## Neuropsychiatry and Quantitative Electroencephalography in the 21st Century

Neuropsychiatry, October, 1(5): 495-514 (doi: 10.2217/npv.11)

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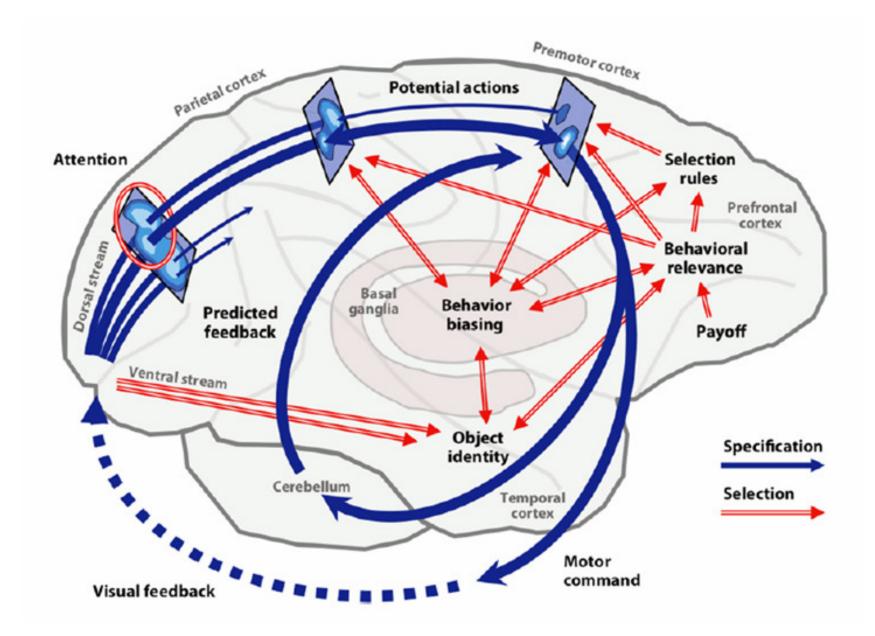
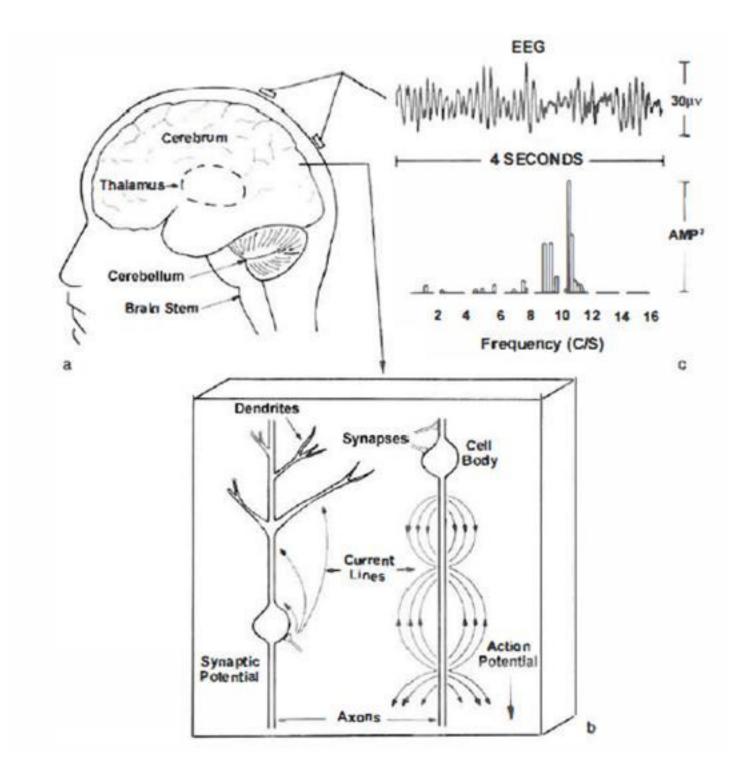
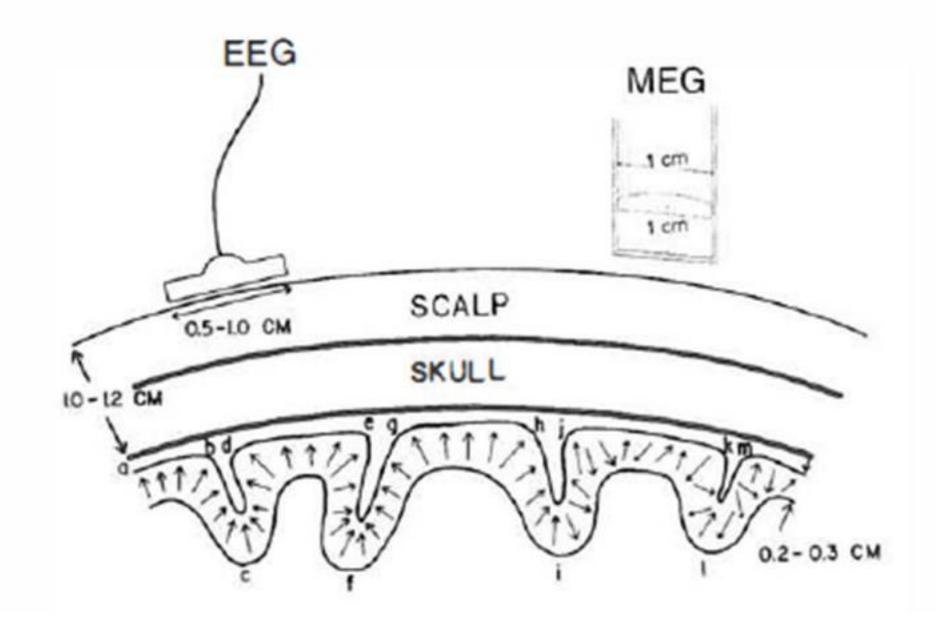


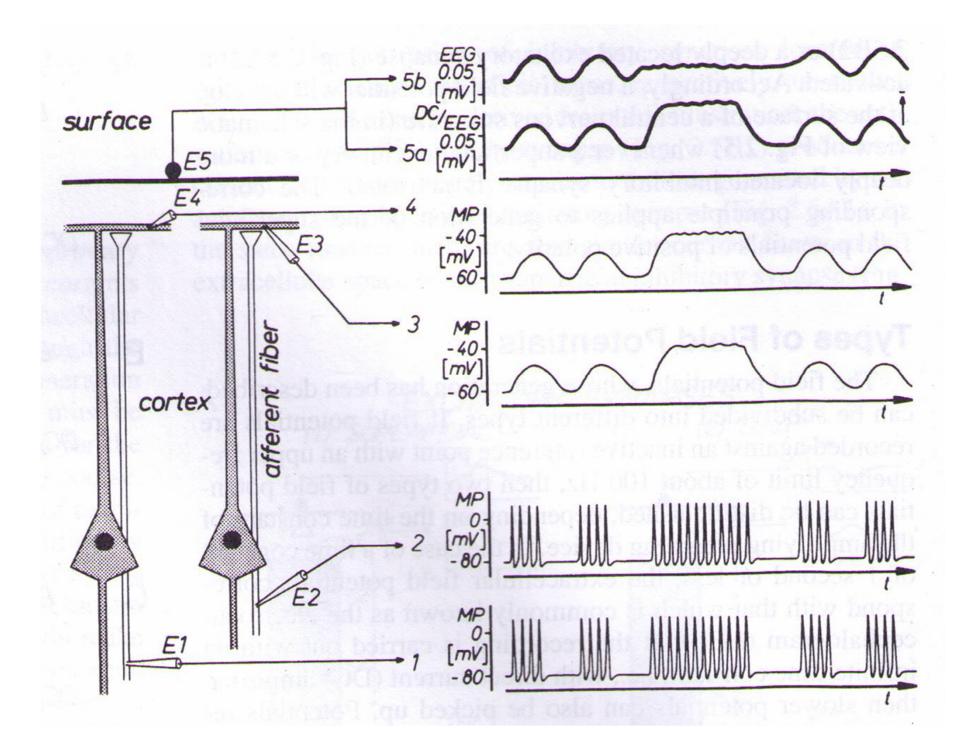
Illustration of brain information flow that can only be measured by the electroencephalogram using computers. Information flow – Millisecond Match-Mismatch From Rabinovich et al, 2012

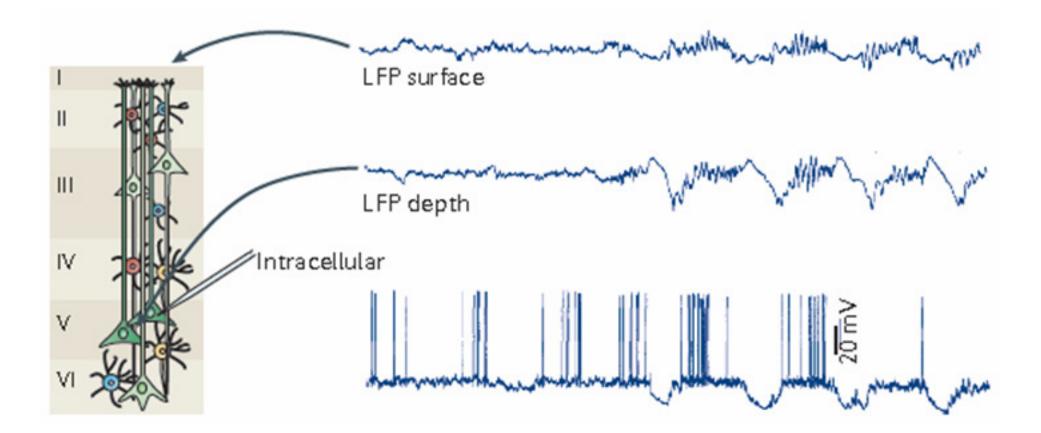
# **Genesis of the Human Electroencephalogram - EEG**

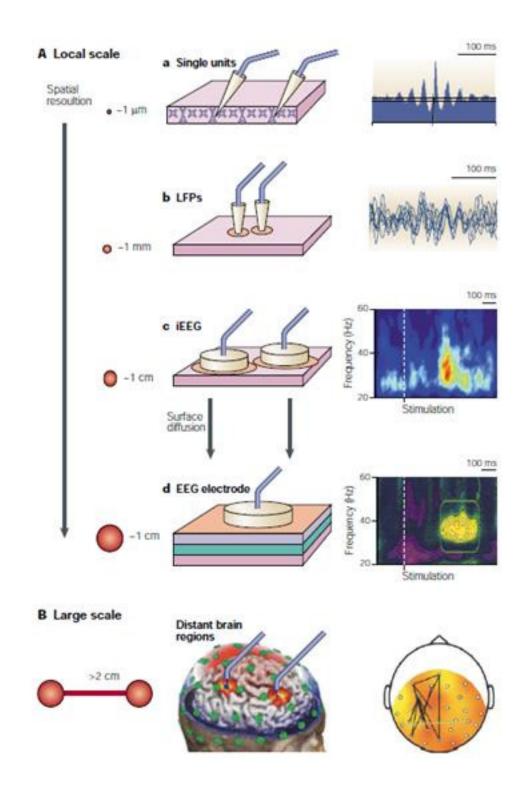
- **1- Pyramidal Neuron Dipoles**
- 2- Oscillations In an Approx. 2mm thick sheet
- **3- Summated Local Field Potentials (LFP)**
- 4- Amplitude = Proportion of Synchronous/Square Root of Proportion of Asynchronous Generators
- **5- Pacemakers and Resonance**

