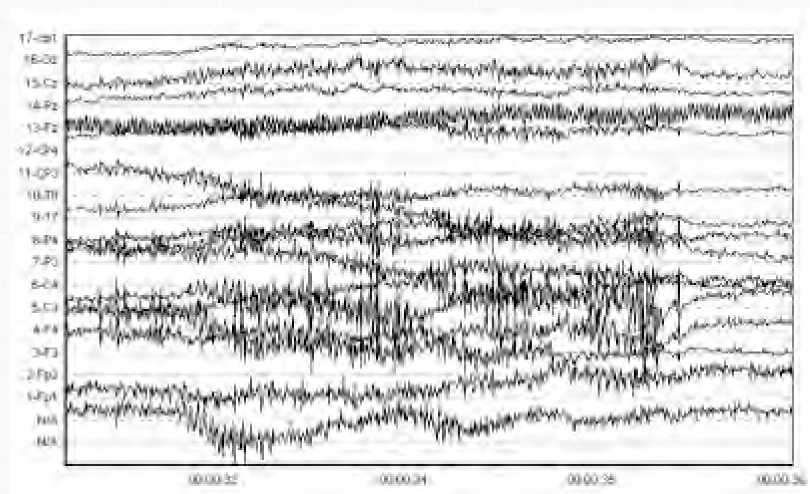

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Slow voltage shifts “drift”

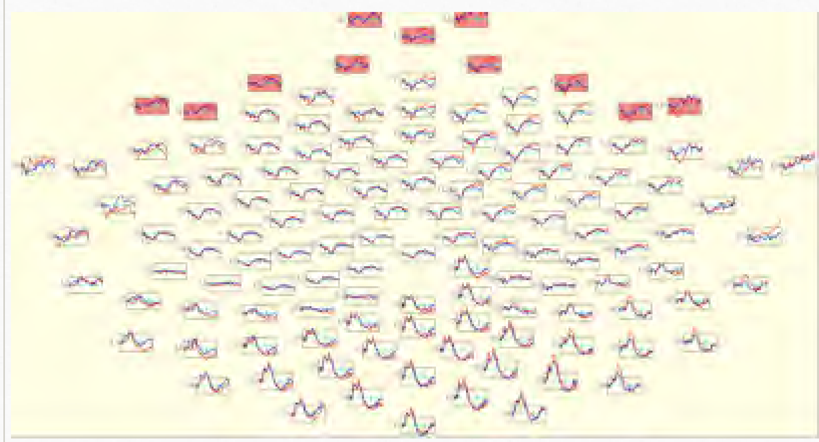
- Change in skin impedance
  - Sweat causes decrease in impedance
- Slight changes in electrode position (movement)
  - Major issue in little kids/infants
  - High pass filter can help this
- Can cause amplifier to saturate, causing EEG to look flat (“blocking”)
  - Use lower gain on amplifier

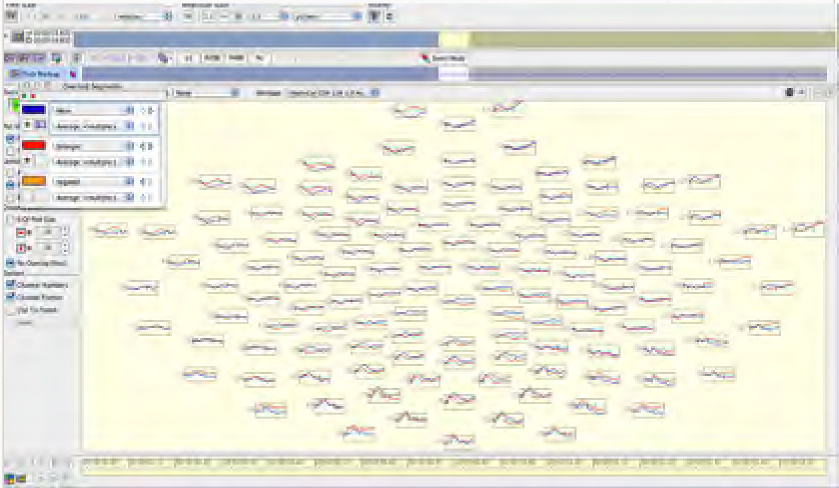
Signal Averaging

- Average segmented data across all trials, per condition and then across subjects
- EEG data from single trial assumed to contain ERP waveform + random noise
- ERP waveform assumed to be same in each trial, whereas noise varies
- Averaging trials reduces noise, increases S:N ratio

Data processing

- Filtering
- Segmentation
- Signal averaging
- Artifact detection and rejection



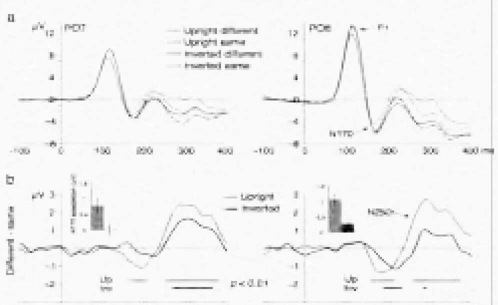


Measurement, plotting, analysis

- Variables of interest: Latency, Peak vs. mean amplitude
  - Depends on component of interest
- Need to establish baseline (100-200 msec) but realize that pre-stimulus interval (ISI) may not be completely neutral
- Amplitude directly affected by latency
- Plot in excel
- Analysis in SPSS, using ANOVA's

Plotting ERP waveforms

- Need to include voltage and time scale
- Superimpose different conditions/groups
- Show prestimulus baseline (100-200 msec)



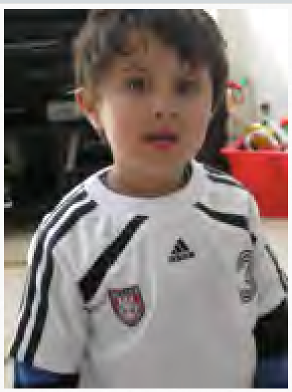
What do differences in waveforms mean?

- Reliably different waveforms can be linked to different activity in the nervous system
- Need a theoretical framework linking biological states and functional states
- Ideally, need apriori hypothesis of nature and source of differences
- Findings then need to be replicated

Key points

- EEG and ERP methodology promising in developmental populations
- Excellent temporal resolution
- Spatial resolution limited, requires inferences
- While post-acquisition data processing can be manipulated, rigorous study design critical in acquiring high quality data

Questions?



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