EEG-fMRI & Language

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Section on Functional Imaging Methods, NIMH
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Purpose of this Talk

- Give an overview of EEG/ERP
- Illustrate converging evidence from fMRI and EEG/ERP of language (reading)
- Highlight the importance of simultaneous EEG-fMRI studies moving forward

Historical Moment

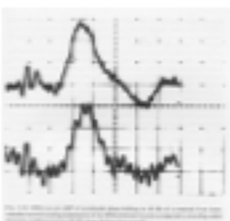
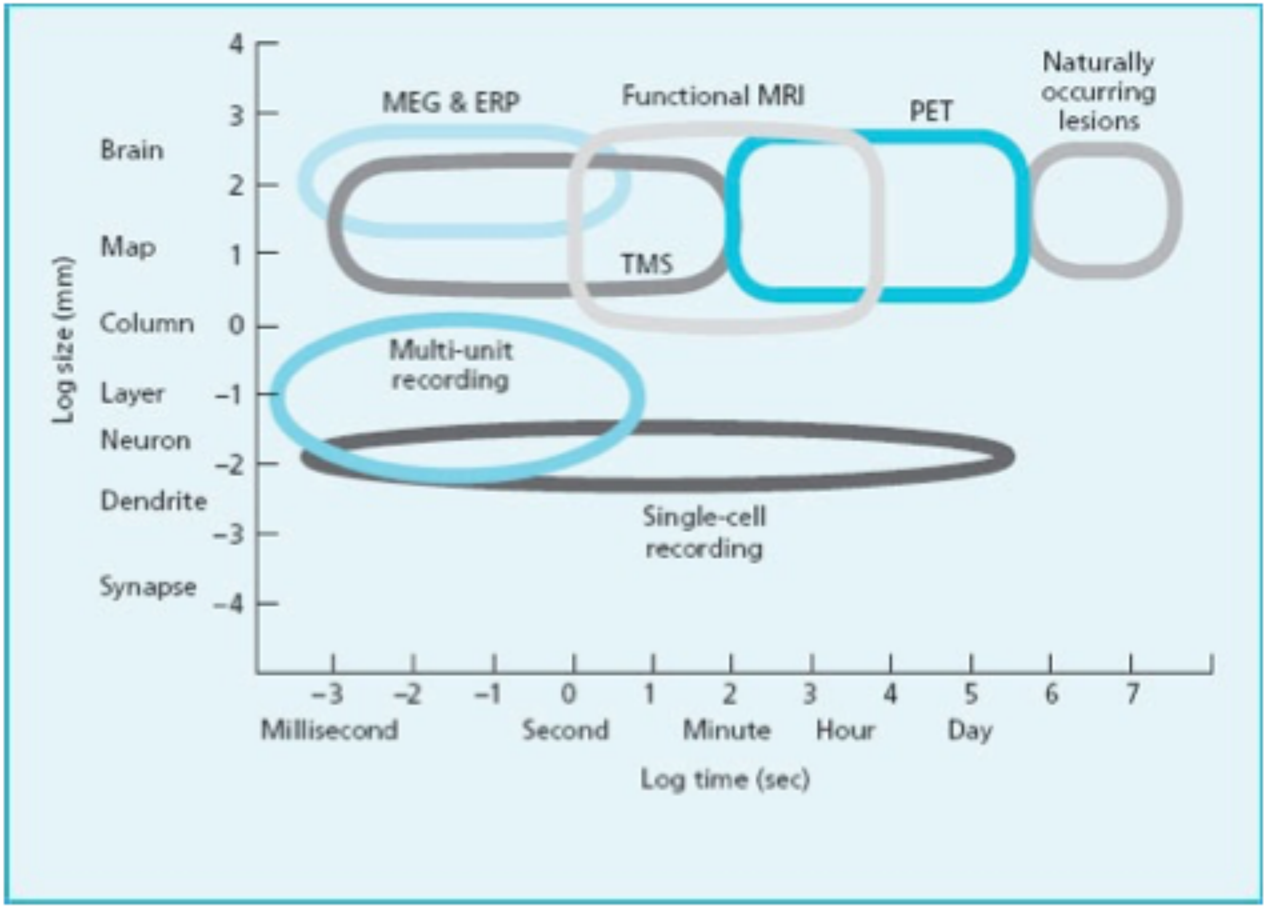


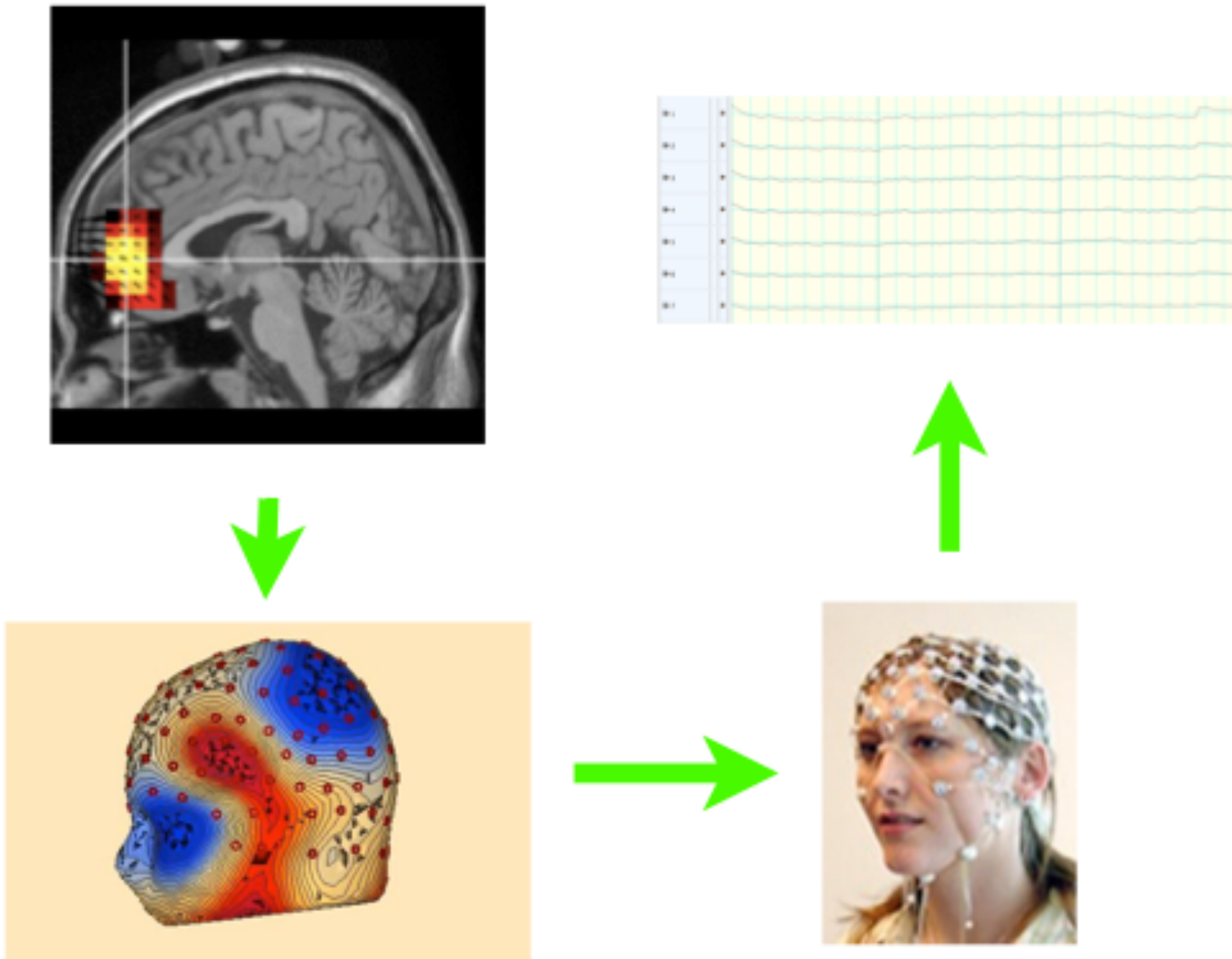
FIG. 1-21. A modern EEG and perceptual laboratory, equipped for EEG, average evoked potential, and CNV recording. 1. Tektronix 502 oscilloscope; 2. Tektronix Polaroid camera; 3. Grass Kymograph camera; 4. Grass physiological stimulators; 5. Tektronix power supply, waveform and pulse generators; 6. Moseley X-Y plotter; 7. Massey-Dickinson control and programming equipment; 8. Power supply; 9. Hewlett-Packard counter; 10. Tapereader; 11. Oscilloscope monitors; 12. Mnemotron computer of average transient (CAT) and accessories; 13. Preset controller and tape coder; 14. Ampex FR-1300 7-channel FM tape recorder; 15. Grass Model 6 8-channel EEG.

Hans Berger, 1924

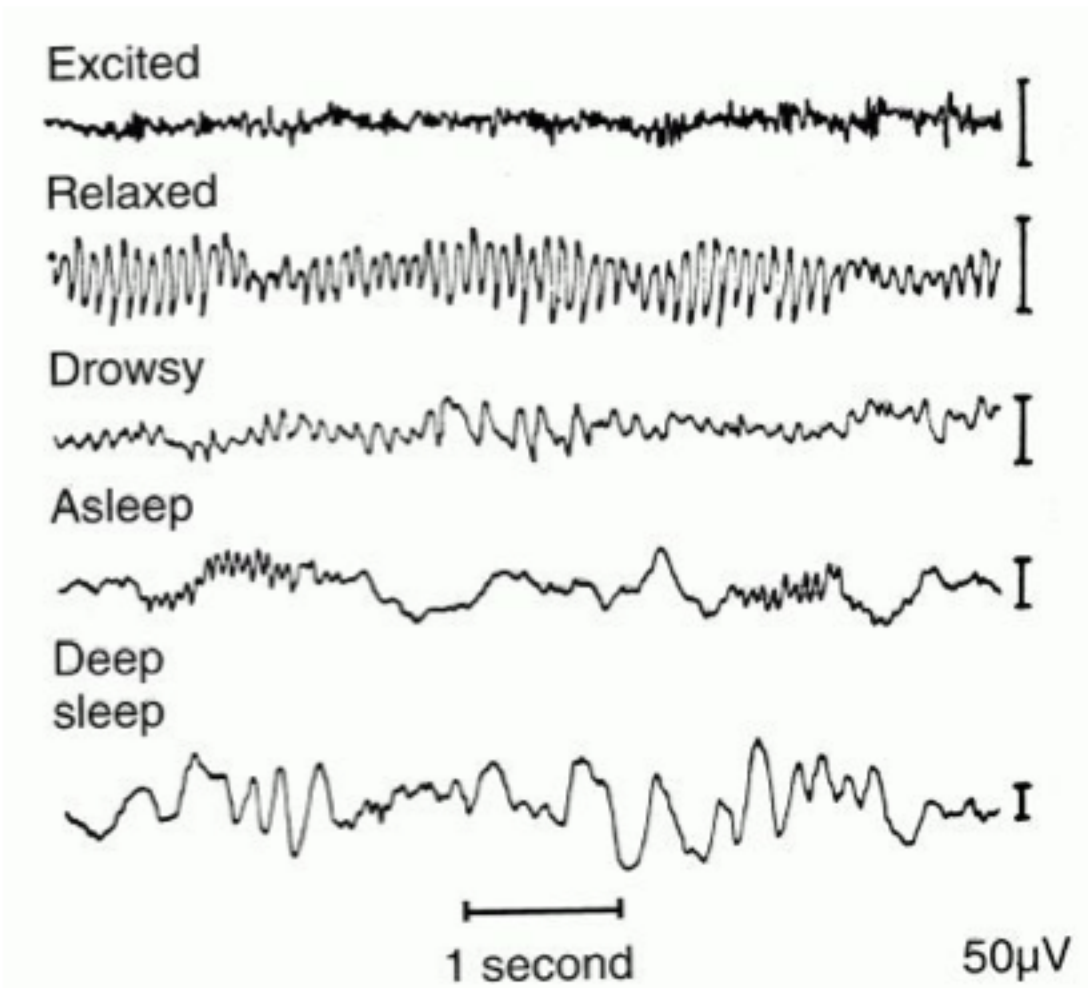
Temporal-Spatial Tradeoffs

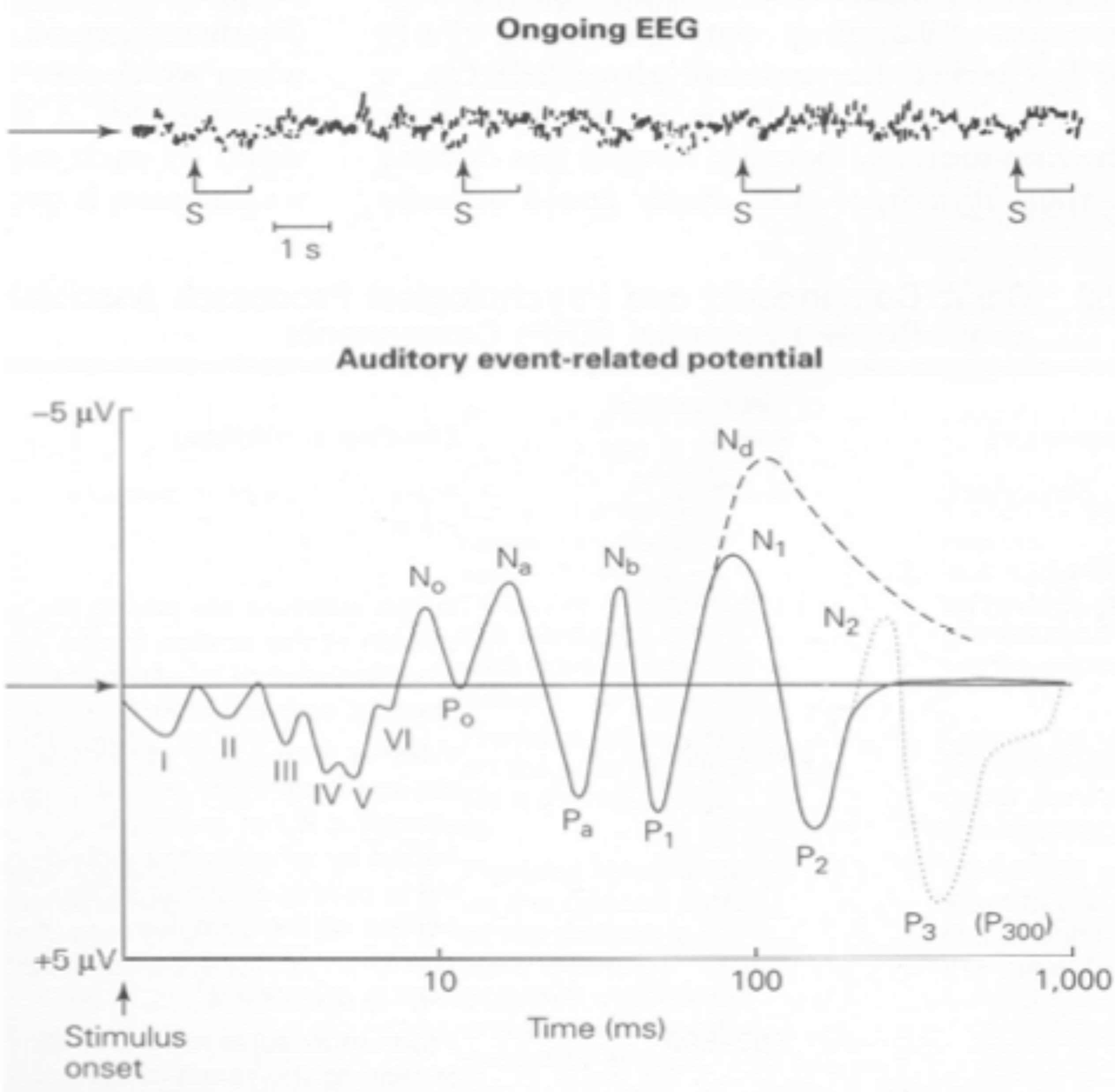


Neural Origins of EEG



EEG Reflects Brain State

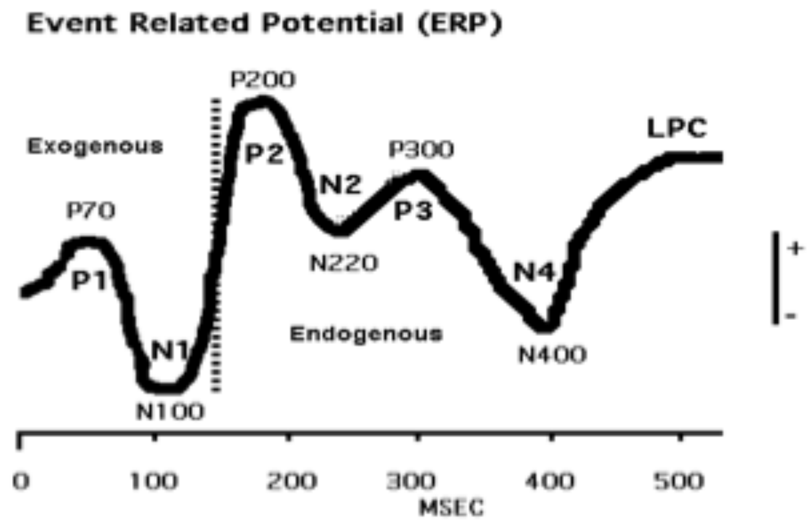




Ongoing EEG
S
S
S
S
1 s
Auditory event-related potential
–5 µV
+5 µV
Nd
N1
Na
Nb
No
N2
Po
I
II
III
IV
V
VI
Pa
P1
P2
P3
(P300)
10
100
1,000
Time (ms)
Stimulus onset