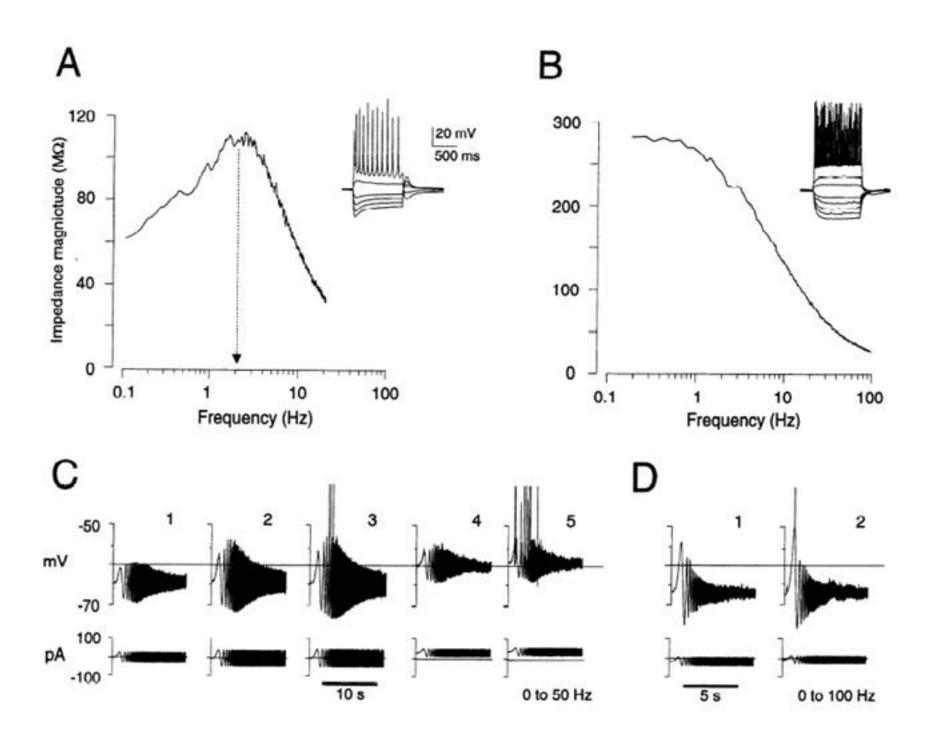


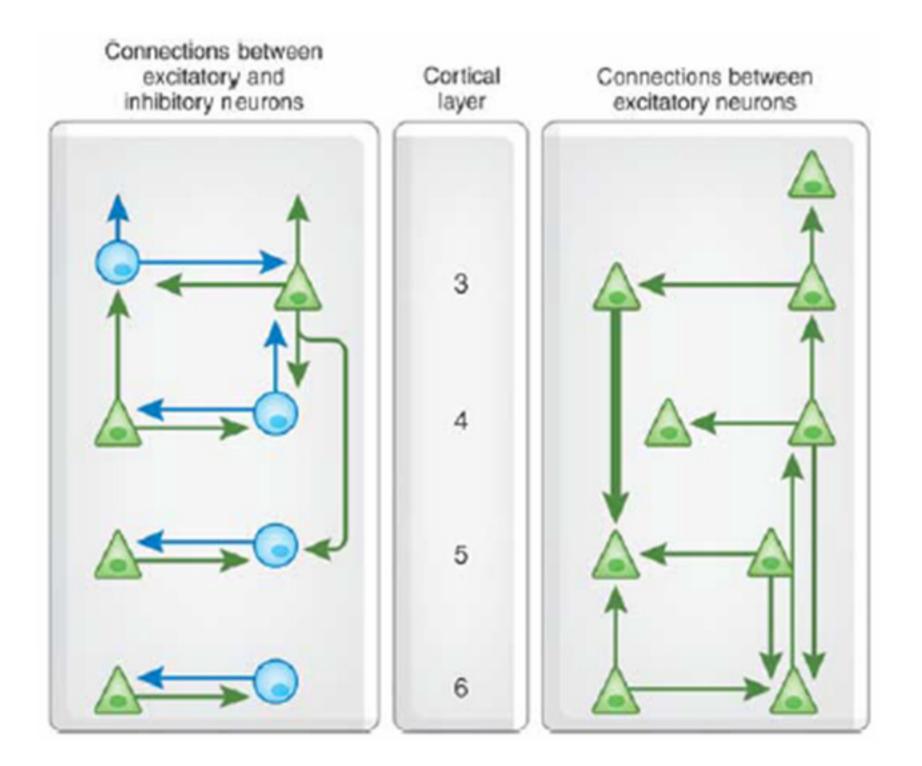


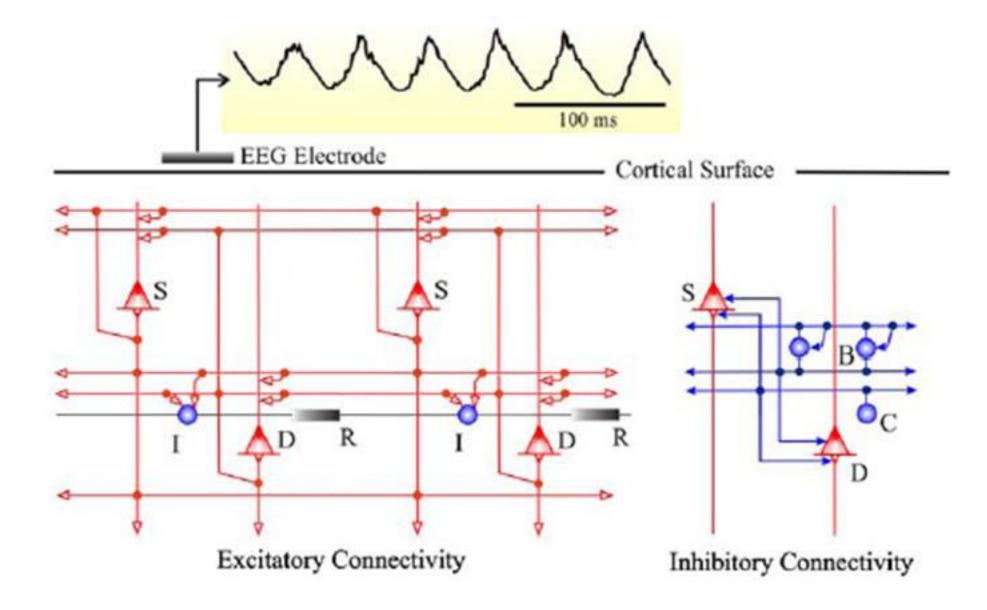


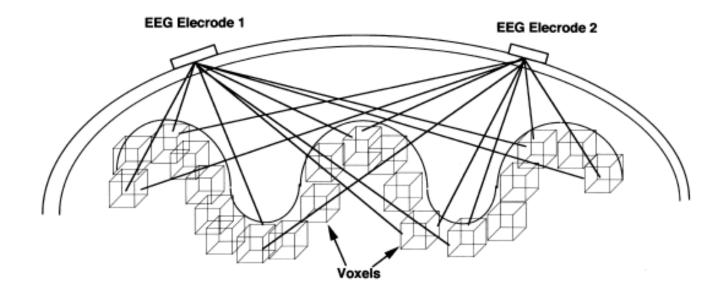


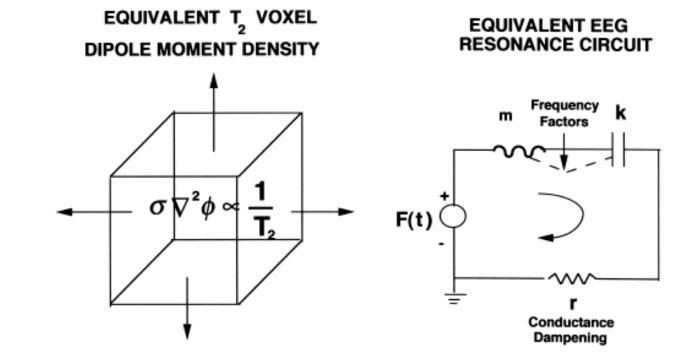


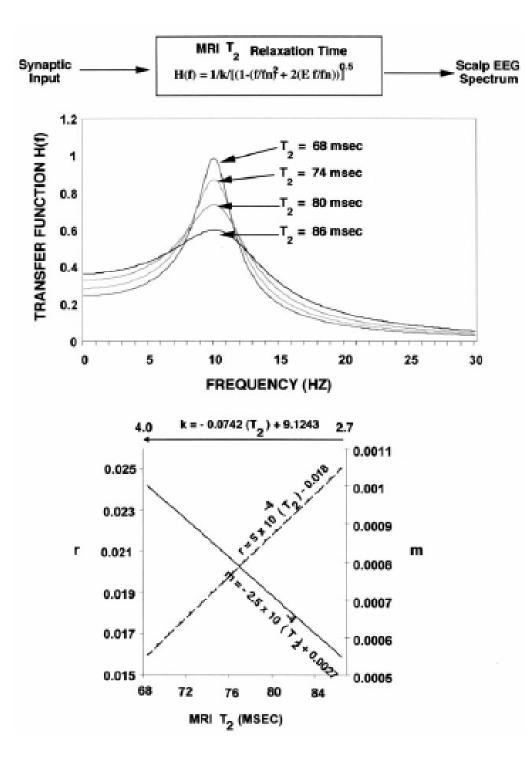






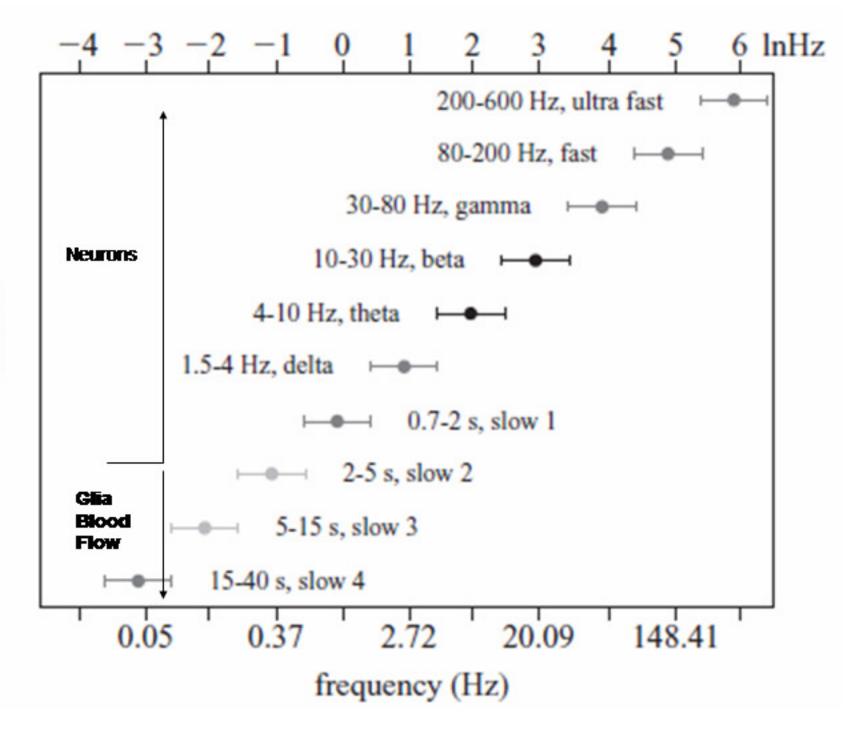






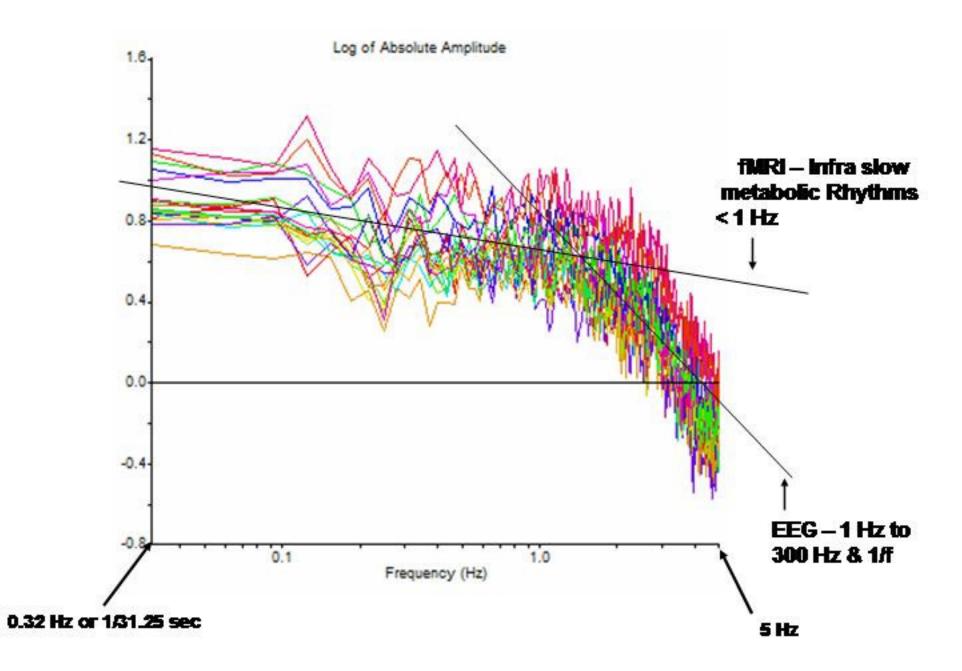
# **Frequencies of the EEG**

All Pyramidal Neurons can Oscillate form approx 1 Hz to 300 Hz
Membrane Potential & Ca++, Na+, K+ ionic conductance 1 – 20 Hz