The Evoked Potential

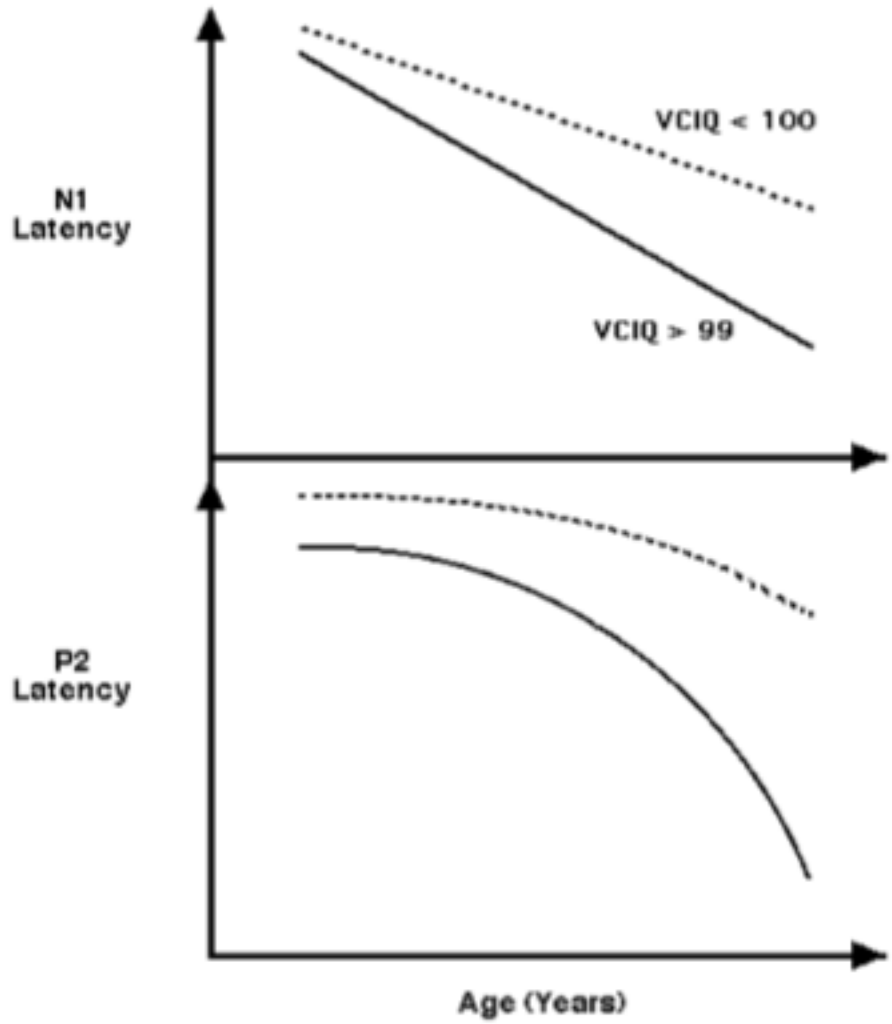
- Event-Related Potential
- Portion of the ongoing EEG
- Time-Locked to Stimulus Onset
- Strong Temporal Information
- Comparability across the lifespan



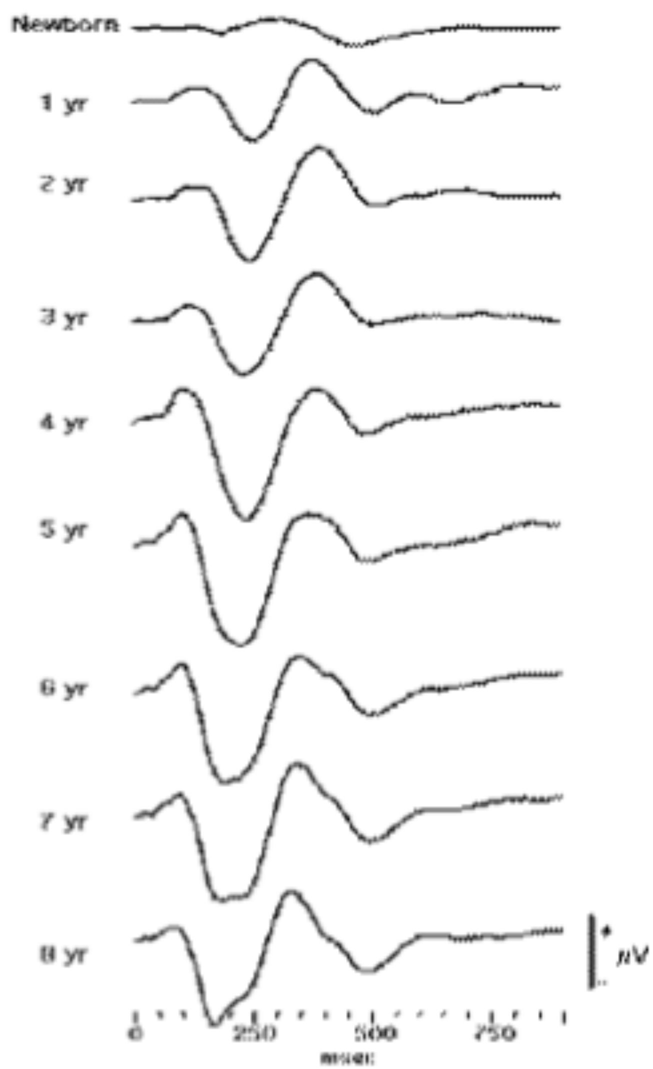
ERP Definition

- Sequence of overlapping components, each perhaps representing activity of different populations of nerve cells and each sometimes standing in different, perhaps orthogonal, relations to experimental variables (Donchin, 1979, p24).

Comparable Across Lifespan

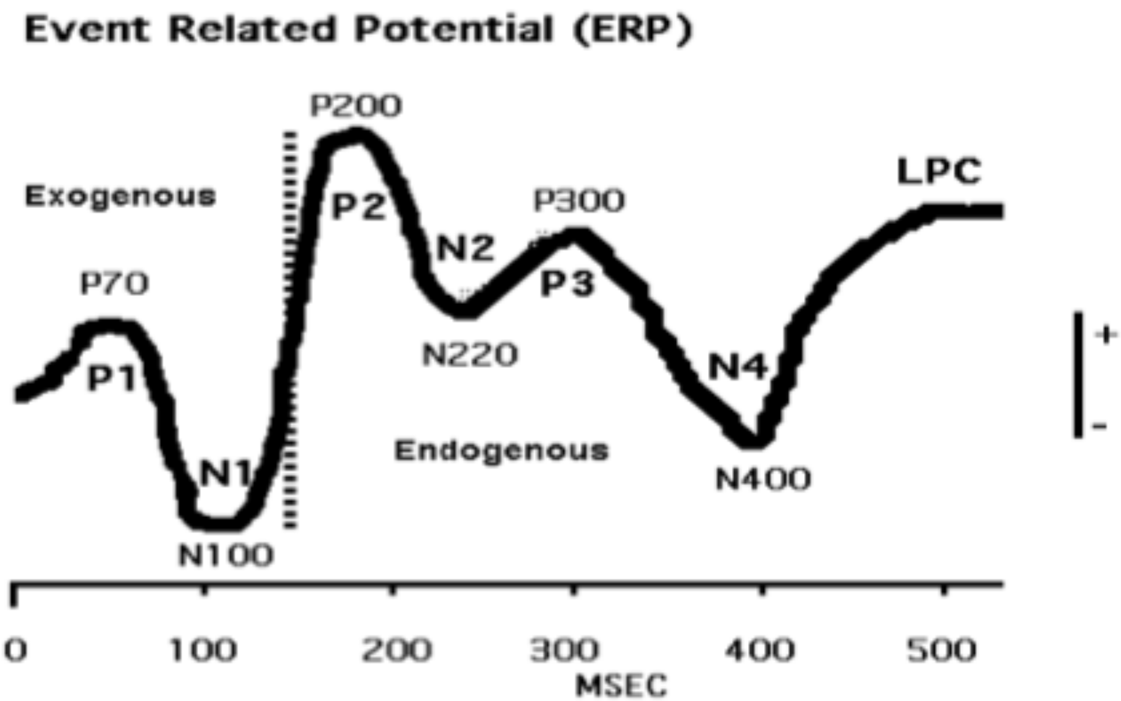


Developmental Changes



Infant ERP Testing

ERP Nomenclature



Exogenous = influenced by external factors
Endogenous = internal factors controlling

Peaks	Latency (ms)	Experiment Manipulation	Max Scalp Amplitude	Interpretation	Source
P1	50 Auditory	None Specific	Anterior	arousal level, suppression of unattended information	primary auditory cortex, superior temporal gyres, medial frontal
	100 Visual		Occipital		striate or extra-striate (posterior fusiform), posterior-parietal regions
N1	100 Auditory	None Specific	Temporal	selective filtering, basic stimulus characteristics, initial selection for later pattern recognition	Primary auditory cortex, superior temporal plane
	100-161 Visual		Central, Midline, Occipital		inferior occipital, occipito-temporal junction, inferior temporal lobe
P2	150-275 Auditory	None Specific	Central	selective attention, stimulus change, feature detection, short-term memory	primary auditory cortex, secondary auditory cortex
	200+ Visual		Occipital, Frontal		inferior occipital region

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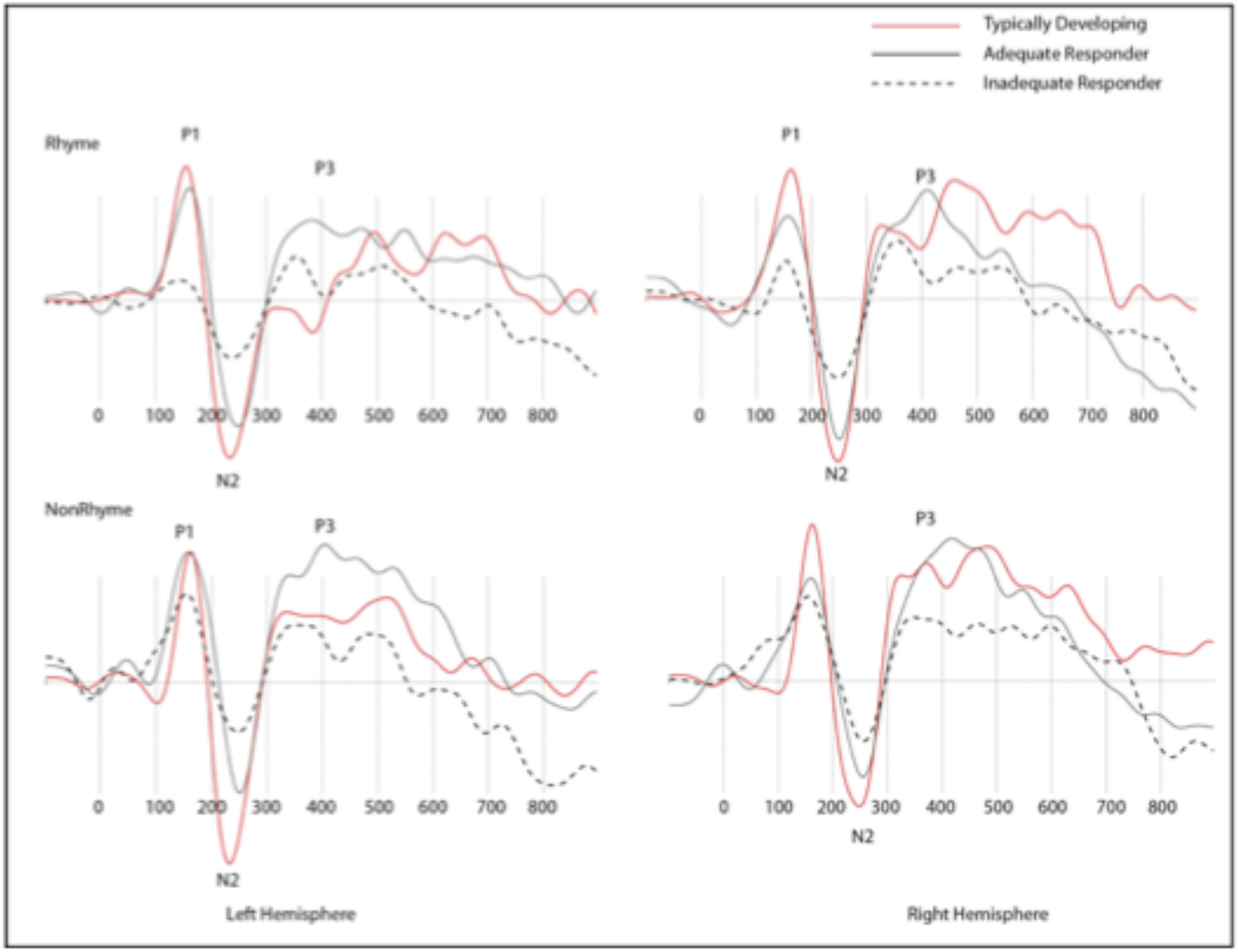
Peaks	Latency	Experimental Manipulation	Max Amplitude	Interpretation	Source
N2	200 ms Auditory	None Specific	vertex, pre-occipital, and frontal	Detect changes in attended stimuli	supratemporal, auditory cortex
	156-189 ms (N170)	Face and Object Recognition	inferior temporal	Facial and Object Expertise	Fusiform Gyrus, lateral occipital-temporal
	100-300 ms	Go/No-Go	frontal, central	inhibition	caudal and astral anterior cingulate
MMN	100-250 ms Auditory	Physically different stimuli	frontal, central	early sensory memory	temporal lobe, right superior temporal gyrus and plane
P3	300 ms	oddball (P3b)	occipito-parietal	memory updating, stimulus discrimination	thalamus, hippocampus, superior temporal gyrus and junction
	300 ms	novel stimuli (P3a)	frontal	involuntary attention, inhibition	medial parietal lobe, left superior prefrontal cortex

Peaks	Latency	Experimental Manipulation	Max Amplitude	Interpretation	Source
N400	475 ms Visual	Sentence Processing with Semantic Violations	Parietal and Temporal	Higher-Order Language Processing	Parahippocampal, anterior fusiform, medial temporal, hippocampus, amygdala, lateral temporal regions
	525 ms Auditory				
P600	400-600 ms Memory	Learned vs. Novel	Left Temporal, Frontaocentral	Memory, Novel identification, can be cross-modal	Prefrontal, anterior temporal lobe, anterior cingulate, hippocampus, frontal and temporal cortex
	500 ms Language	Syntactic Violation	Frontocentral	Syntactic violation, phrase structure, subcategorization	Superior Parietal, Precuneus, Posterior Cingulate, Basal Ganglia

Peaks	Latency	Experimental Manipulation	Max Amplitude	Interpretation	Source
ERN	80-150 ms (Response Locked)	Forced Choice RT/ACC (e.g. Flanker)	Frontal & Central	Intent and Motivation	Anterior Cingulate Cortex, DLPFC
FRN	250-350 ms	Any reward feedback	Anterior Frontal Central	Expectation differs from feedback Feedback positive vs. negative	Anterior Cingulate Cortex
CNV	Pre-stimulus negative deflection	Go/No-Go Set ITIs	Vertex	Anticipation	Premotor (BA 6)

Amplitude and Latency

Amplitude and Latency



Molfese, Fletcher, & Denton (2013)

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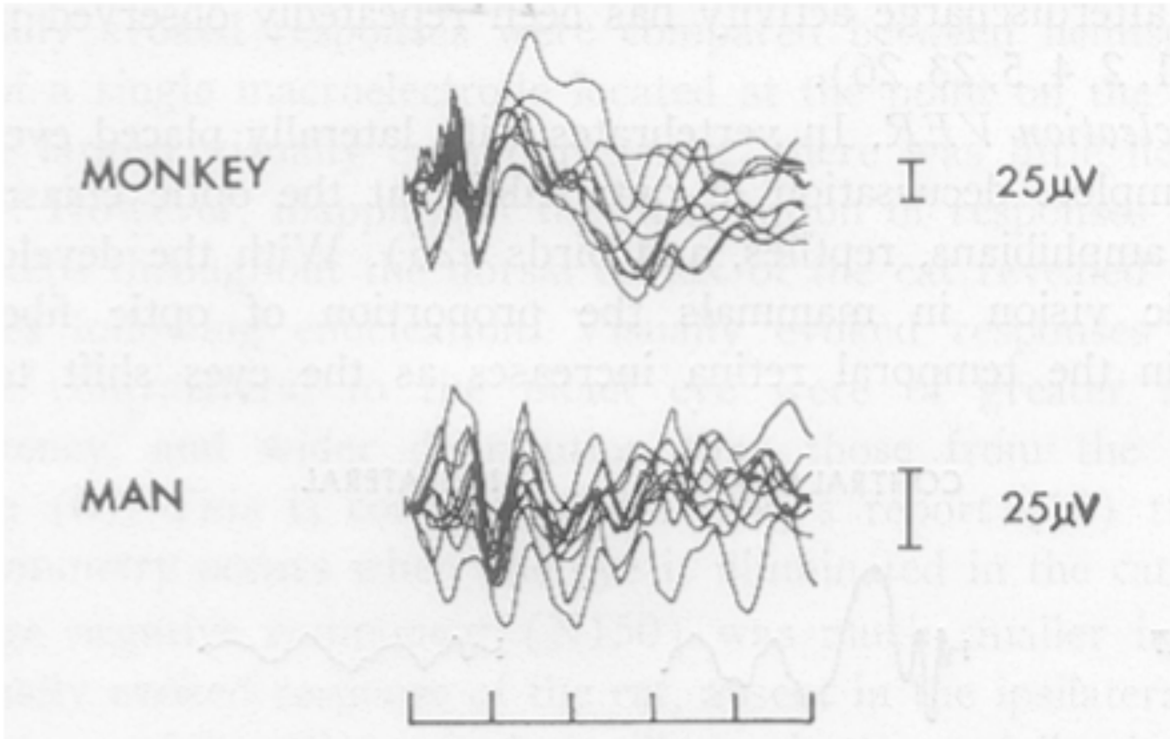
Variation in ERP Trials

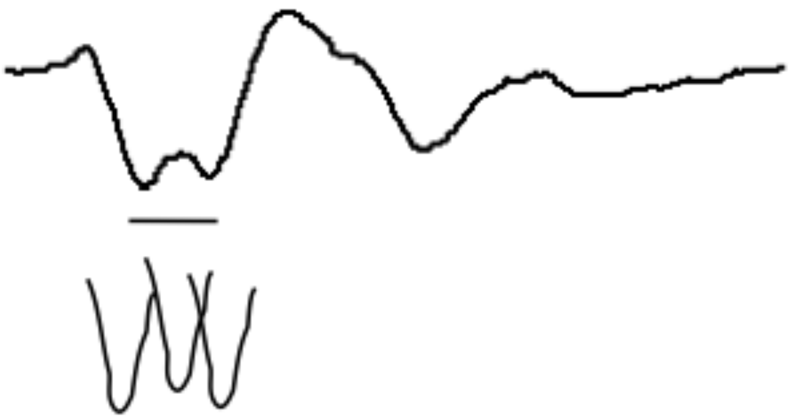
Variation in Amplitude & Latency



10 trials evenly selected from 100

Variation in Peaks

Variation in Peaks

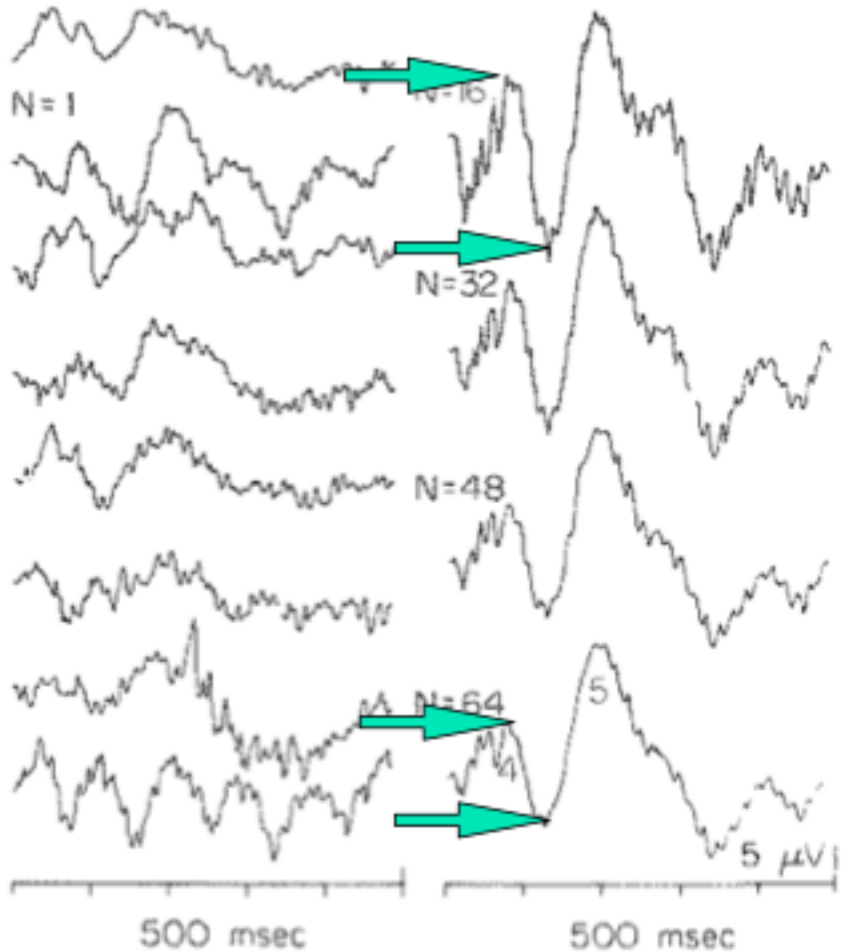


More variation, wider peaks

Less variation, often “higher” peaks

ERP Averaging

ERP Averaging



The more TRIALS Averaged together, the smaller the ERP.

More TRIALS also changes shape of ERP

Goff, 1971

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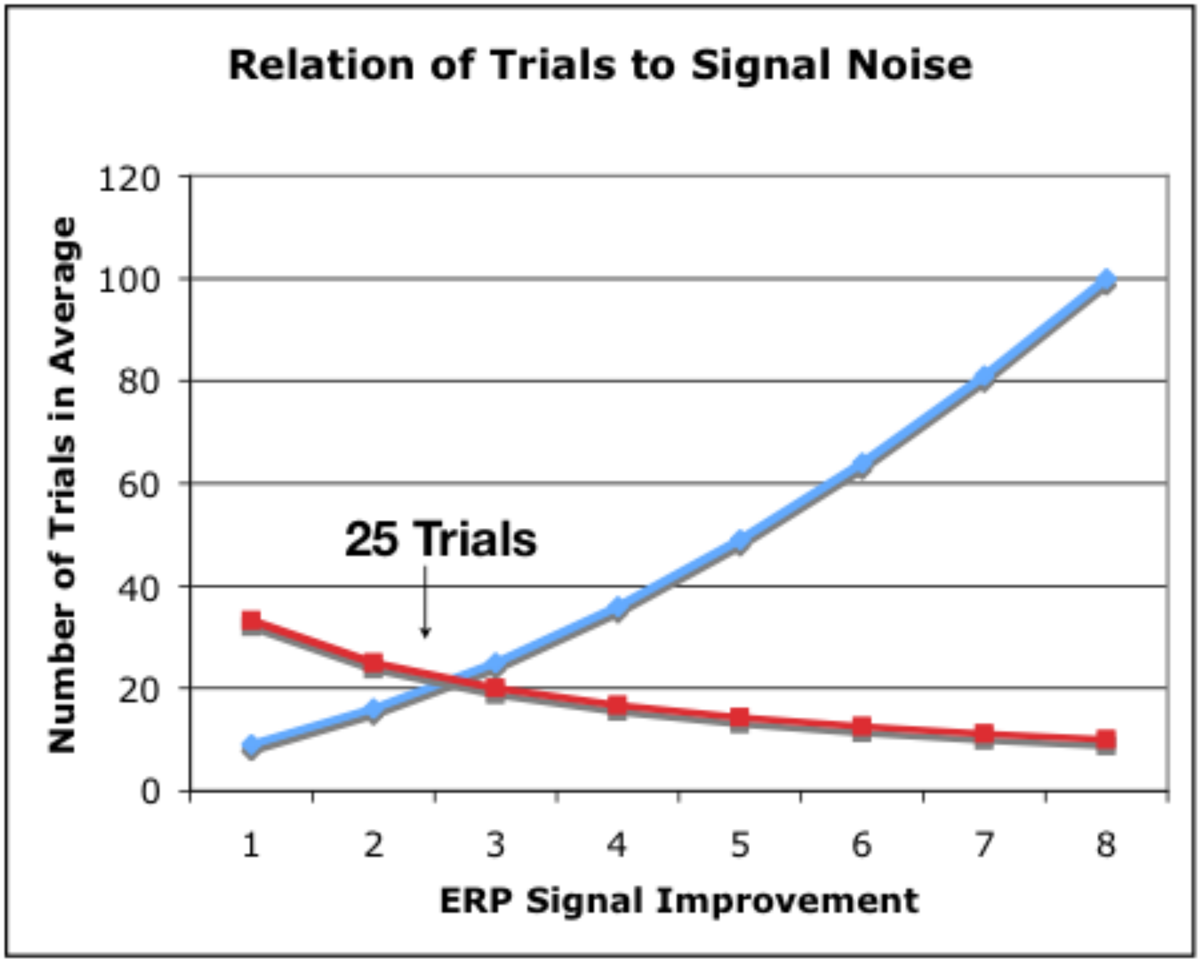
ERPs & Averaging

ERPs & Averaging

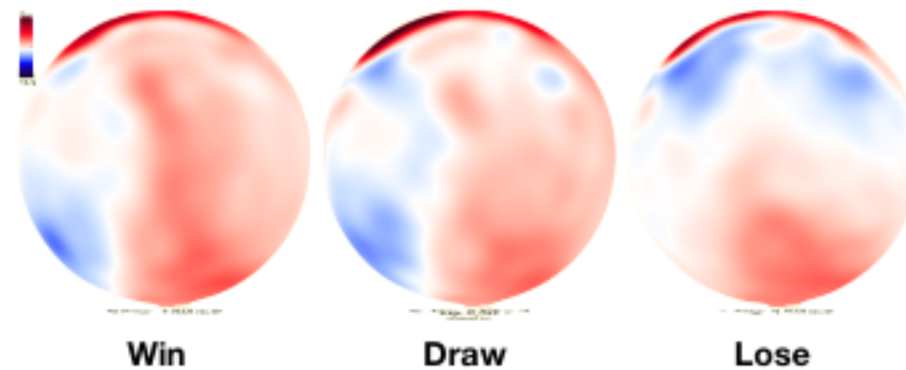


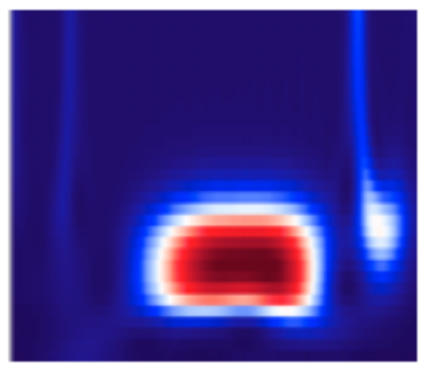
Trade-off between improving S/N and completing an experiment.

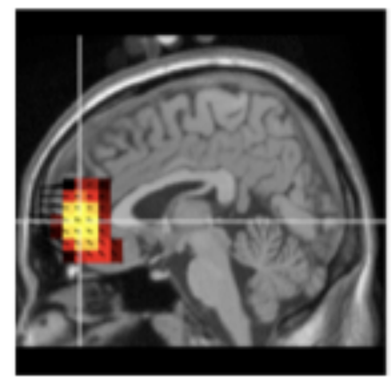
Multiple Metrics of

Comparison

- In addition to peak amplitude & latency
  - Scalp Topography
  - Frequency Analysis
  - Wavelets
  - Source Analysis