Pacemakers in Limbic, Thalamic and Cortical systems
Local Inhibitory Feedback

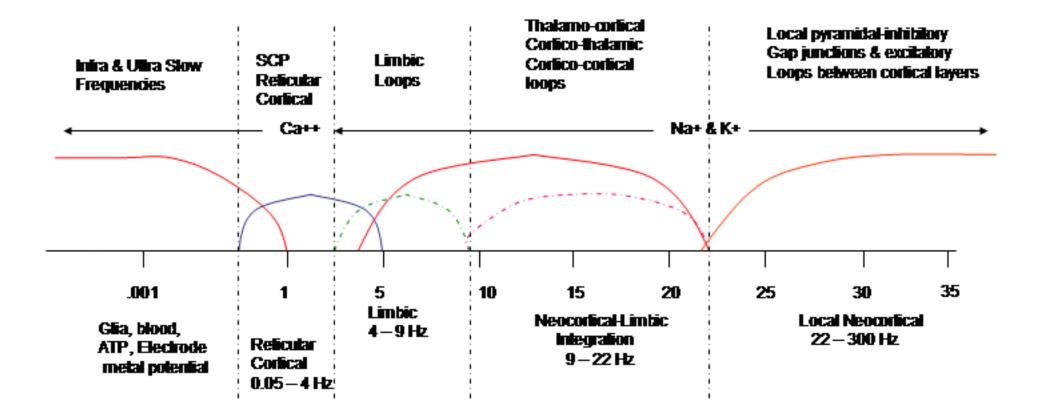


Classes

### Two Compartments of the Frequency Spectrum of Bursts in EEG Absolute Amplitude



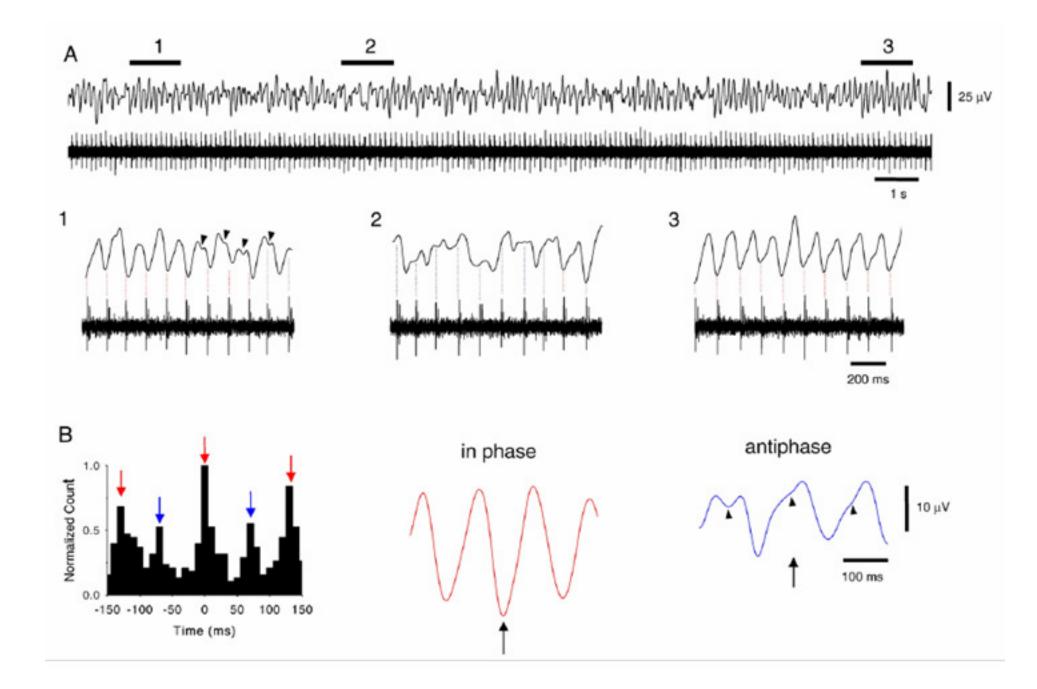
## Cross-Frequency Phase Lock and Phase Shift Spectrum



Frequency (Hz)

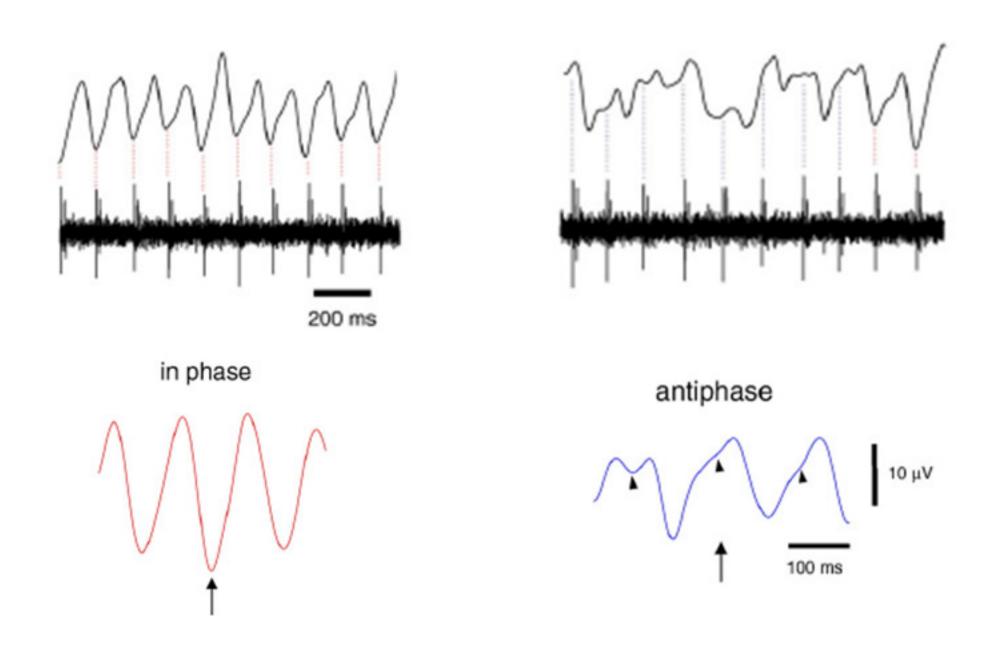
## **In-Phase vs Anti-Phase**

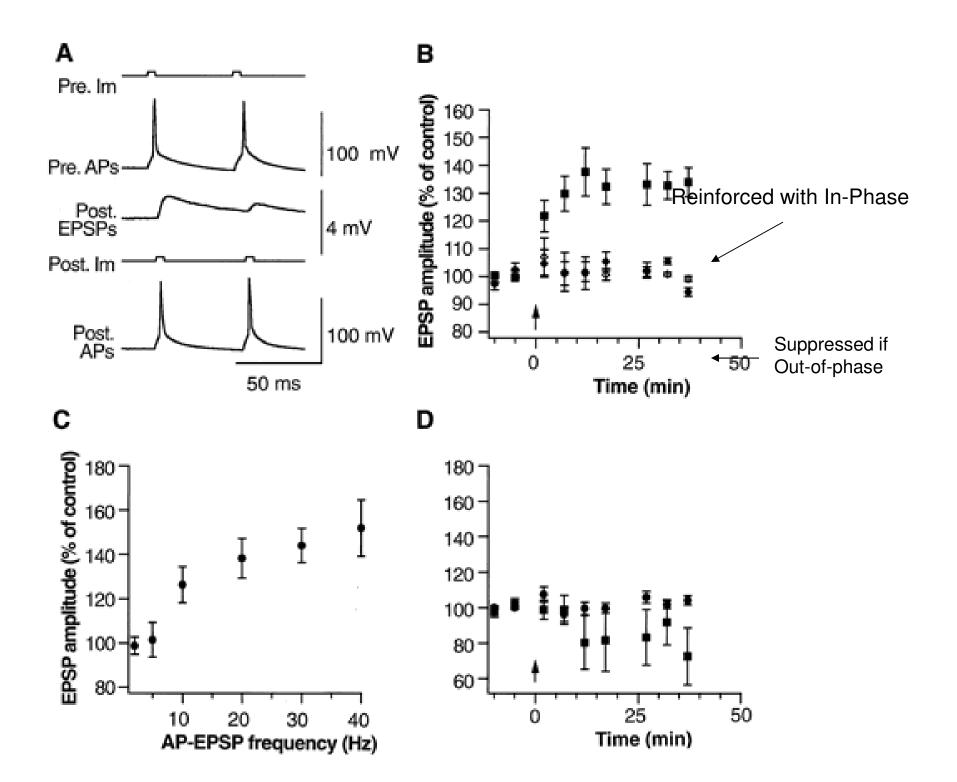
# How Neurons are Selected for Brief Periods of Time

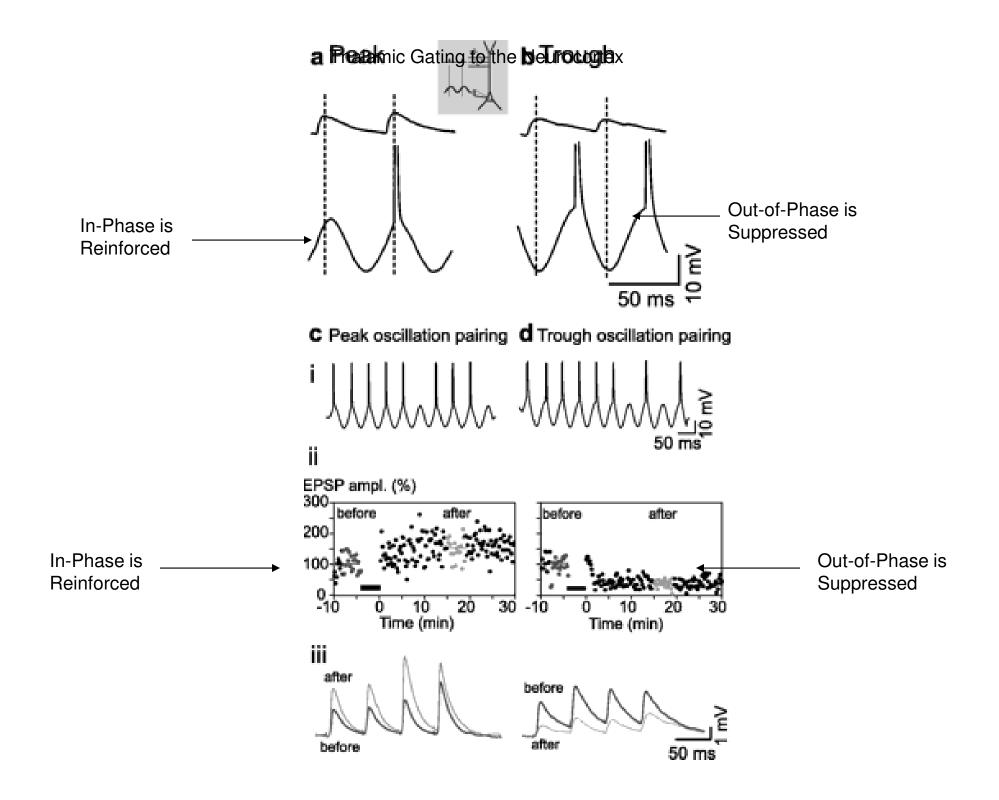


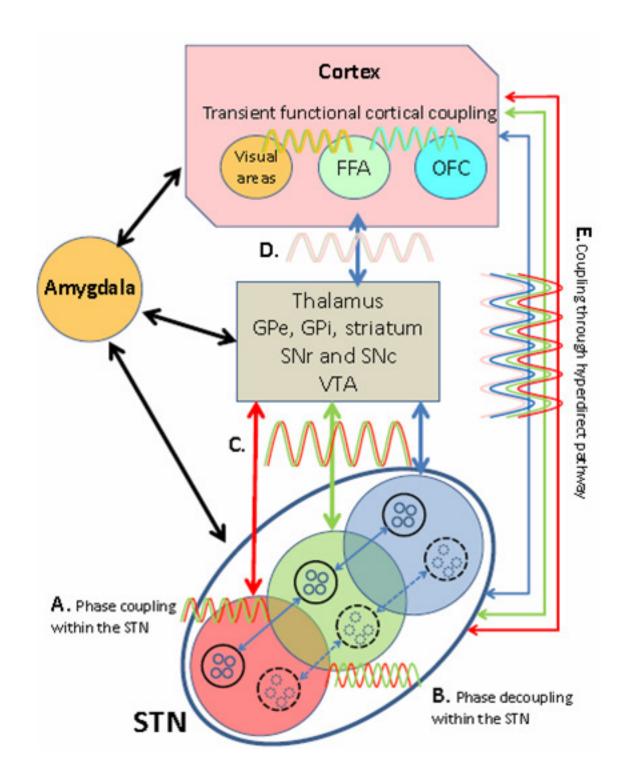
#### LFPs & In-Phase Action Potentials

LFPs & Anti-Phase Action Potentials



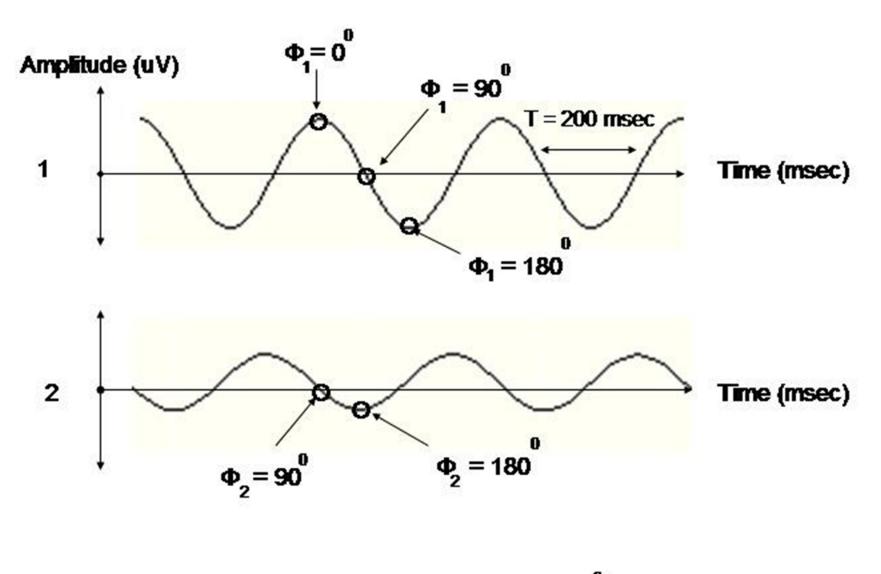






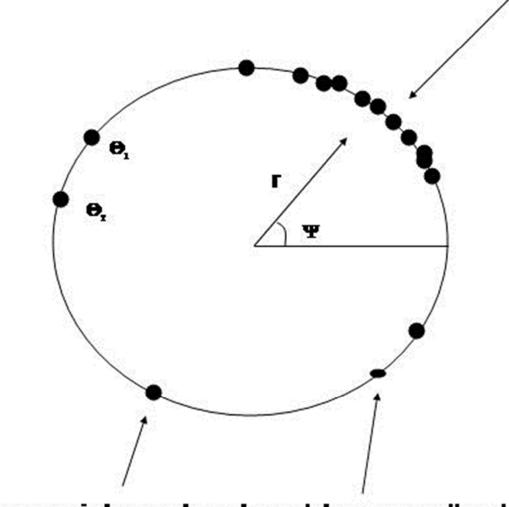
What is EEG Phase Difference and Coherence

Note: ICA & PCA Reconstruction Obliterate the Phase Differences Present in the Original EEG Recording



Phase Difference =  $\Phi_1 - \Phi_2 = 90^{\circ}$ 

Coherence is high when phase delays are clustered or grouped together. Magnitude of coherence = r

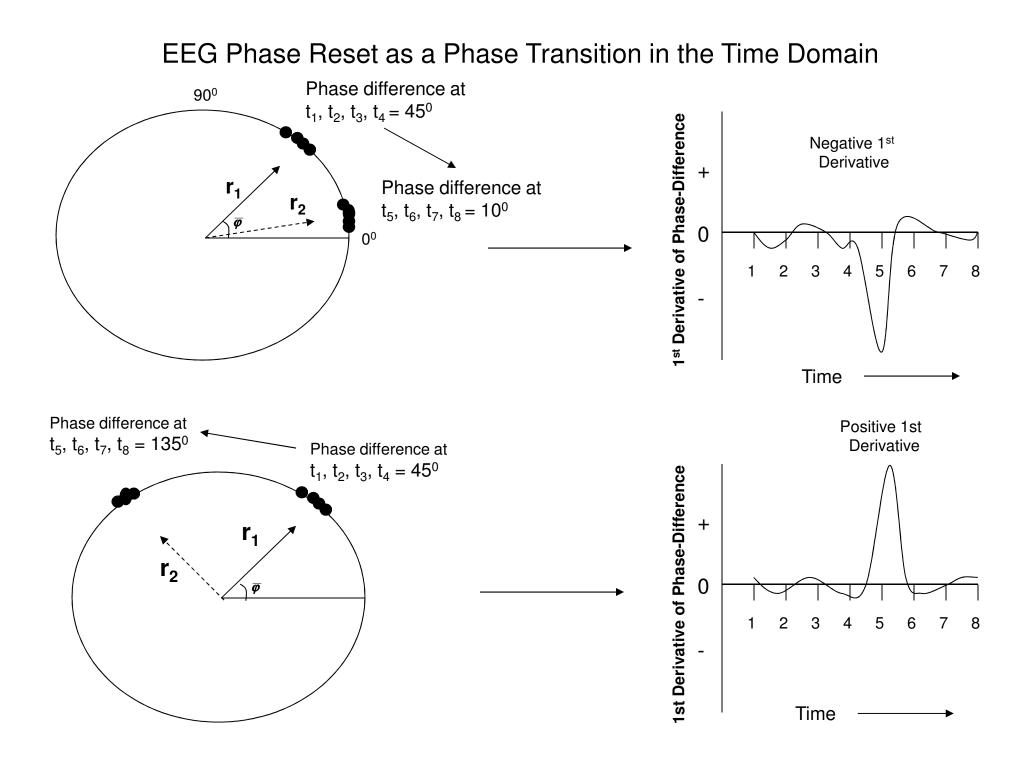


Coherence is lower when phase delays are scattered

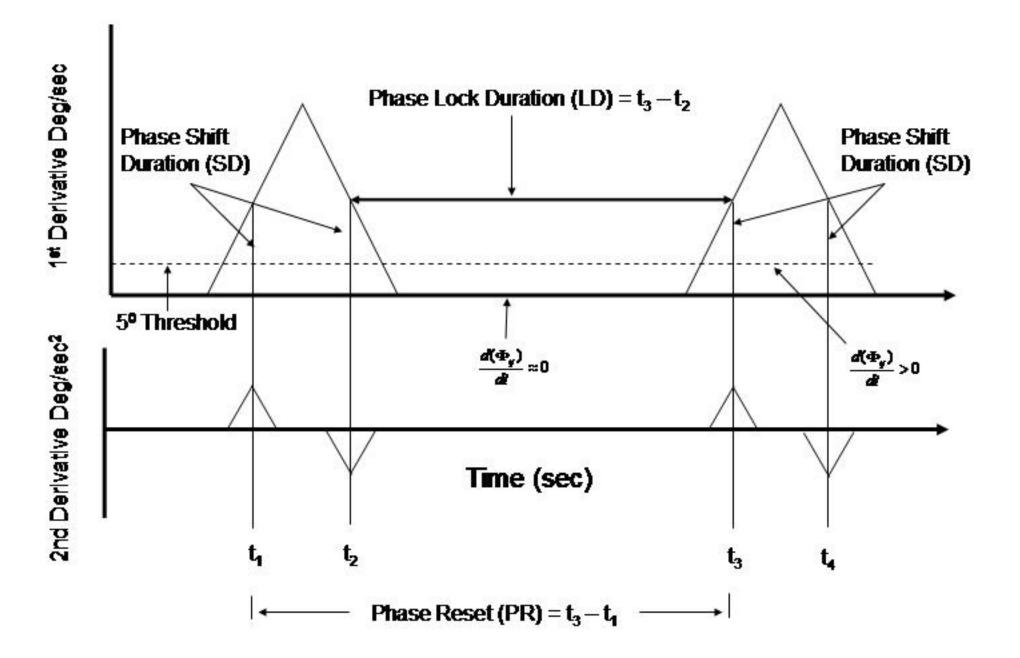
How to Measure Phase Shift and Phase Lock