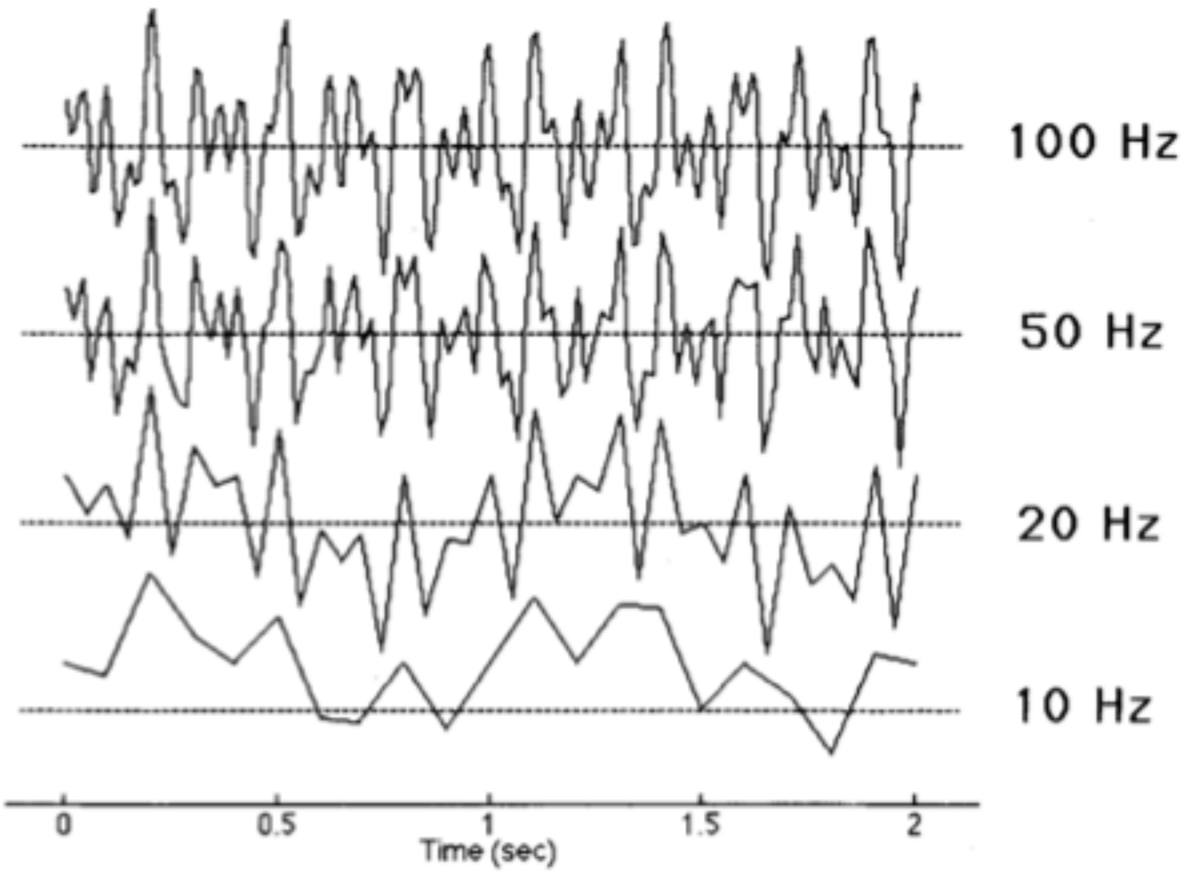






Temporal Nyquist

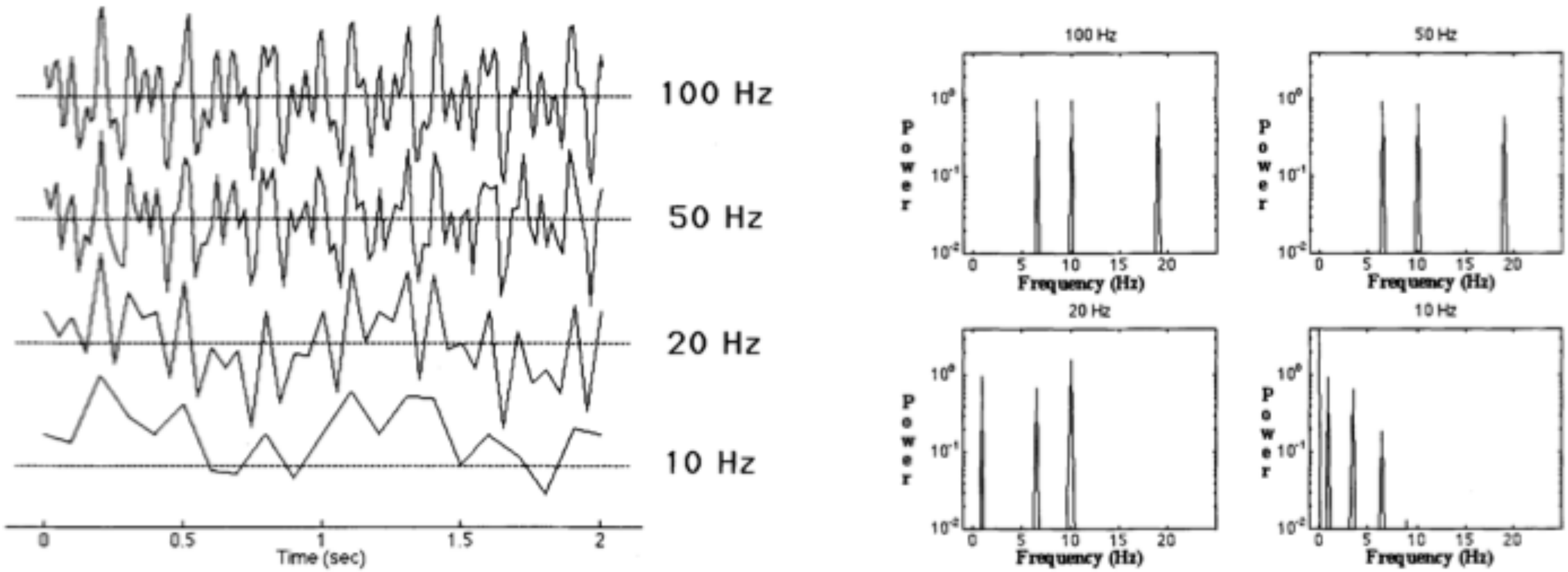
Temporal Nyquist



Composite Sine waves (6.5, 10, 19Hz)

Temporal Nyquist

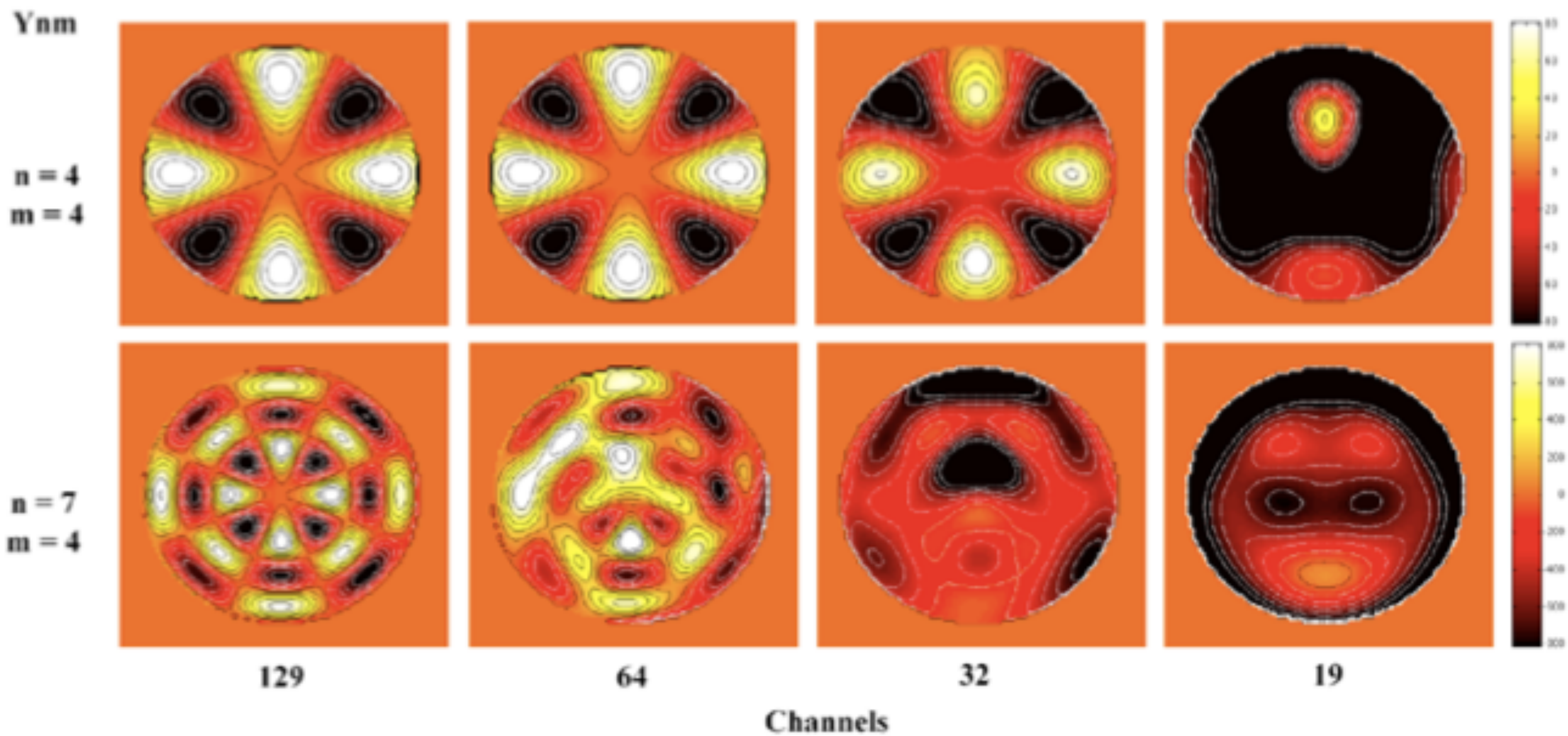
Temporal Nyquist



Composite Sine waves (6.5, 10, 19Hz)

Spatial Sampling

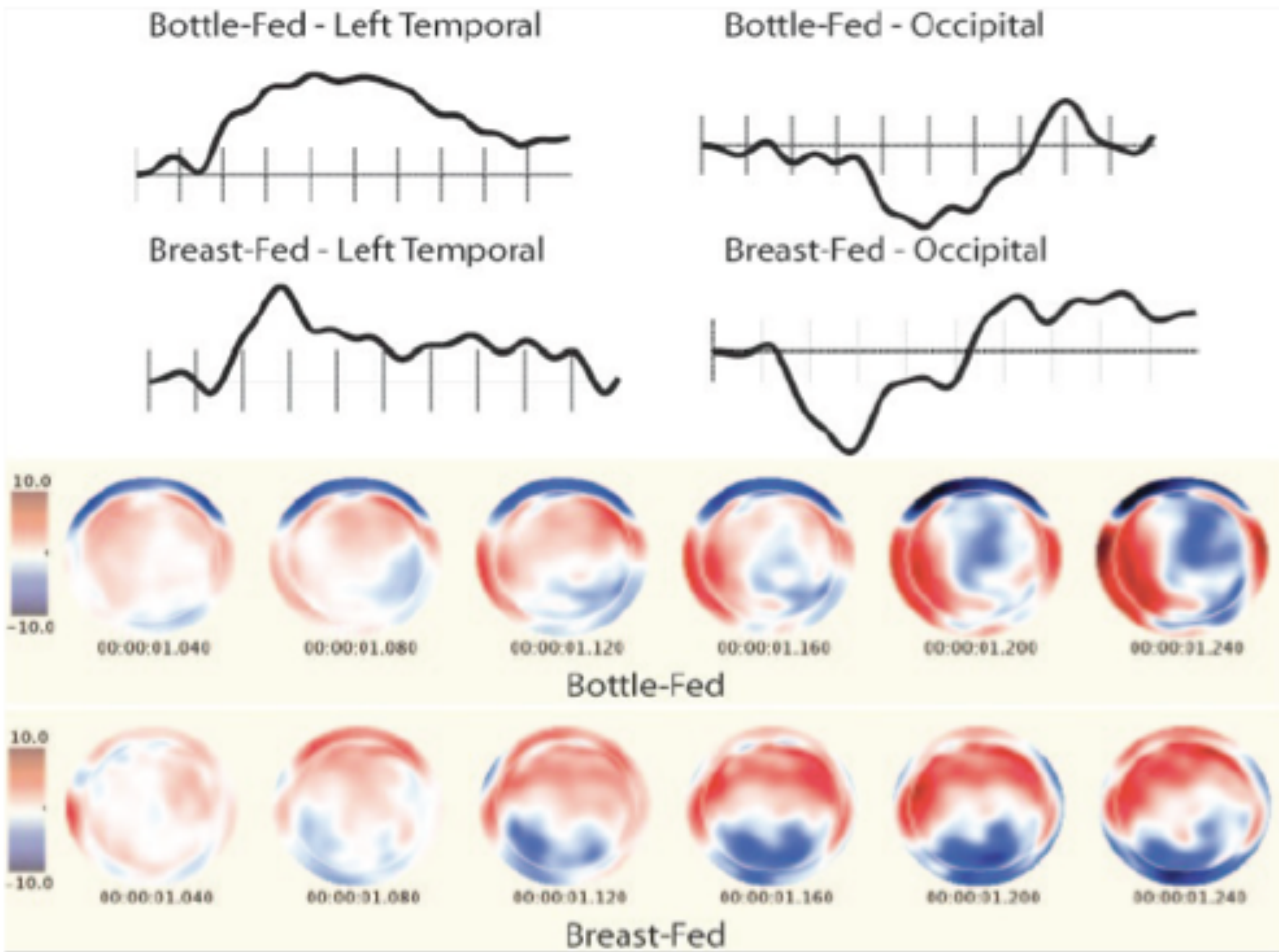
Spatial Sampling



Srinivasan, Tucker, & Murias (1998)

Link between amplitude and topography

and topography



Furguson & Molfese (2007)

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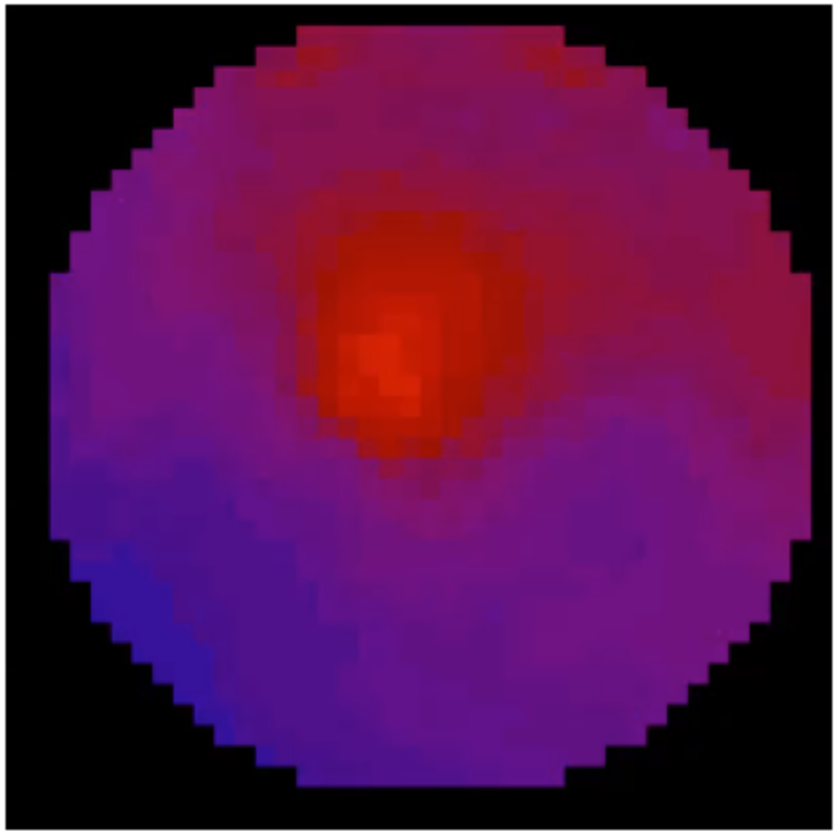
Changing Scalp

Topography

Topography



Infant Data

Courtesy of D. L. Molfese

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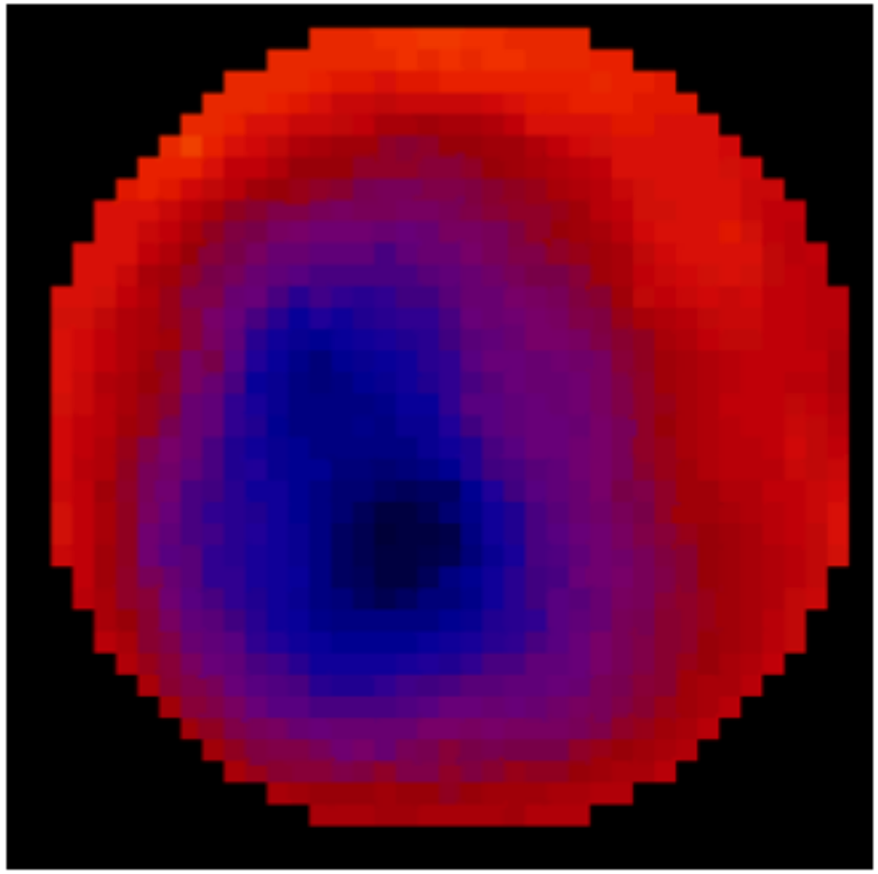
Changing Scalp

Topography

Topography



Adult Data

Courtesy of D. L. Molfese

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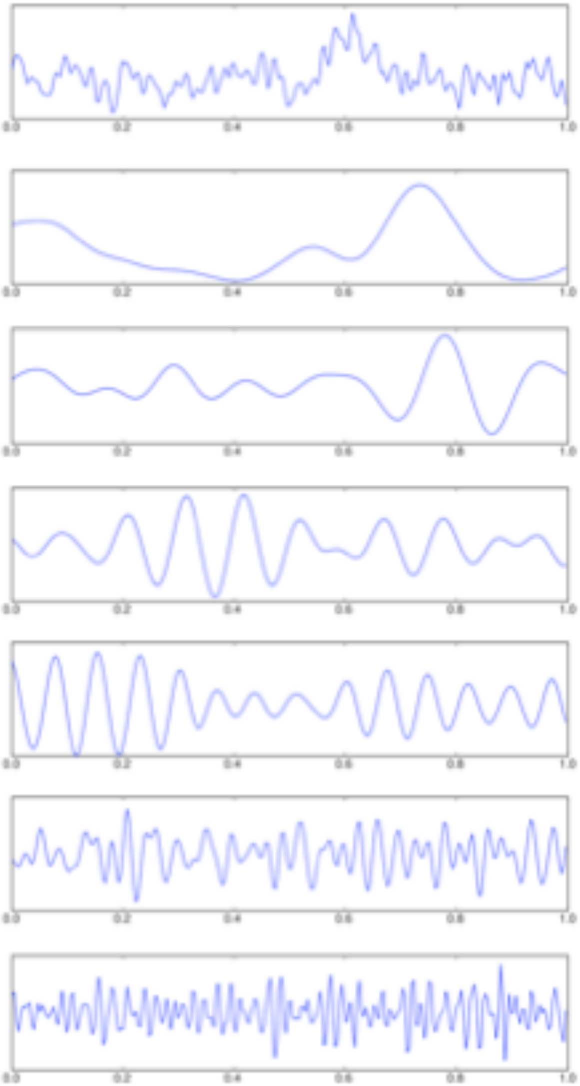
Frequency Analysis



Ongoing EEG

Delta 0-4 Hz

Theta 4-7 Hz

Alpha 8-11 Hz

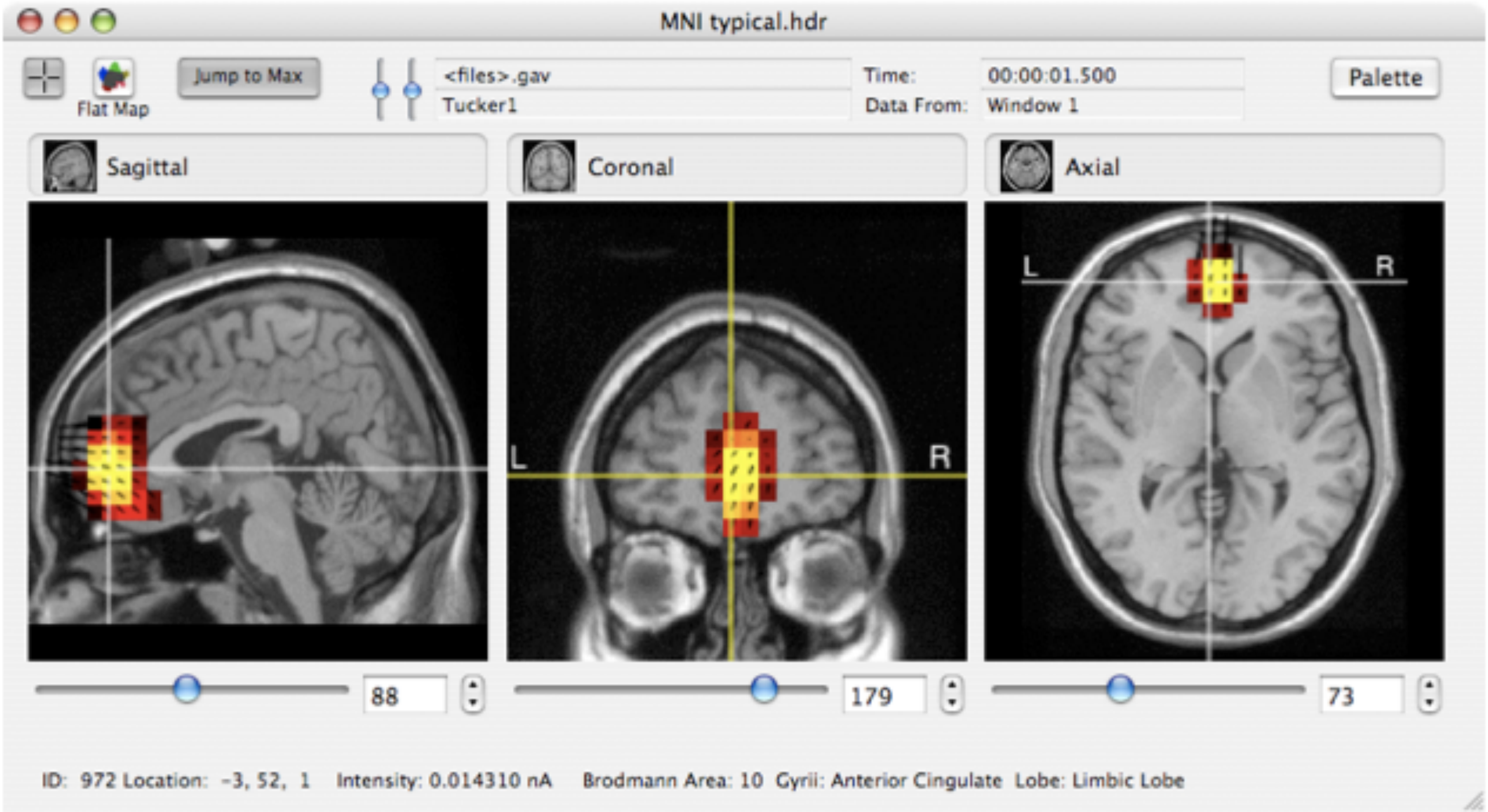
Sensory Motor Rhythm (SMR) 9-12 Hz

Beta 12-25 Hz

Gamma 26+ Hz

Figures courtesy of Wikipedia

Source Analysis



Source Analysis Terminology

Terminology

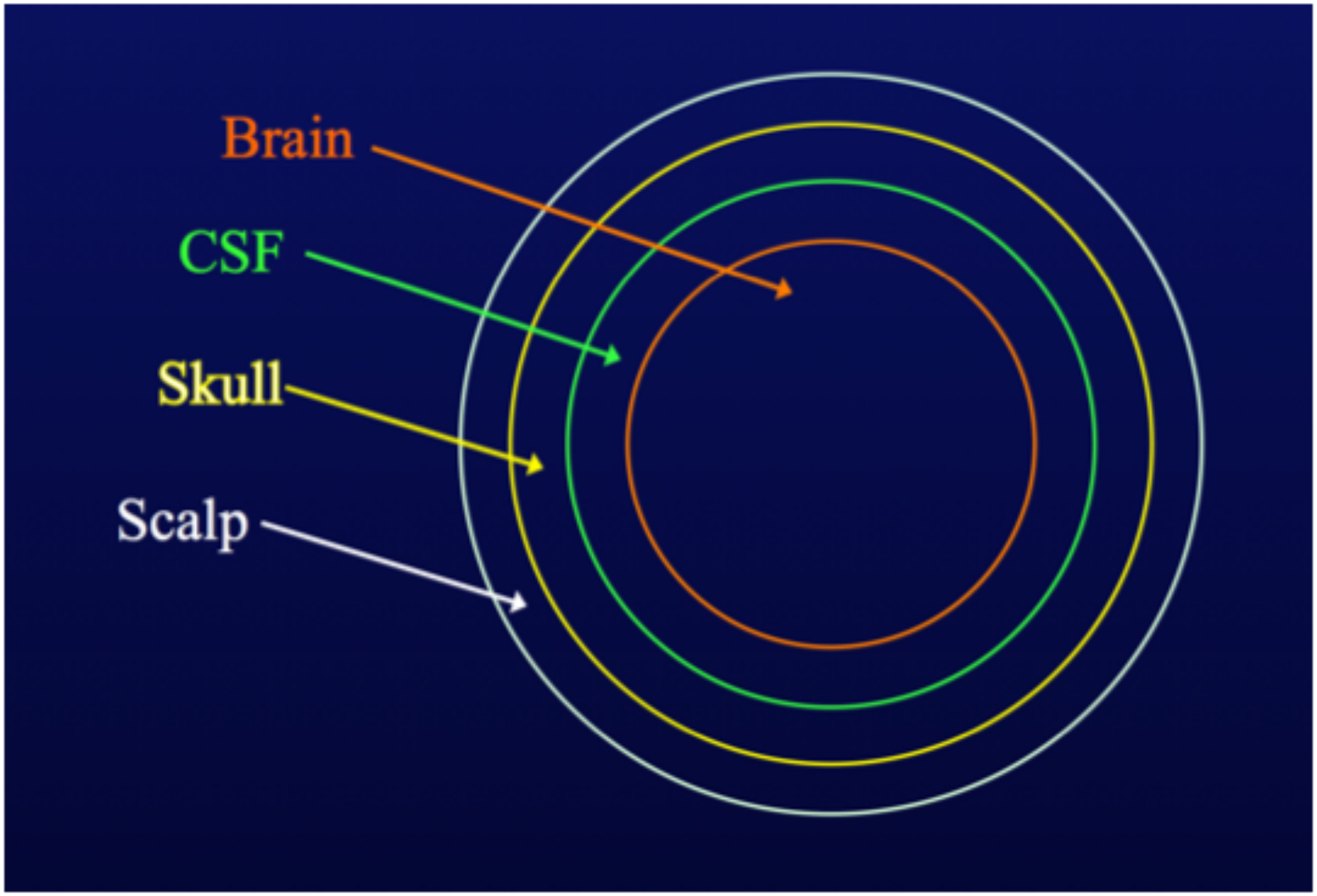
- Forward Problem: Given the sources and a propagation model, what does the scalp topography look like?
- Inverse Problem: Given scalp topography and propagation model, what are the generators?

Best Practices in Source Analysis

Source Analysis

- Adequate Number of Sensors
- Know the Geometry of Head & Sensors
- Accurate Head Model
- Know Conductivity of the head
- Make due with some propagation model

Head Models



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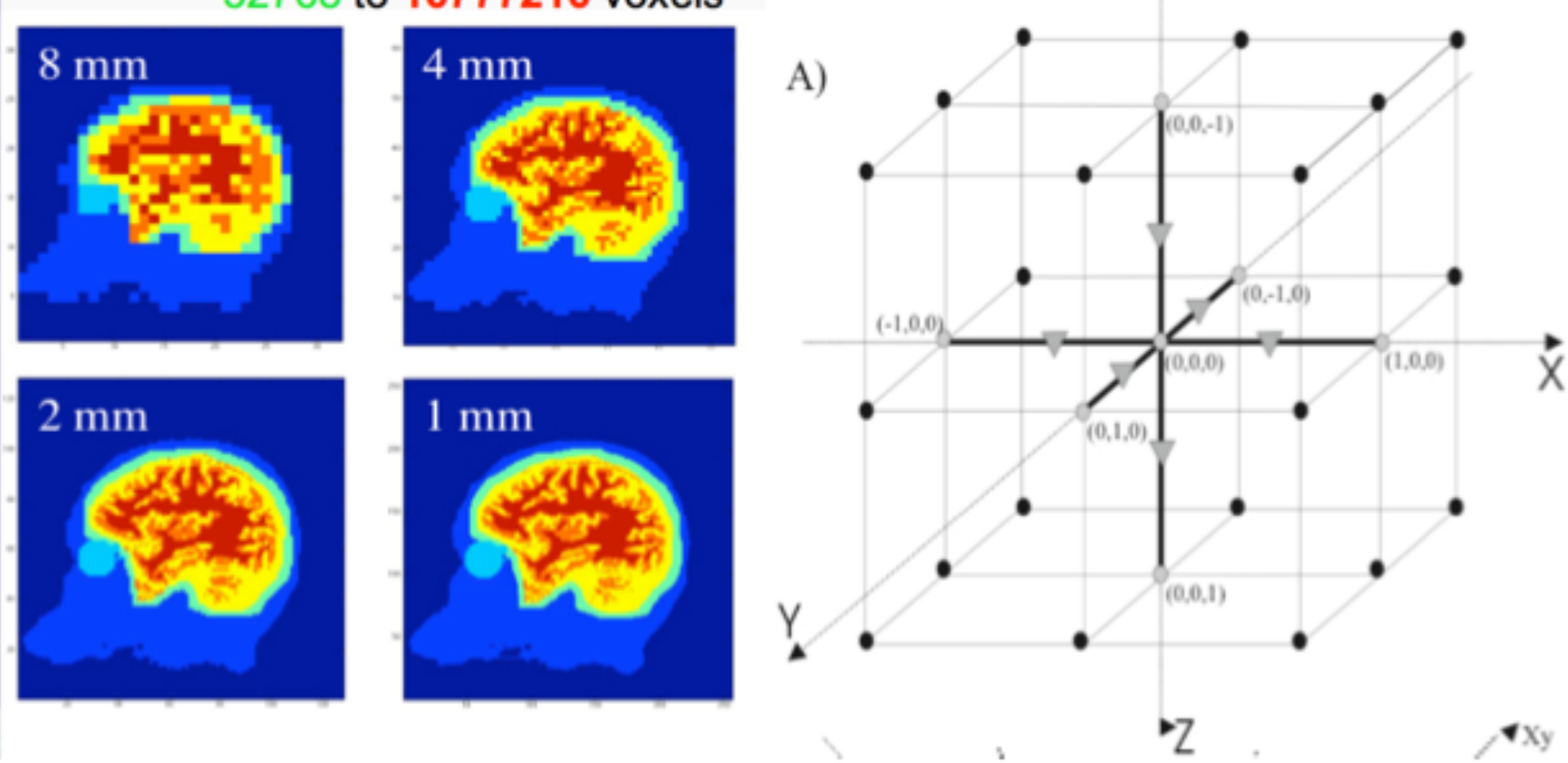
Head Models

Finite Difference Models:Role of Resolution: from 32768 to 16777216 voxels

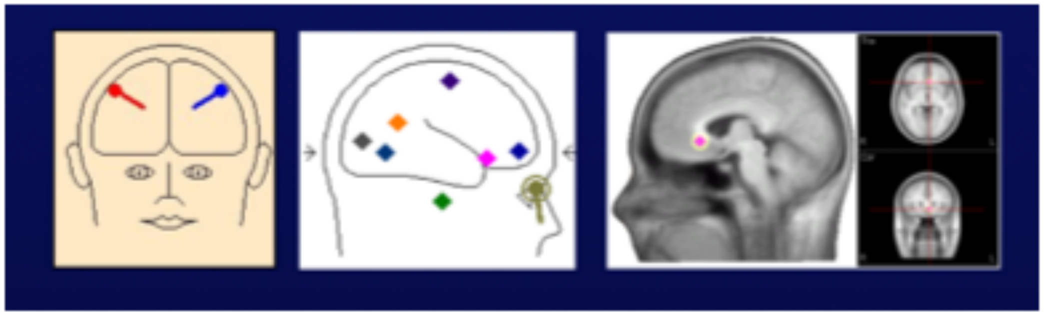


Types of Source Models

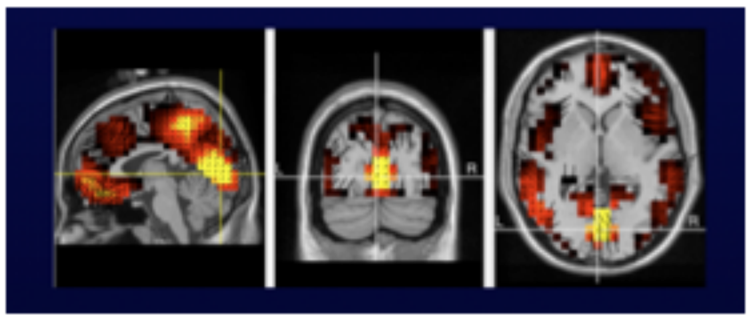
	Name	Most Useful	Notes
Spherical Model	Spherical Model "Shell"	Fast Calculation	Ignores head shape and complex geometry
BEM	Boundary Element Method	Surfaces	Great for surface models
FEM	Finite Element Method	Volumes	Easier to Calculate
FDM	Finite Difference Method	Volumes	Most Complex Calculation