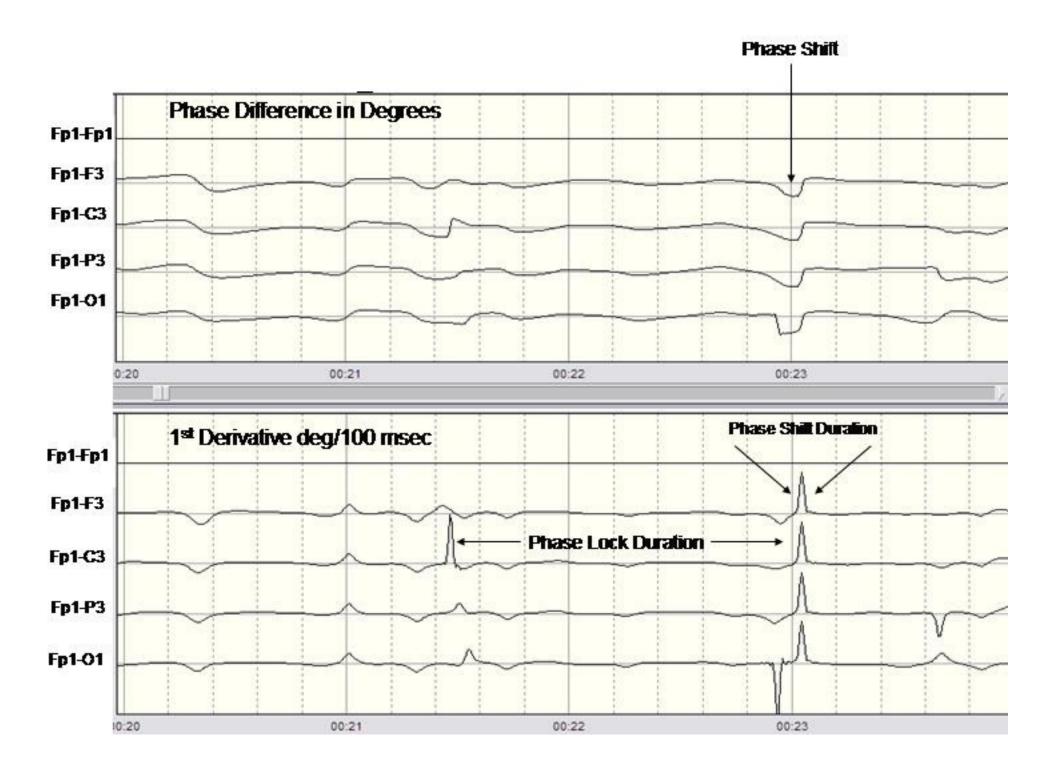
# Phase Reset and Neural Resource Selection and Allocation

Note: ICA Obliterates Time & Phase Differences Between Channels and Cannot be Used for These Type of Analyses

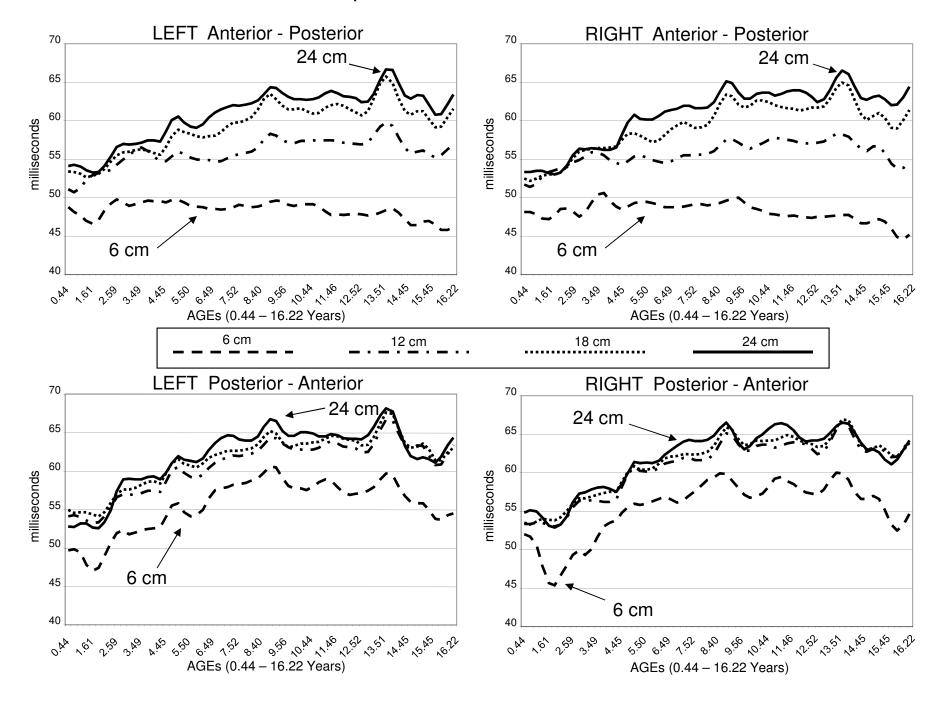


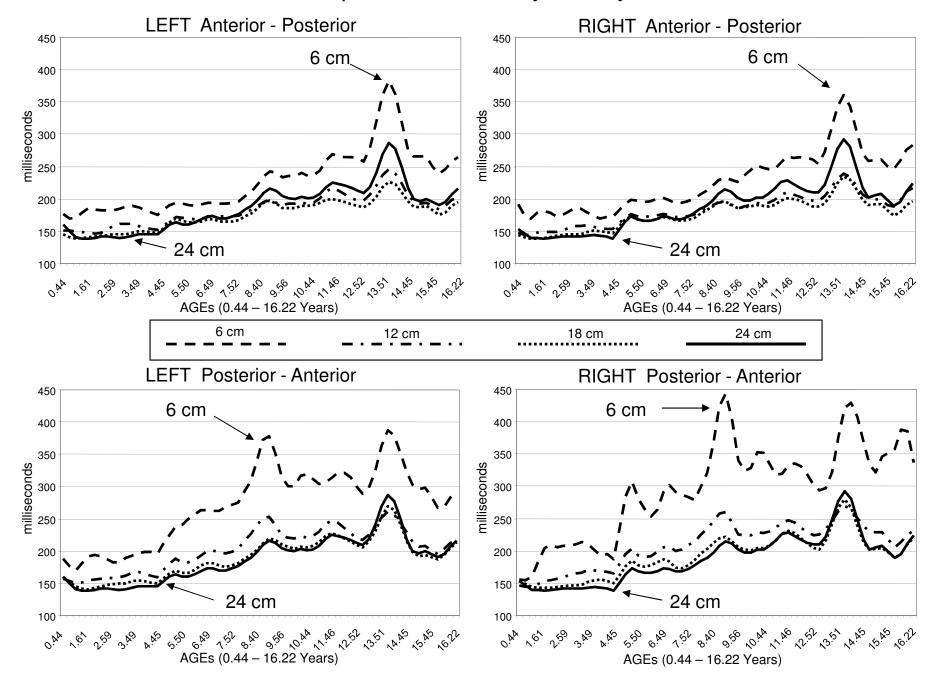
## **Phase Reset Metrics**





**Development of Phase Shift Duration** 





### **Development of Phase Synchrony Interval**

Co		Table V tween Coherence Phase Synchrony (	and Phase Shift (C Stability)	haos)
		Chaos	Stability	
	Coherence	- 0.547	0.863	

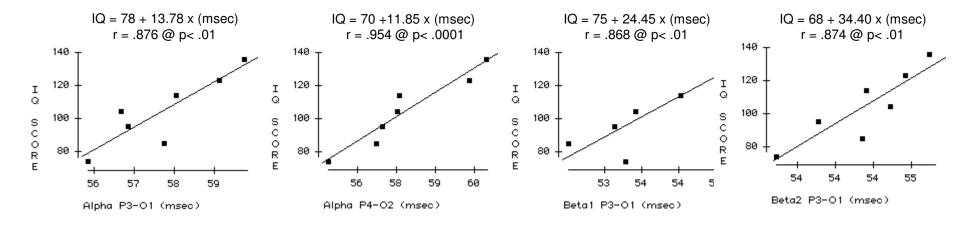
Chaos 0.386	Coherence	- 0.547	0.863
	Chaos		- 0.386
Stability - 0.386	Stability	- 0.386	

Published in NeuroImage – NeuroImage, 42(4): 1639-1653, 2008.

## INTELLIGENCE AND EEG PHASE RESET: A TWO COMPARTMENTAL MODEL OF PHASE SHIFT AND LOCK

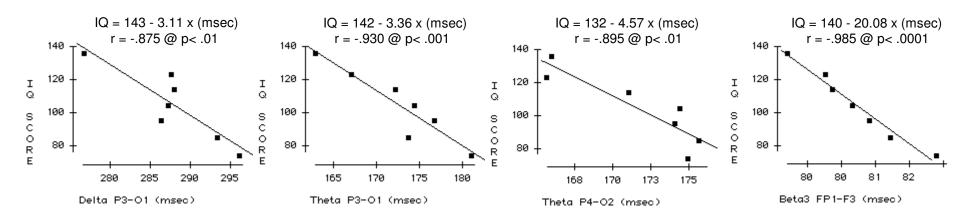
Thatcher, R. W. 1,2, North, D. M.1, and Biver, C. J.1

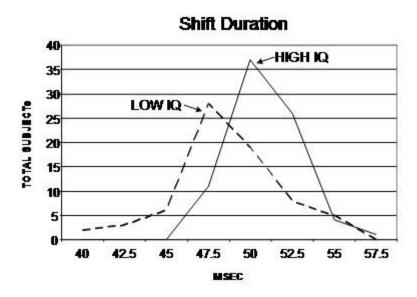
EEG and NeuroImaging Laboratory, Applied Neuroscience Research Institute. St. Petersburg, FI1 and Department of Neurology, University of South Florida College of Medicine, Tampa, FI.2