Types of Source Analysis

- Equivalent Current Dipole (ECD)



- Distributed Linear Inverse (LORETTA)



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ECD

- Assumes a small number of sources can model surface topography
- Iteratively nonlinear search for location that accounts for largest proportion of variance in scalp topography
- Repeat and add more sources until percentage variance desired is accounted for
- Challenges:
  - High user involvement (low replication)
  - Have to balance time window, number of dipoles, and orientation of dipoles

Distributed Linear Inverse

- Often synonymous with Minimum Norm Solutions
- Linear mapping of scalp data to distributed sources within the brain
- All dipoles are active in the brain to different degrees
- Underdetermined

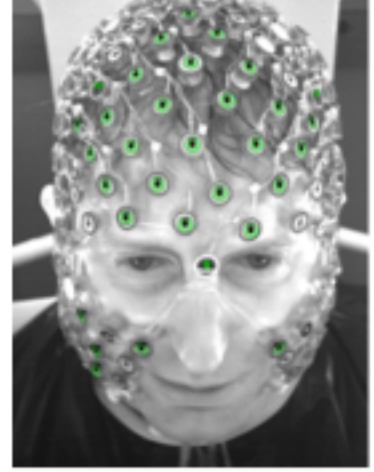
Distributed Linear Inverse

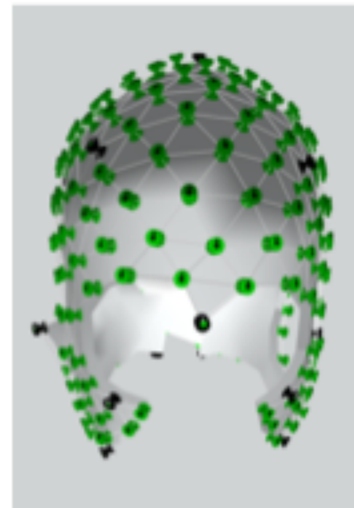
- No true/unique solution. Need to apply constraints:
  - Minimum Norm: smallest overall intensity of activation
  - Weighted Minimum Norm: Apply weights to compensate for superficial sources (smoothing)
  - Regularization - reduce the effect of random noise

Options for Source Analysis

- Best: MRI + EEG Electrode Locations (GPS) + EEG
  - Individual Head Models
- Good: EEG Electrode Locations (GPS) + EEG
  - Template Head Models with custom sensor loc
- OK: EEG
  - Template Head Models only

Electrode Coordinates

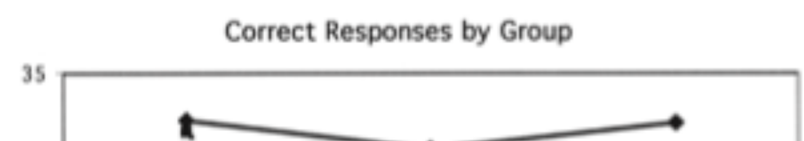




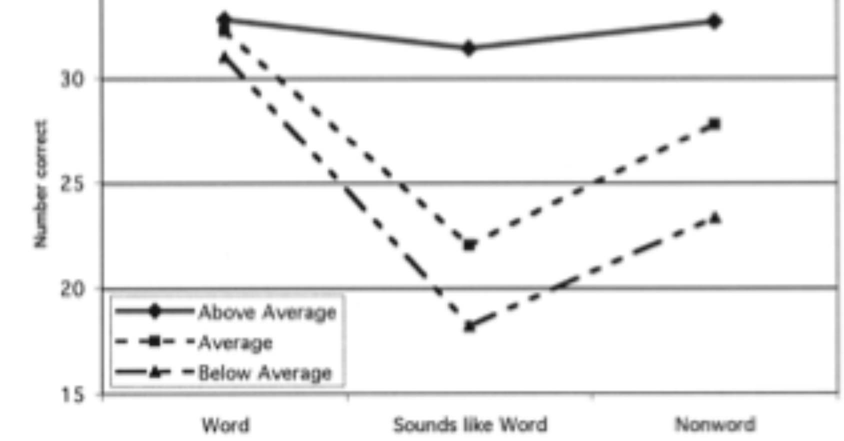
EEG and fMRI Similar Results

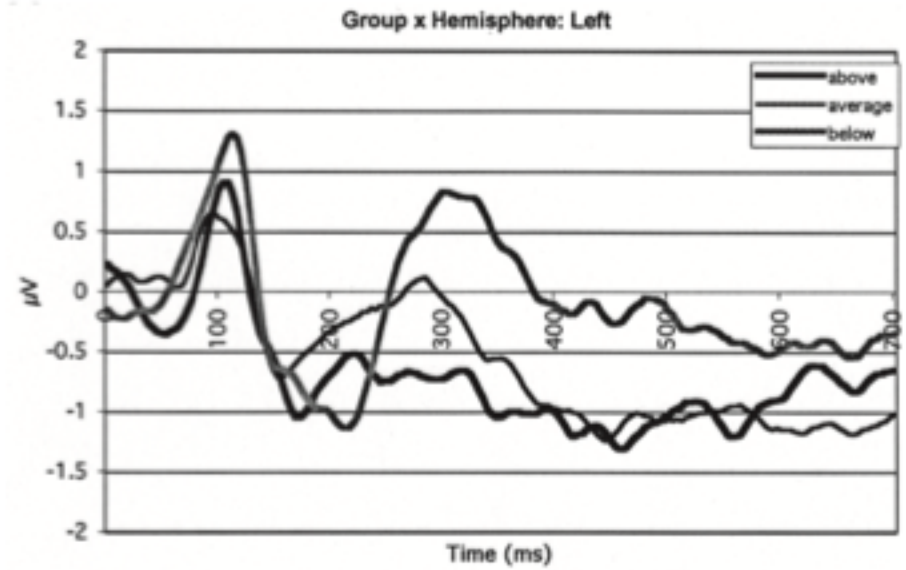
- Limited research covering language and simultaneous EEG-fMRI
- Extensive research in both fMRI and EEG showing
  - Differences between TD and RD/Dyslexia
  - Changes in brain with development of language
  - Changes in brain following reading intervention
- Converging findings

ERPs of Reading Groups



- N=27 children
- 9-12 years of age
- ERP amplitudes and peak latencies decreased as reading skills in- creased
- Hemisphere differences increased with higher reading skill levels
    - LH > RH is more proficient reading skill





D. L. Molfese, et al. (2006)

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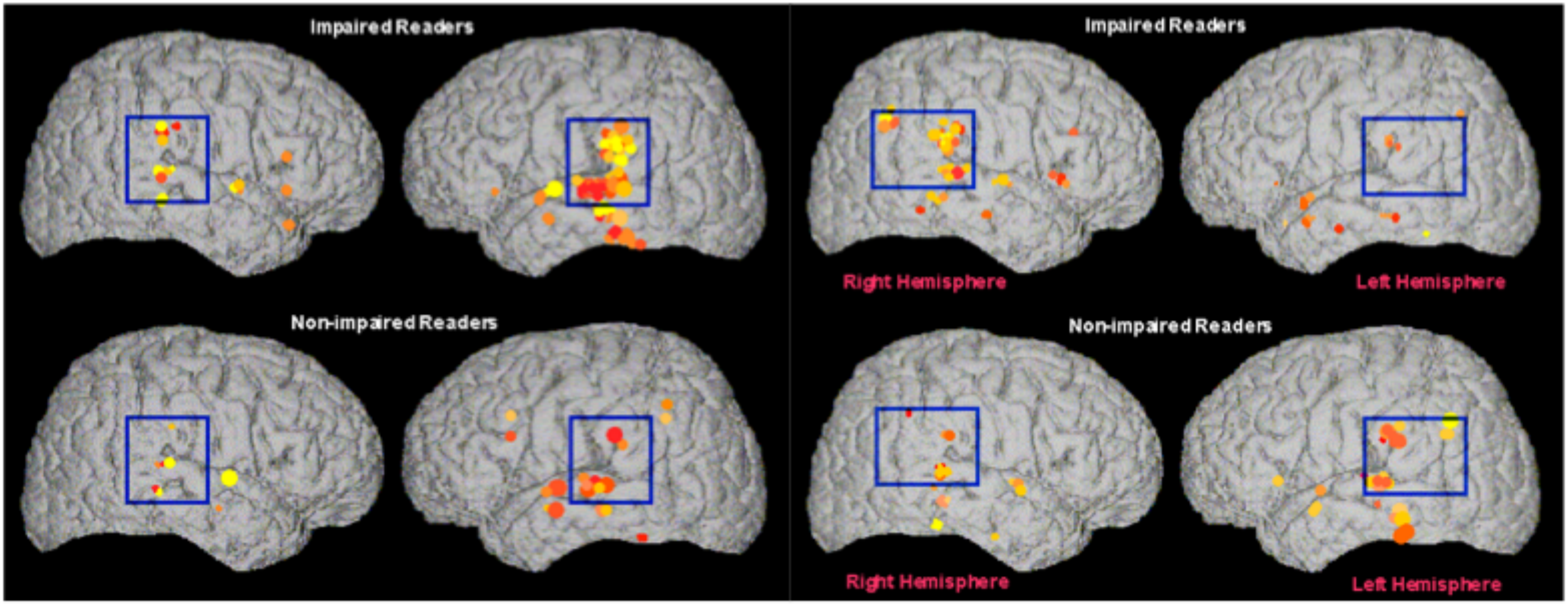
MEG of Reading Groups



Listening to Words **Reading Words**

Simos, et al. (2003)

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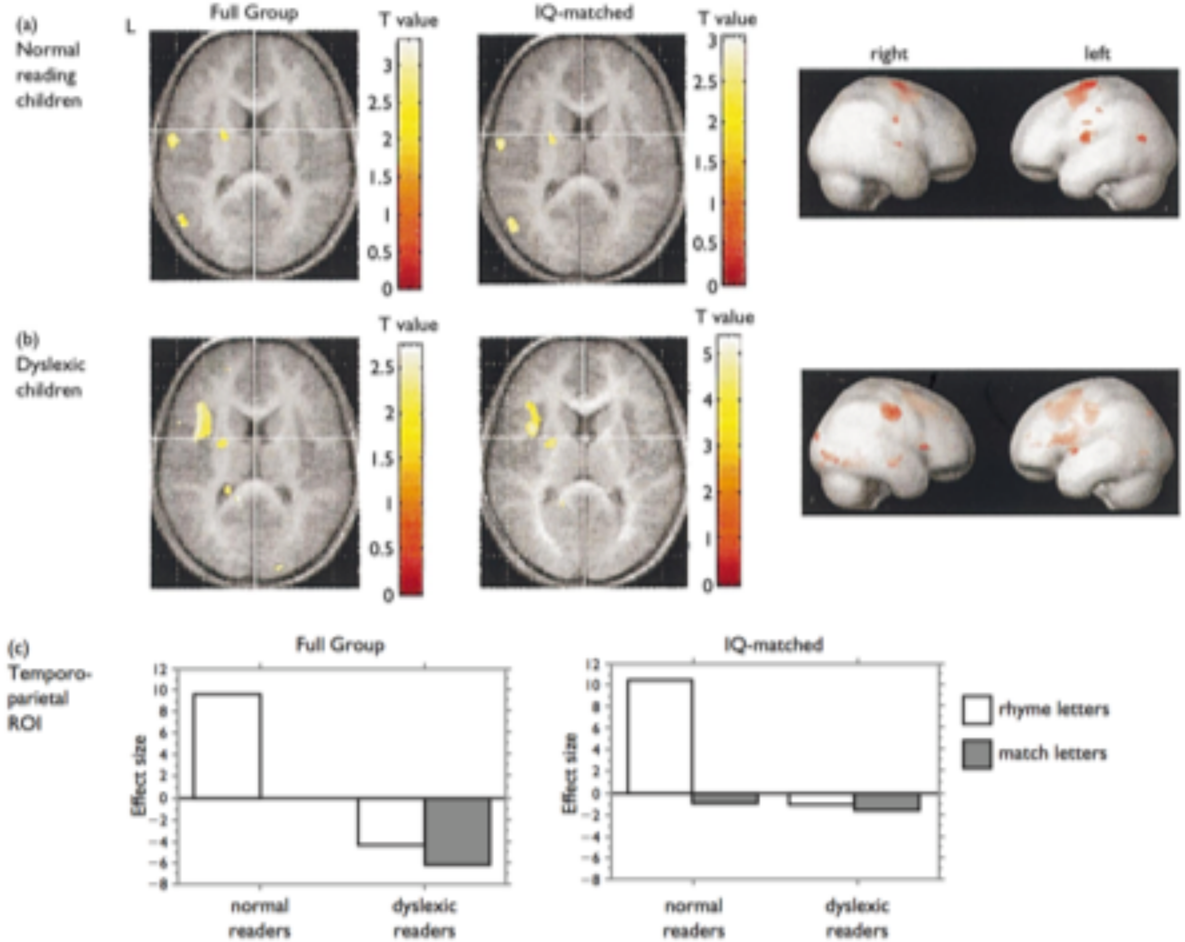
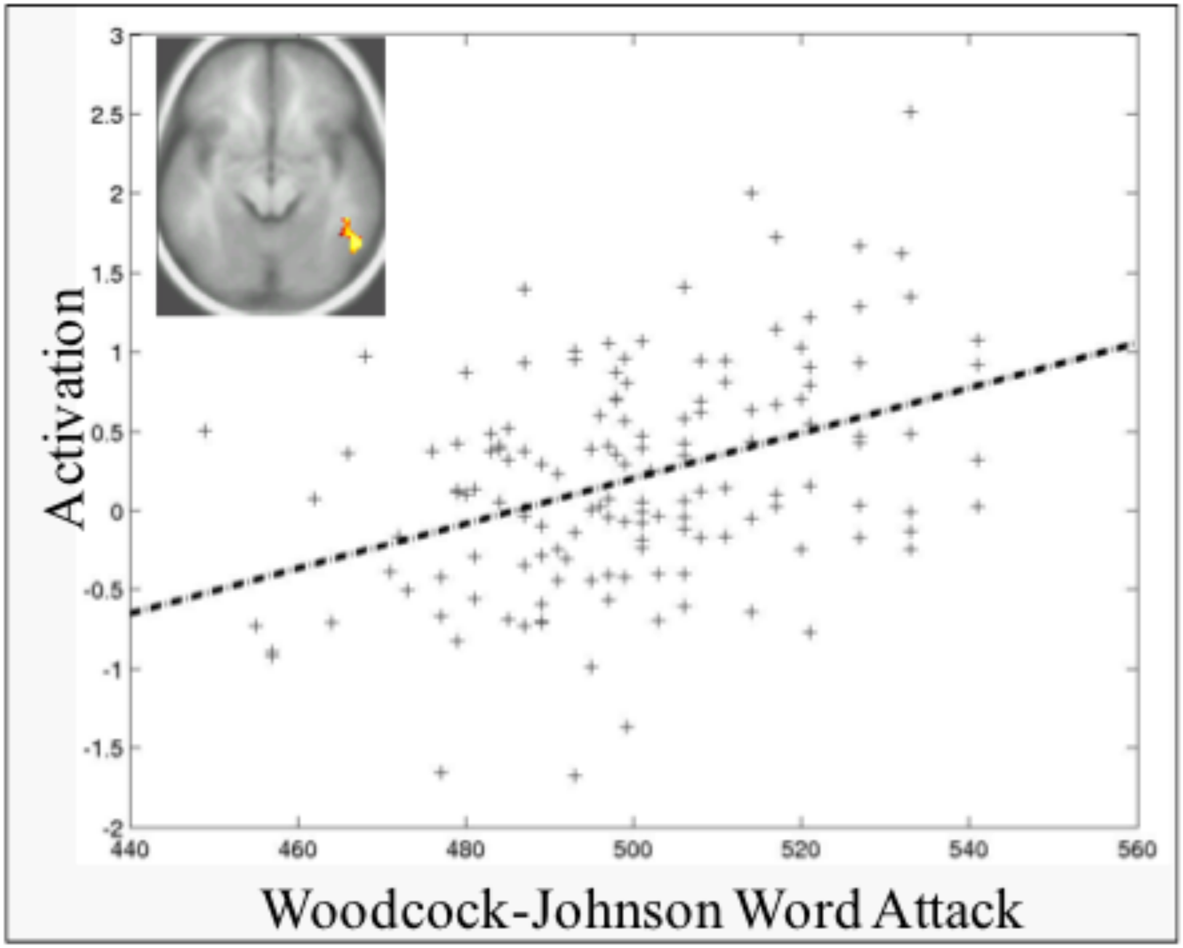
fMRI Differences RD and TD