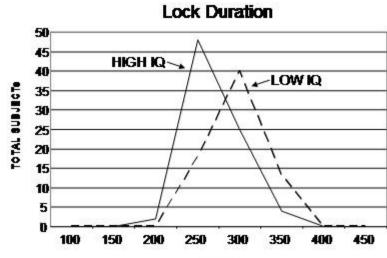


### Regressions & Correlations of Phase Shift Duration Short Distances (6 cm)

### Regressions & Correlations of Phase Locking Interval Short Distances (6 cm)

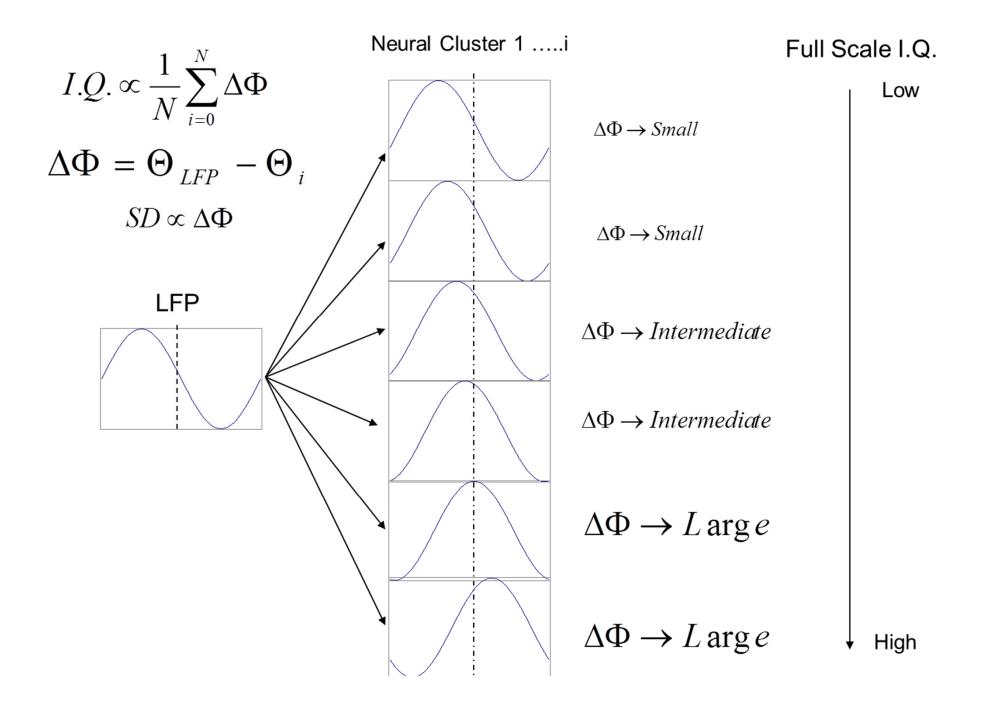


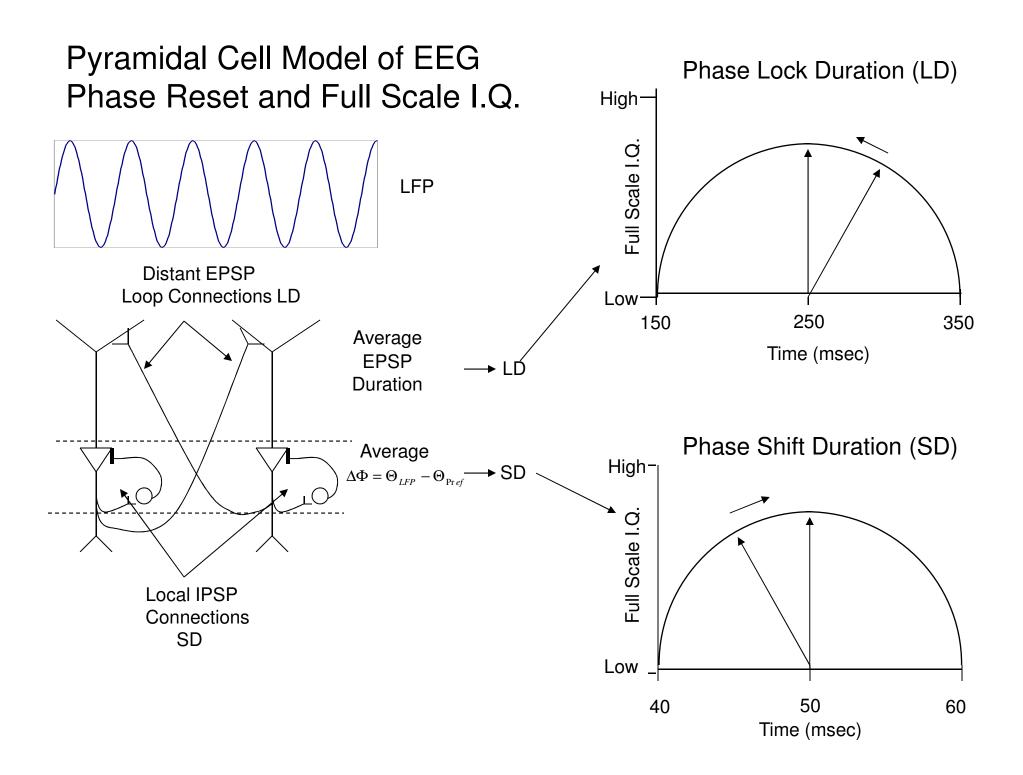






Local Field Potential (LFP) Model of Phase Shift Duration and Full Scale I.Q.

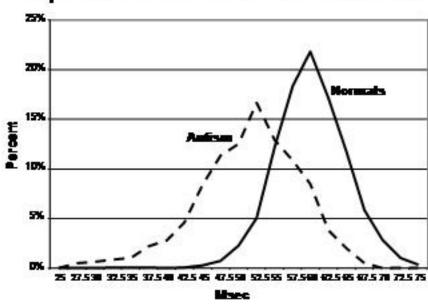




## AUTISM AND EEG PHASE RESET: A UNIFIED THEORY OF DEFICIENT GABA MEDIATED INHIBITION IN THALAMO-CORTICAL CONNECTIONS

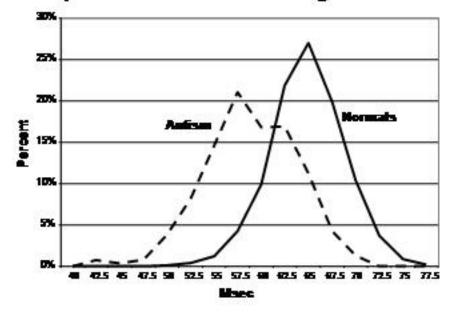
Thatcher, R. W. 1,2, Phillip DeFina2, James Neurbrander2, North, D. M.1, and Biver, C. J.1

EEG and NeuroImaging Laboratory, Applied Neuroscience Research Institute., St. Petersburg, FI1 and the International Brain Research Foundation, Menlo Park, NJ2

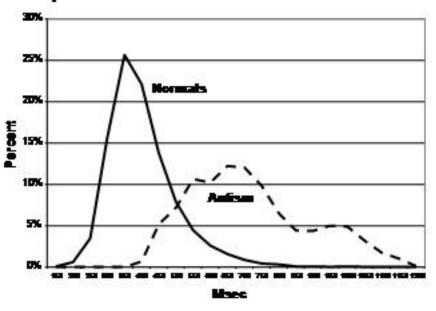


### Alpha1 Shift Duration Short Distances

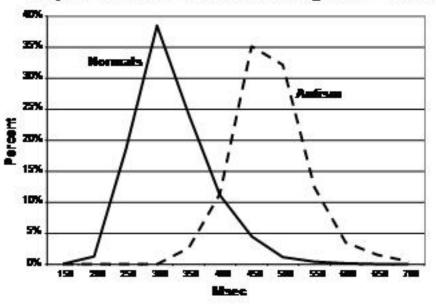
Alpha1 Shift Duration Long Distances

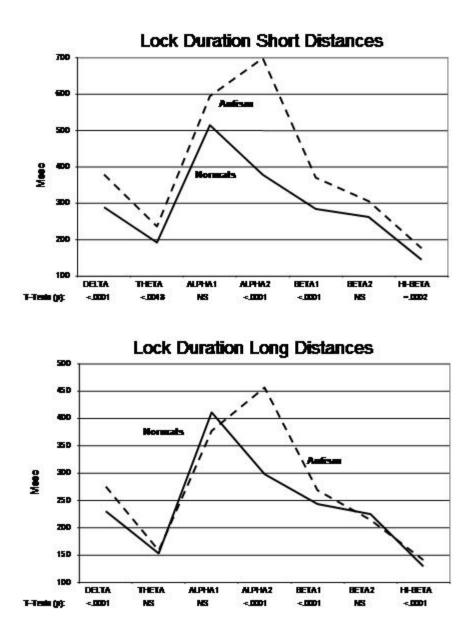


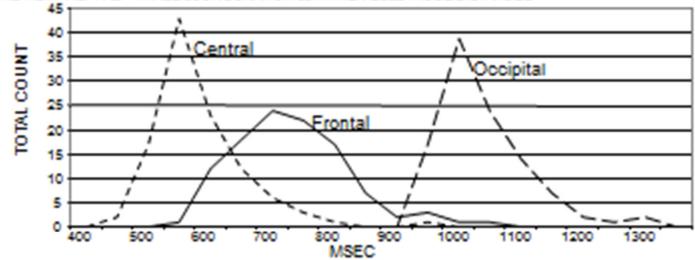
Alpha2 Lock Duration Short Distances



## Alpha2 Lock Duration Long Distances



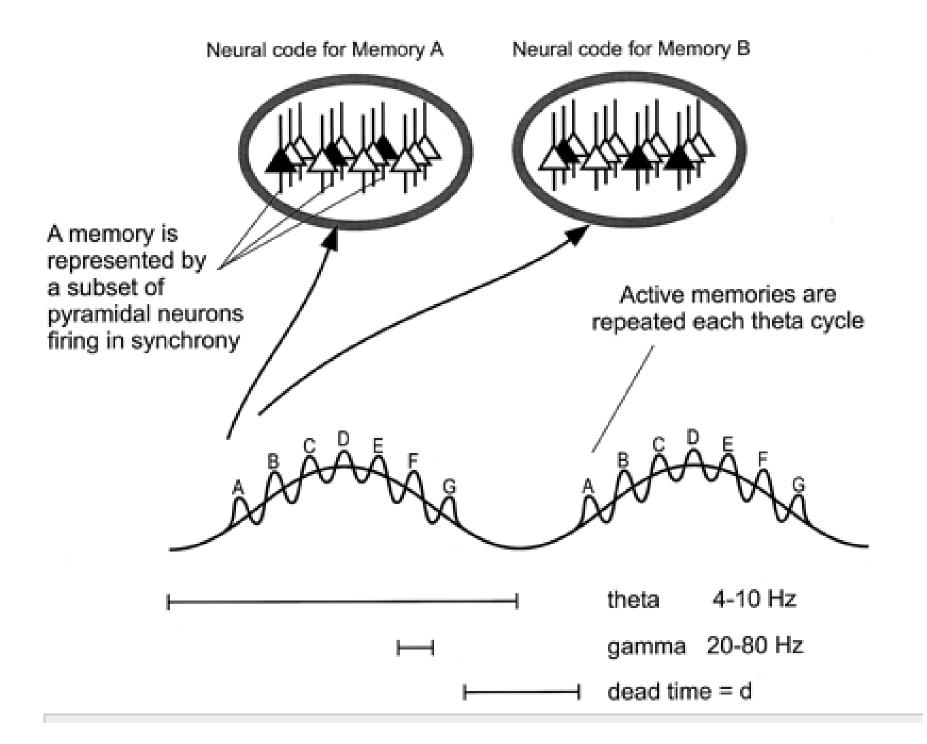


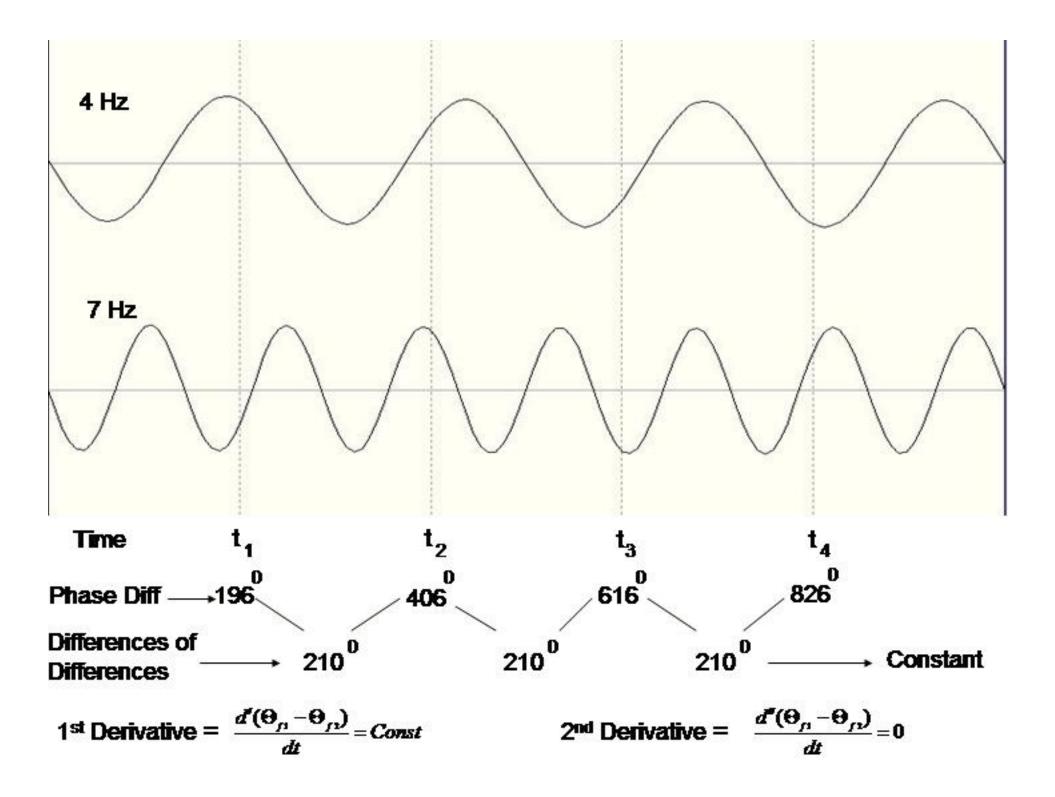


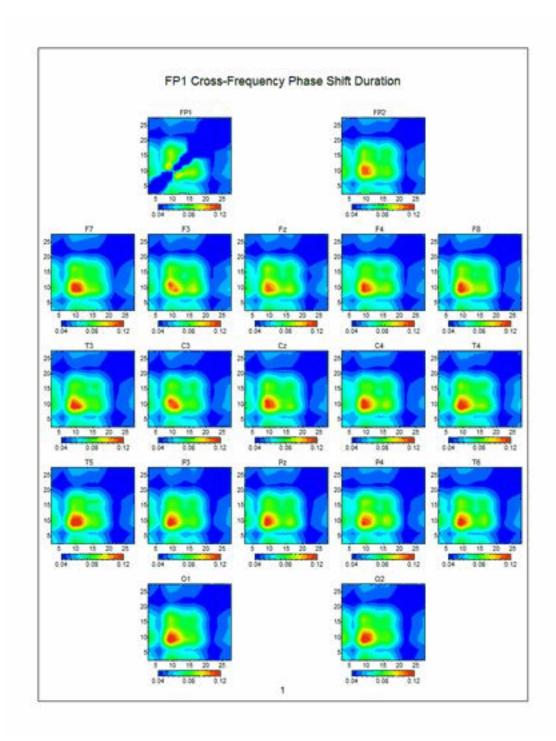
AUTISM - ALPHA2 - PHASE LOCK DURATION 6cm INTER-ELECTRODE DISTANCES

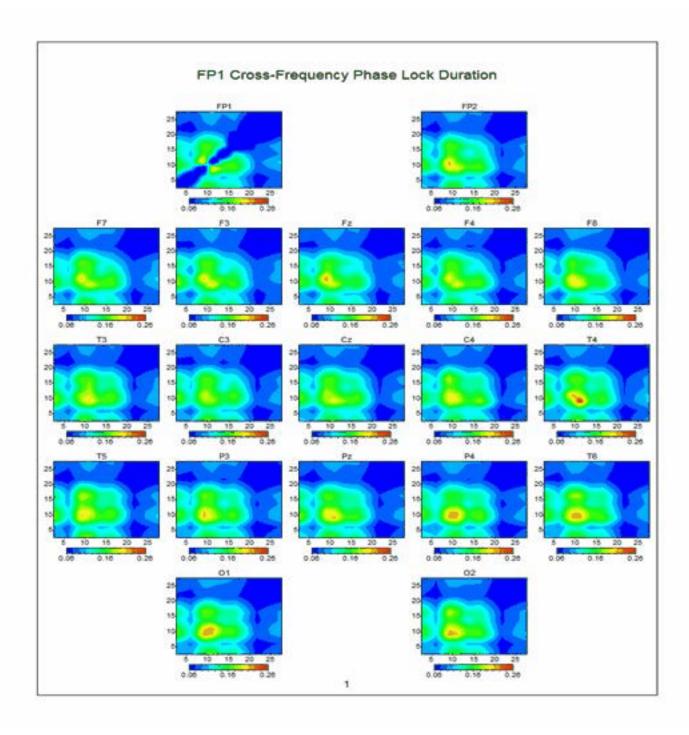
# **Cross-Frequency Phase Shift and Phase Lock**

Note: ICA Obliterates Time & Phase Differences Between Channels and Cannot be Used for These Type of Analyses



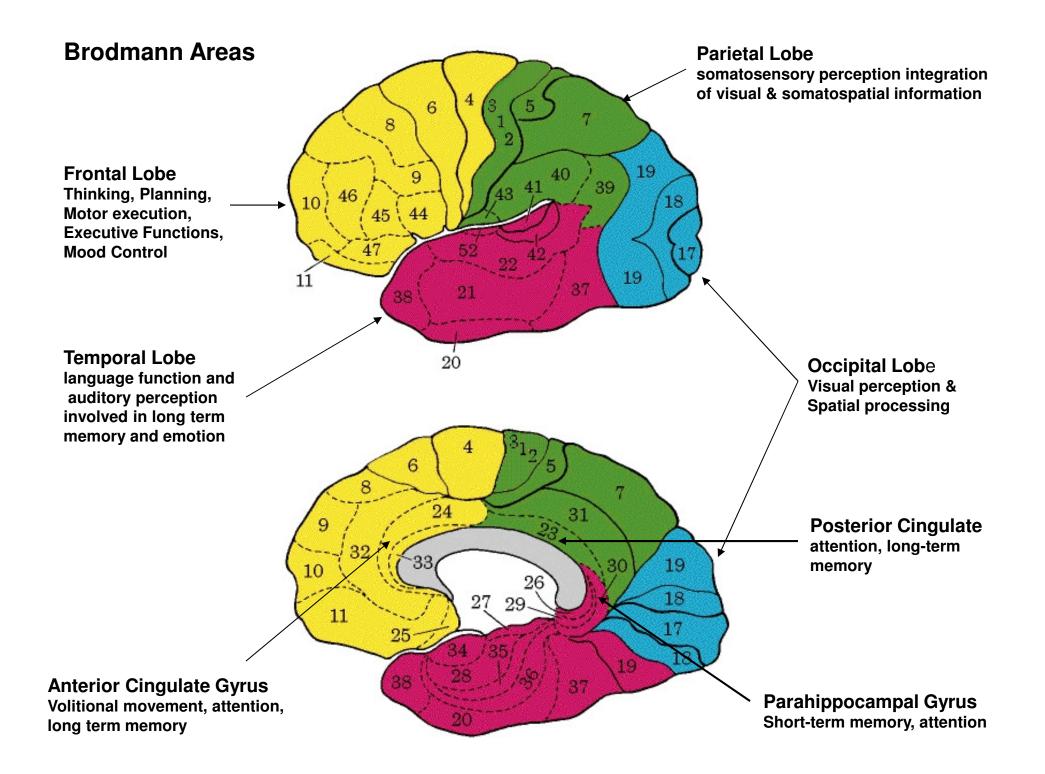


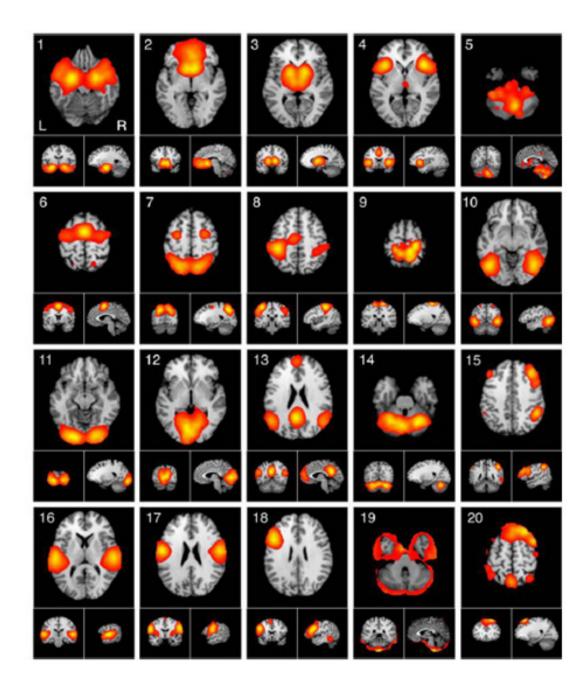




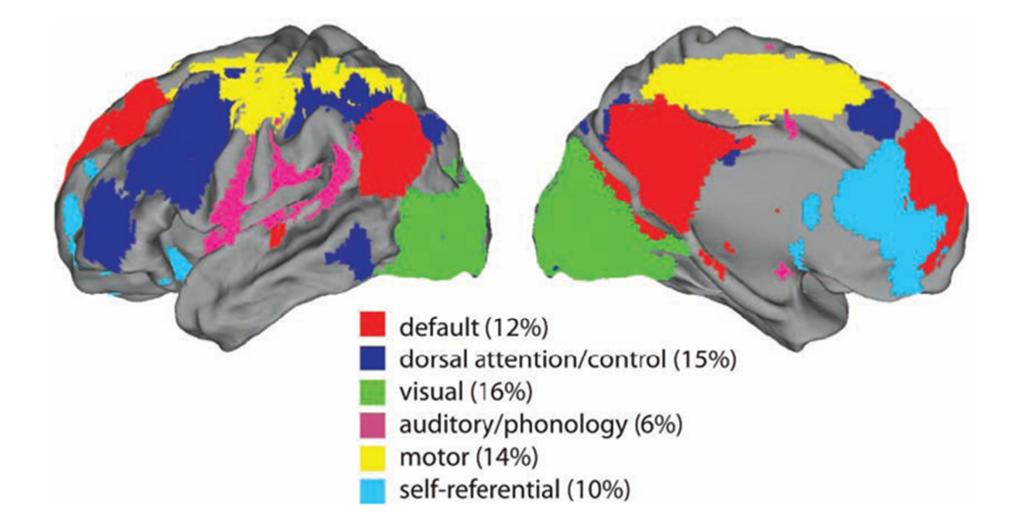
# Electrical Neurolmaging of Functional Modules and Hubs as Measured by fMRI and PET

Phase Shift and Phase Lock Switch Dynamics that "Animate" Information Flow Within and Between Modules and Hubs





Laird et al (2011) summarized the various "intrinsic connectivity networks" or ICNs into eighteen specific groupings based upon 30,000 fMRI and PET studies



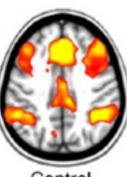
## Six Functional Modules as Measured by fMRI