Temple et al. (2001)

Reading Skill & VWFA



Shaywitz et al. (2002)

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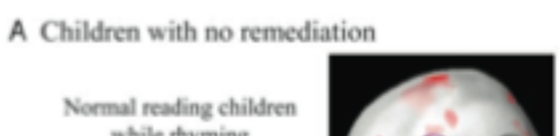
Intervention Studies

- Looking at changes in reading circuit associated with improvement in reading ability
- fMRI
- MEG
- ERP

fMRI Reading Intervention I



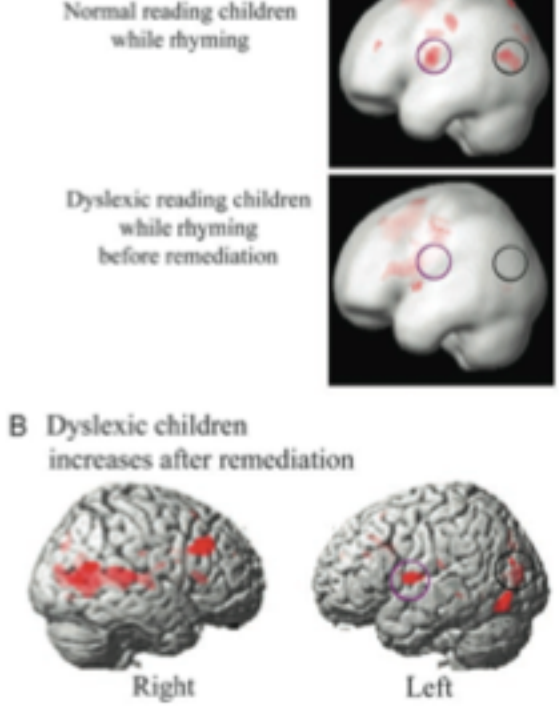


Fig. 1. Neural effects of remediation in children with developmental dyslexia. (*A*) Left hemisphere activations of control children and children with dyslexia are shown during rhyming (as compared with matching) letters ($P < 0.025$, 20-voxel threshold; ref. 12). (*B*) Brain areas that showed increased activity during phonological processing in the dyslexic group after remediation. Shown at $P < 0.01$, 20-voxel threshold. Black circles highlight left temporo-parietal region, which is disrupted in children with dyslexia and affected by remediation. Purple circles highlight the left frontal region that is active in control children and is affected by remediation in children with dyslexia.

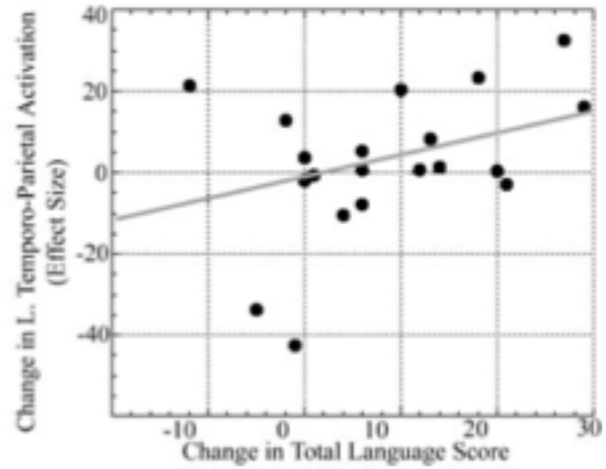
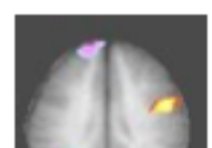


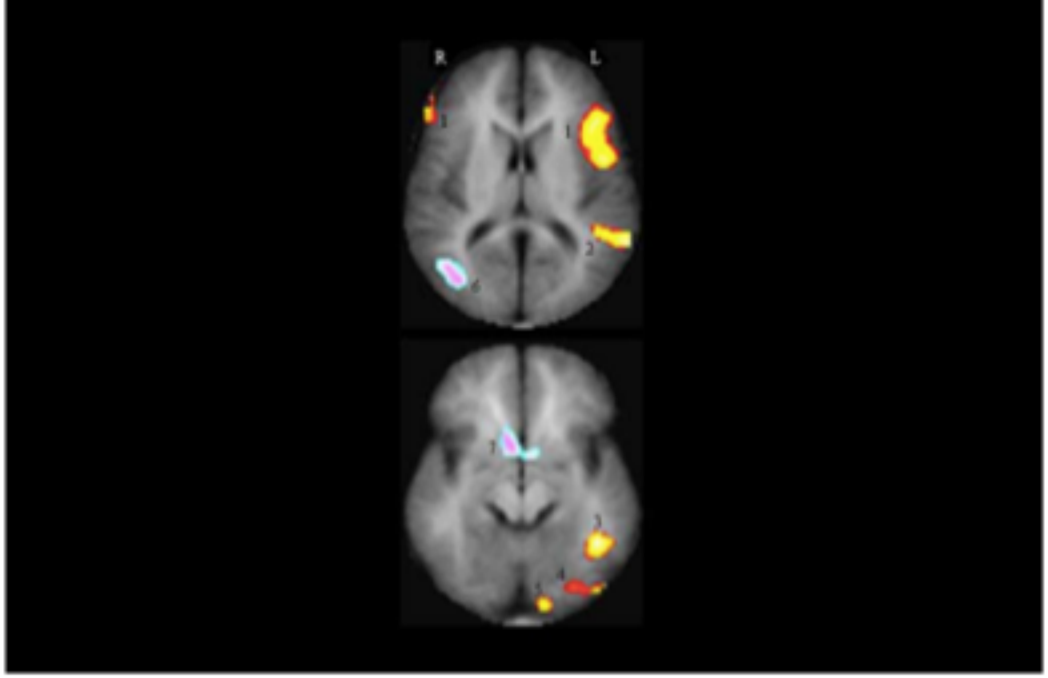
Fig. 2. Language improvement and increased brain function. Correlation between magnitude of change in left temporo-parietal ROI (BA 39) and improvement in oral language ($r = 0.41$, $P = 0.03$). Left temporo-parietal ROI encompassed brain areas that showed underactivation and increases after training in children with dyslexia. Change in effect size is on the vertical axis; change in total language score (CELF-3) is on the horizontal axis. Effect size is the weighted sum of parameter estimates from the multiple regression for rhyme vs. match contrast pre- and posttraining.

Temple, et al. (2003)

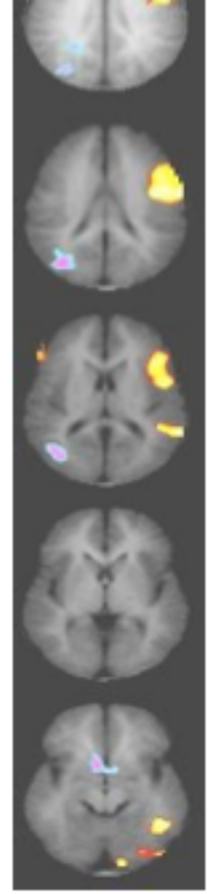
National Institute of Mental Health

fMRI Reading Intervention II



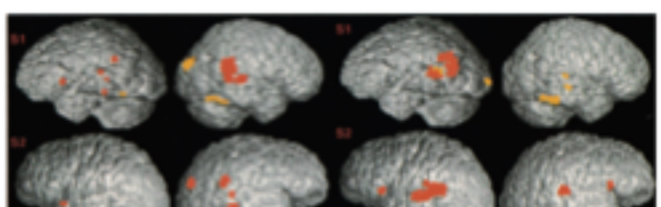


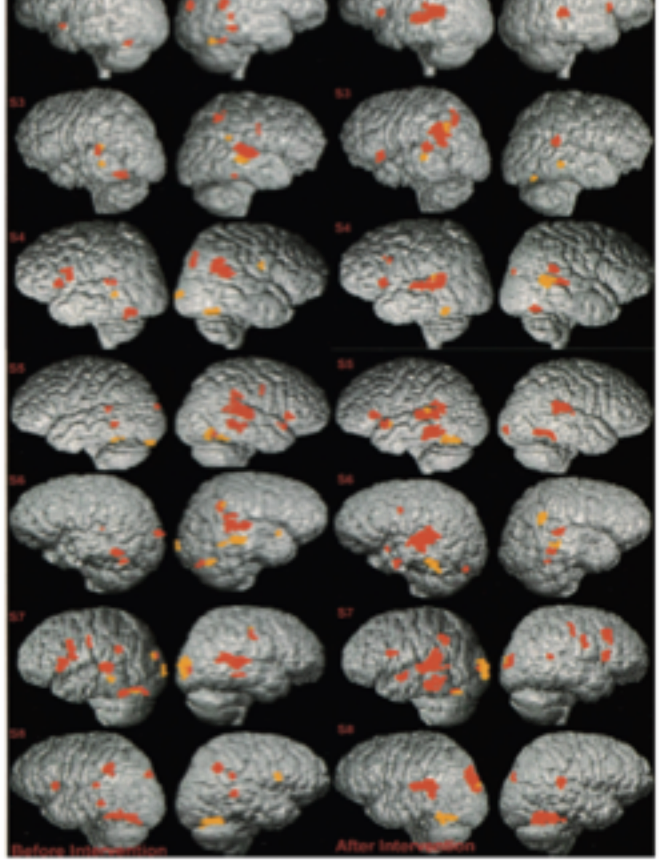
Year 3 - Year 1



Shaywitz, et al. (2004)

MEG Reading Intervention

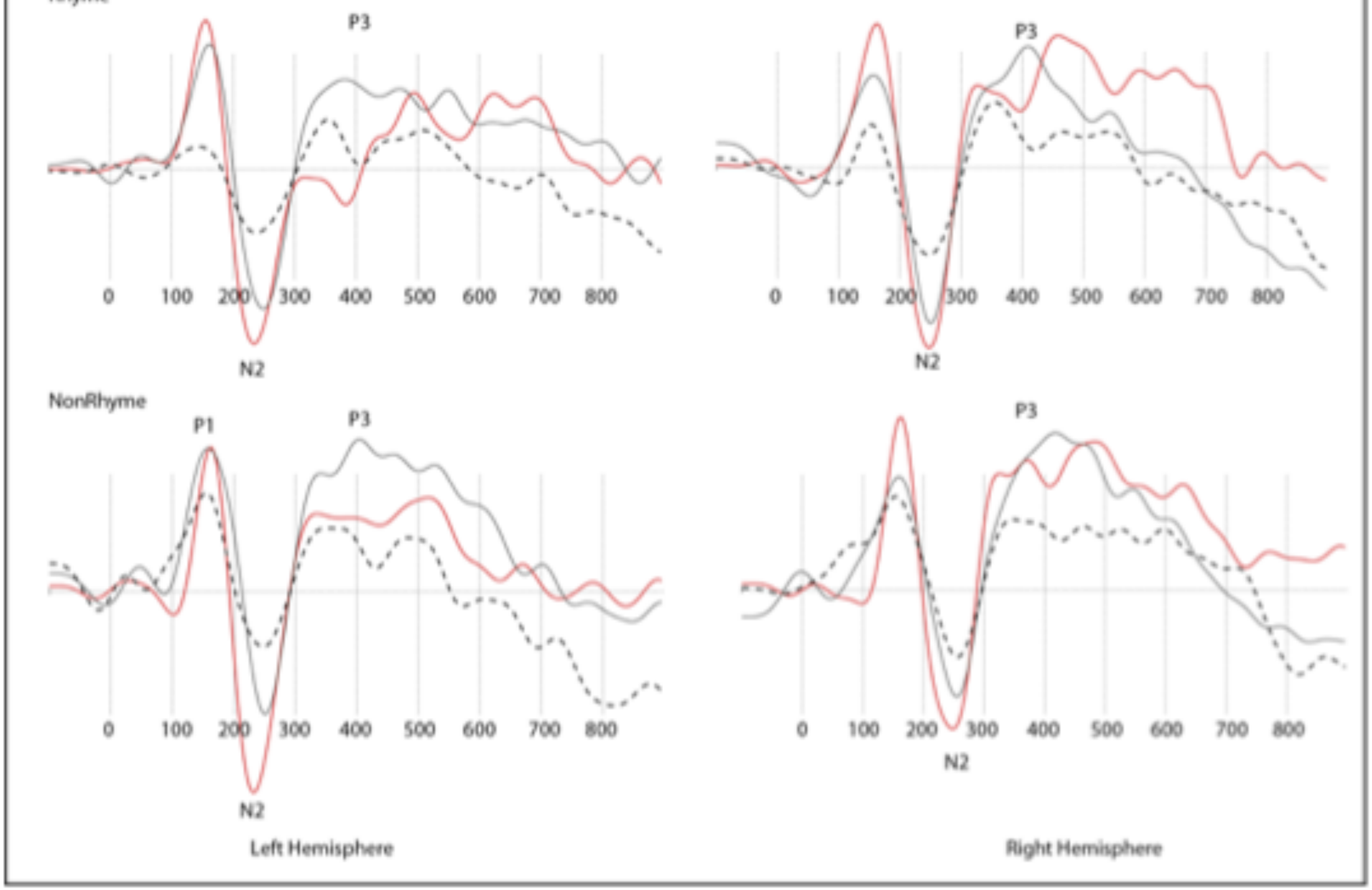




Pre Post

Simos, et al. (2003)

ERP Reading Intervention



Molfese, Denton, & Fletcher (2013)

National Institute of Mental Health

Classifying Intervention

- Discriminant Function - $p<0.003$

	TD	AR	IR
TD	5	3	
AR	2	6	
IR		1	7

	Reading >= GL	Reading < GL	
Reading >= GL	16		96%
Reading < GL	1	7	

General Themes

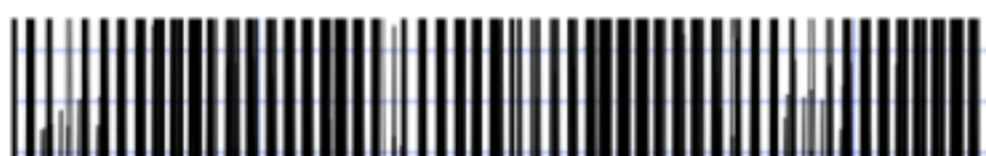
- Activation differences between good and poor readers
- Modulation of parts of the reading circuit
- Laterality differences
- Reading Intervention leads to “normalization” of the reading circuit and in some cases “compensatory” activation

The Advantages to Simultaneous EEG-fMRI

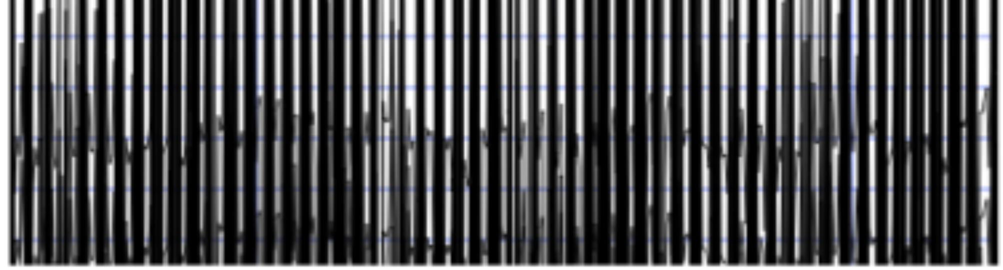
- Quite a bit of information can be gathered from separate sessions of EEG and MRI sessions of EEG and MRI

- The real benefits are:
  - Same environment in both cases (inside an MRI)
  - Looking at individual trial modulation of either ERP/ BOLD
  - Looking at coherence and resting state relationship at the same time

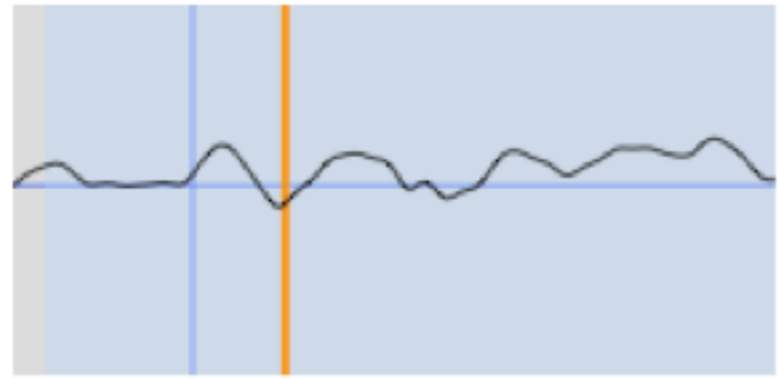
Artifacts



- MR Artifacts



  - Caused by the gradients
- Ballistocardiogram (BCG)

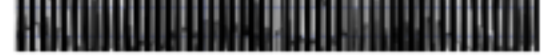


  - Caused by movement of the electrode within the magnetic field

Artifact Removal

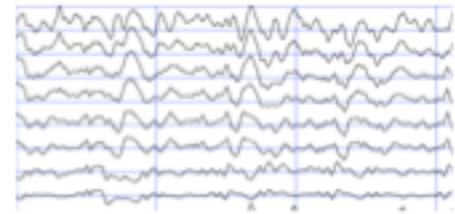
Raw Signal

- Gradient Artifacts



- Fairly straightforward to remove
- Template subtraction

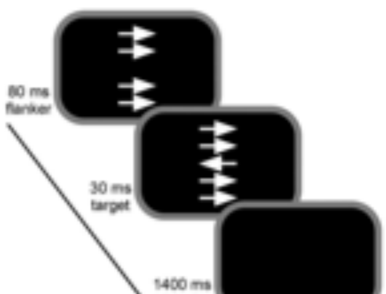
Artifact Removed

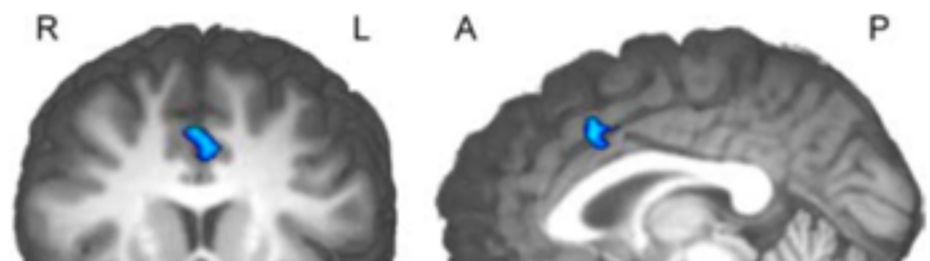


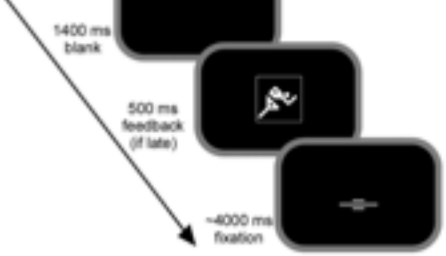
- BCG Artifacts
  - More prominent on the facial electrodes
  - Follows the heartbeat by ~250 ms
  - PCA to model the artifact, remove, reconstruct

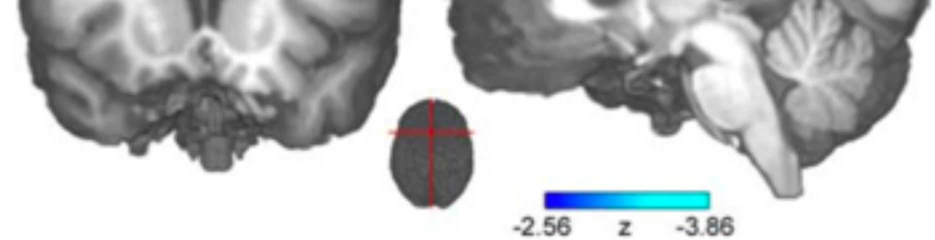
BCG Removal

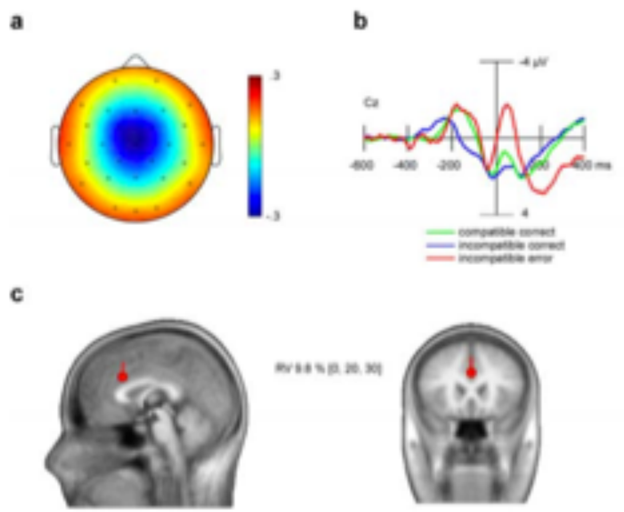
Flanker Example

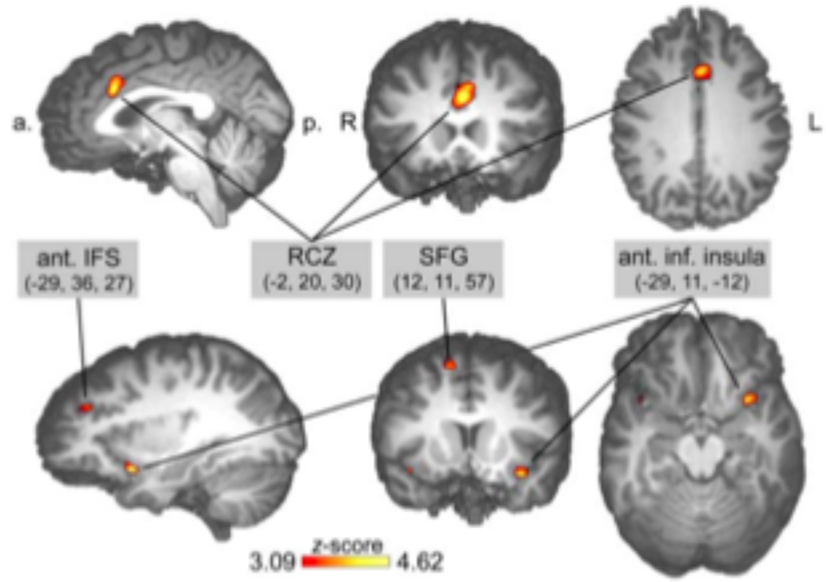












Debener et al. (2005)

“Most” Source Analysis

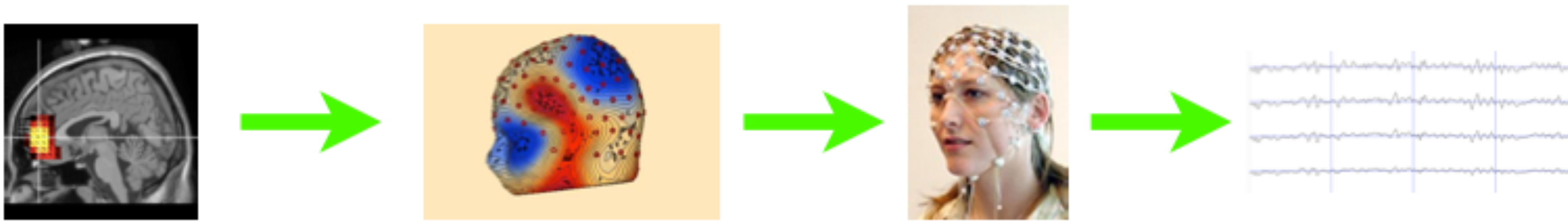
- Collect EEG Data (this is the hardest part)
- Grand Average all of your data

- Grand Average all of your data

- Pretend all of your subjects had the same brain and same electrode coordinates

- Plot out sources in the brain using some minimum norm method

- Declare victory, publish a paper

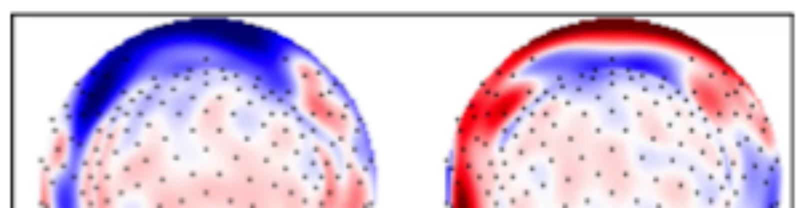


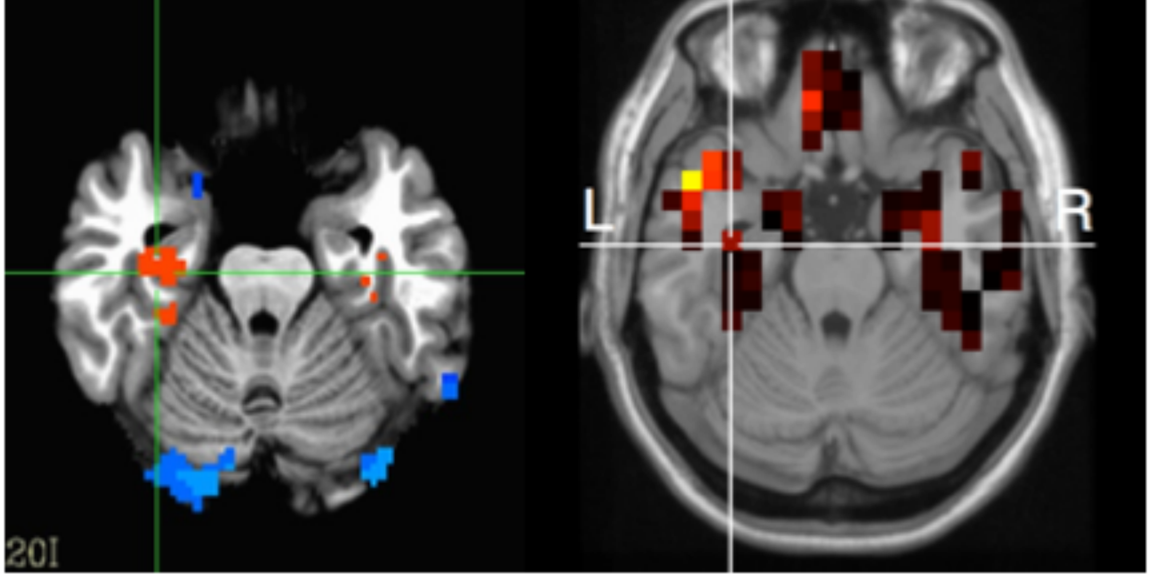
Is Source Space the Answer?

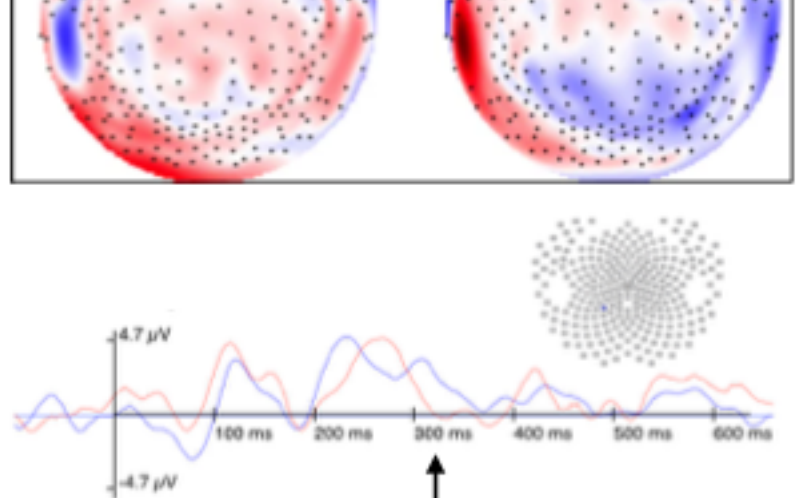
- Advantages

- Able to overlay EEG and fMRI data
- Numerous softwares out there that can do it!
- Disadvantages
  - How do you deal with the temporal domain? Peak picking?
  - How to deal with individual differences?

Difficulty of Source Space



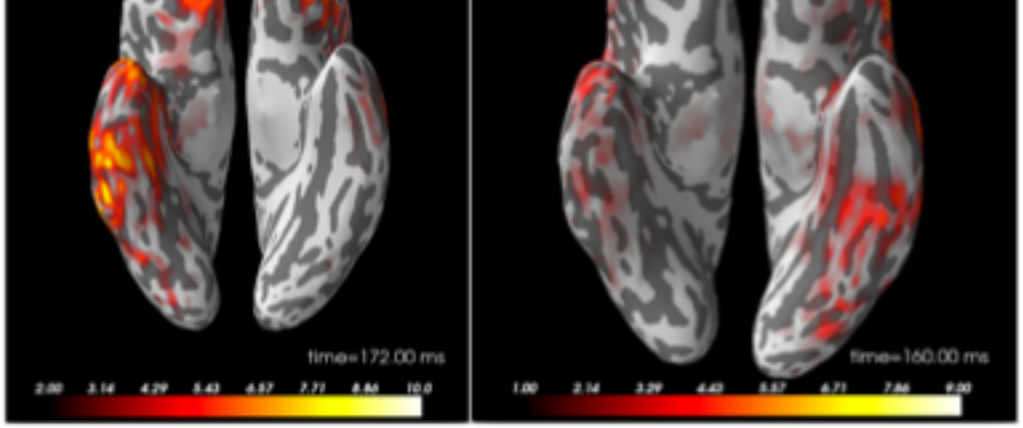




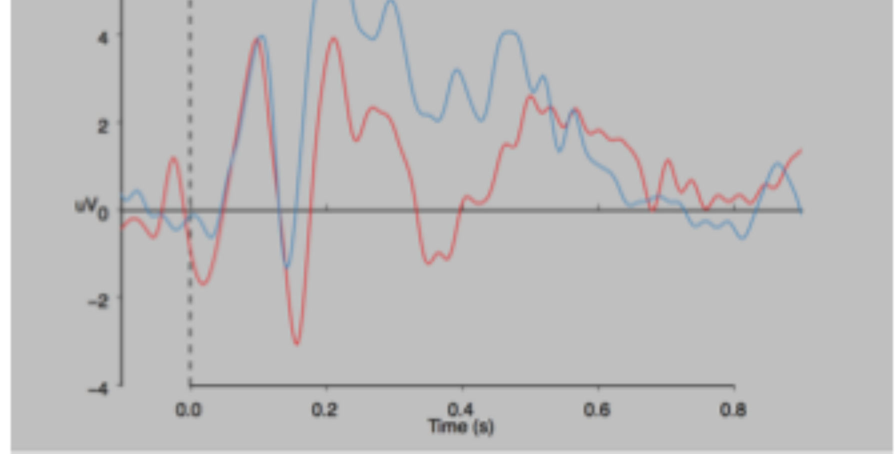
Parahippocampal Activation to P300

N170 Faces / Characters

R L



Faces Characters



Left FF

Questions?

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