Somato-motor



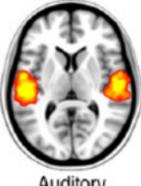
Dorsal attention



Control



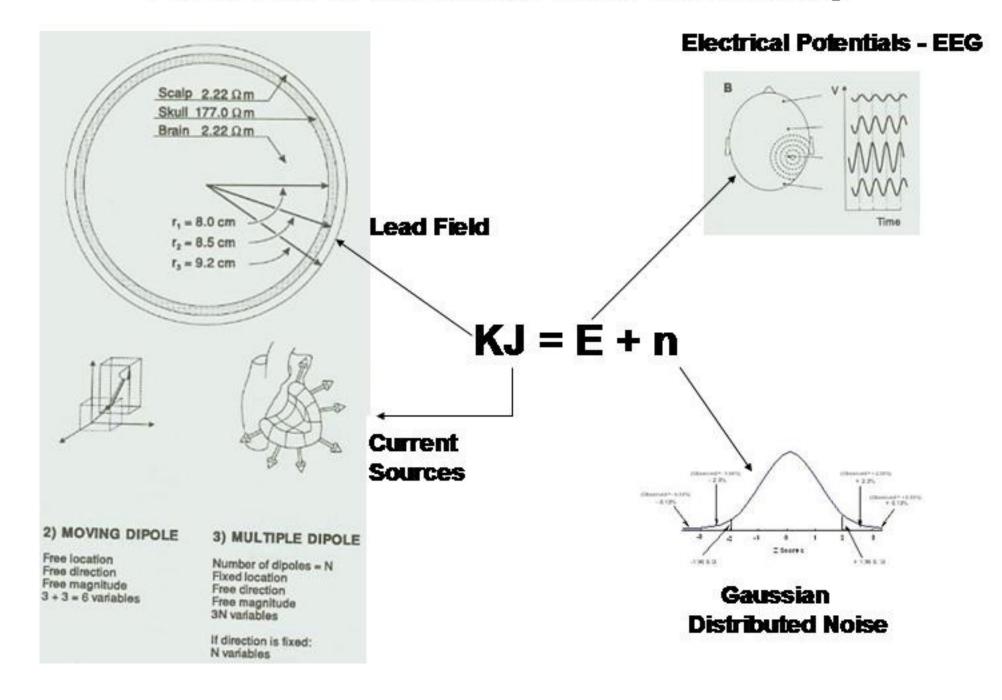
Default mode



Auditory

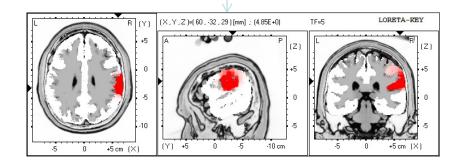


## **Estimation of Cortical Source Current Density**

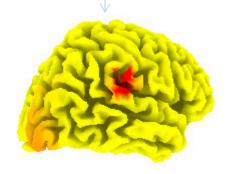


# Electrical Neuroimaging and Cortical Source Localization

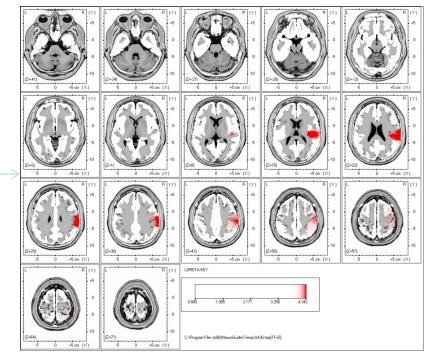
## Horizontal, Sagital & Coronal Views of a Single Slice



**Cortical Surface Projection** 

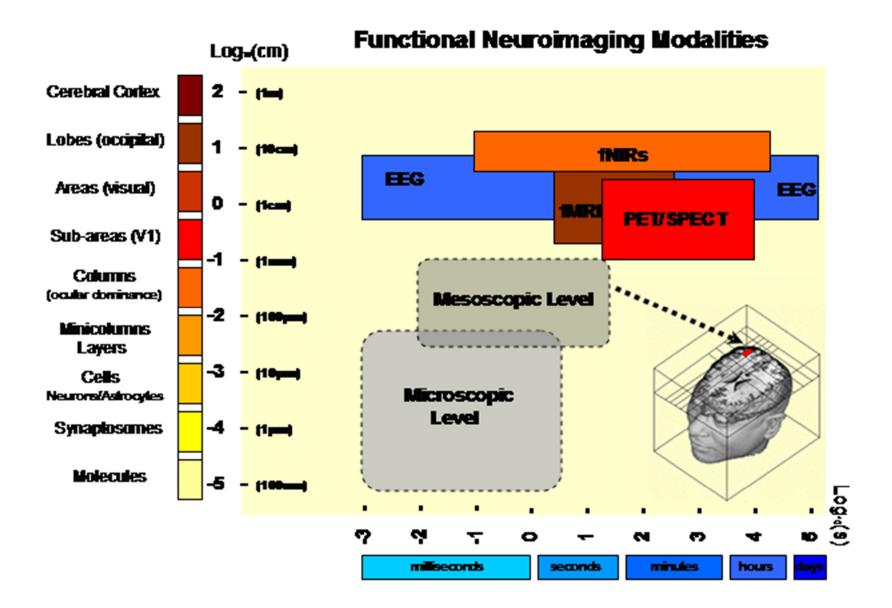


Tomographic Slice Display



EDI Regularised SNR/dB 10 15 25 5 Layer WMN  $3.46 \pm 0.42$  $2.10 \pm 0.28$  $1.34 \pm 0.11$  $1.13 \pm 0.03$ Surface Middle 5.08 ± 0.50  $3.94 \pm 0.38$ 2.95 ± 0.21  $2.40 \pm 0.03$ Deep 5.91 ± 0.39 5.31 ± 0.36  $4.61 \pm 0.24$ 3.89 ± 0.15 **SLORETA** Surface  $0.99 \pm 0.1$  $0.49 \pm 0.08$  $0.11 \pm 0.04$  $0.00 \pm 0.00$  $1.61 \pm 0.13$  $0.84 \pm 0.11$ 0.25 ± 0.07  $0.00 \pm 0.00$ Middle  $1.79 \pm 0.25$  $0.95 \pm 0.16$  $0.39 \pm 0.13$  $0.00 \pm 0.00$ Deep LORETA Surface  $2.32 \pm 0.08$  $2.18 \pm 0.04$  $2.16 \pm 0.03$  $2.21 \pm 0.02$ Middle  $1.51 \pm 0.13$  $1.15 \pm 0.08$ 0.95 ± 0.07  $1.05 \pm 0.06$  $2.30 \pm 0.21$  $1.81 \pm 0.13$  $1.59 \pm 0.11$ 1.53 ± 0.09 Deep SLF Surface 5.27 ± 0.30 4.50 ± 0.28 3.81 ± 0.20  $2.98 \pm 0.13$ 3.50 ± 0.31 2.51 ± 0.15 Middle 4.53 ± 0.39 4.09 ± 0.35 Deep 3.89 ± 0.55 3.70 ± 0.45 3.27 ± 0.48  $1.73 \pm 0.30$ 

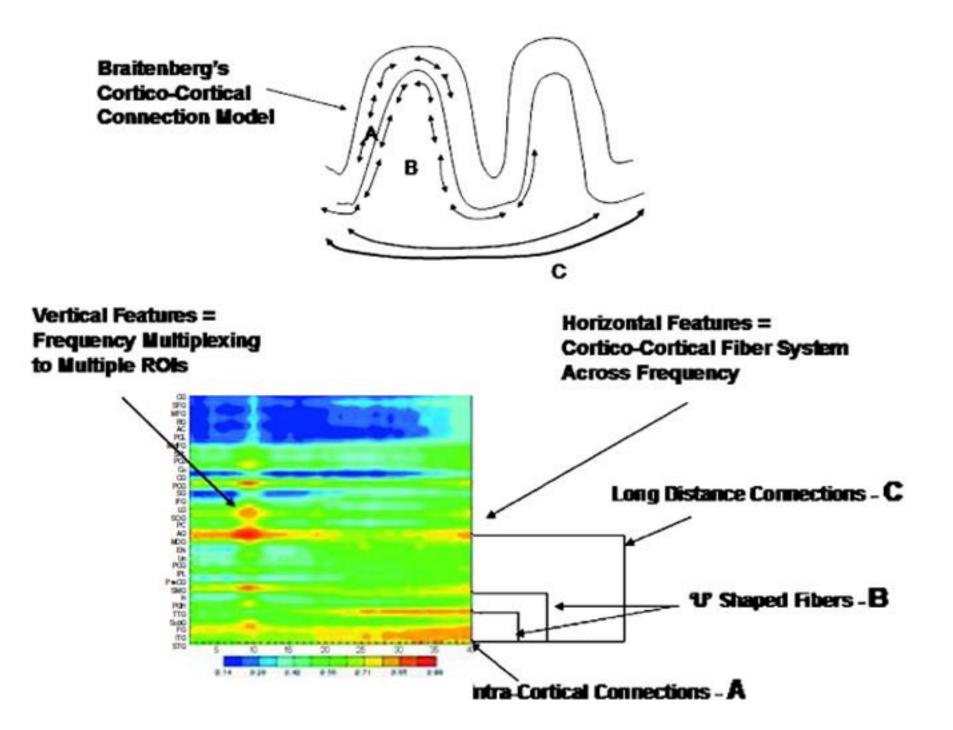
Table 5: Error measure ED1 for the four inverse algorithms, with regularization, under four different noise levels: 25 dB, 15 dB, 10 dB and 5 dB. Each cell value gives the mean and standard deviation.



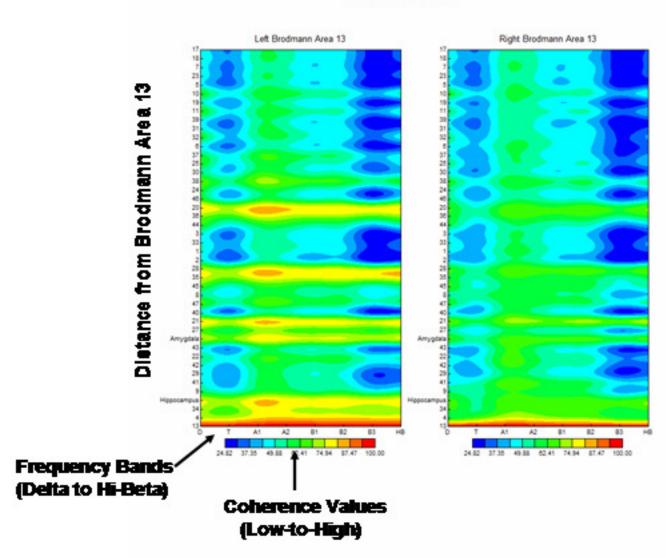
# Electrical Neuroimaging – Assessment and Treatment

# **Advantages of Electrical Neuroimaging**

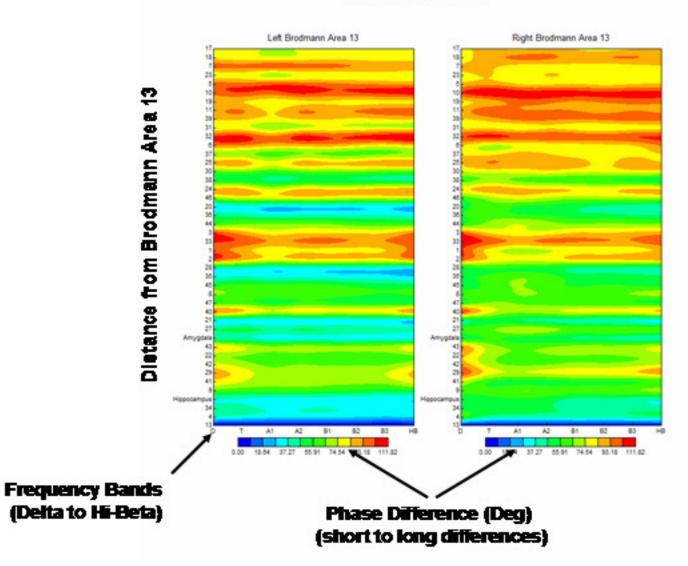
- 1- Spatial Resolution 1 cm to 3 cm
- 2- Temporal Resolution 1 msec
- **3- Imaging of Current Sources**
- **4- Imaging of Network Connections**
- 5- Integration with DTI & fMRI (Brodmann Areas)
- 6- Inexpensive (\$10,000 vs \$3,000,000)
- 7- Dry Electrodes & Wireless Caps
- 8- Portable
- 9- Integration with Smart Phones & Tablets
- 10- Can Assess & Treat in Real-Time1



#### LORETA Coherence



#### LORETA Absolute Phase



## **Graph Theory and Neural Topology**

1- A Node is the principle unit of a network in which nodes are connected (linked) to other *nodes*,

2- A Network consists of a number of nodes connected by links. Nodes are also called *vertices*.

3- A link is a connection between two nodes in the network. Links are also referred to as *edges* or simply *network connections. Axons are the links between neurons.* 

4- The degree of a node is the number of nearest neighbors to which a node is connected. The mean degree of the network is the mean of the individual degrees of all nodes in the network.

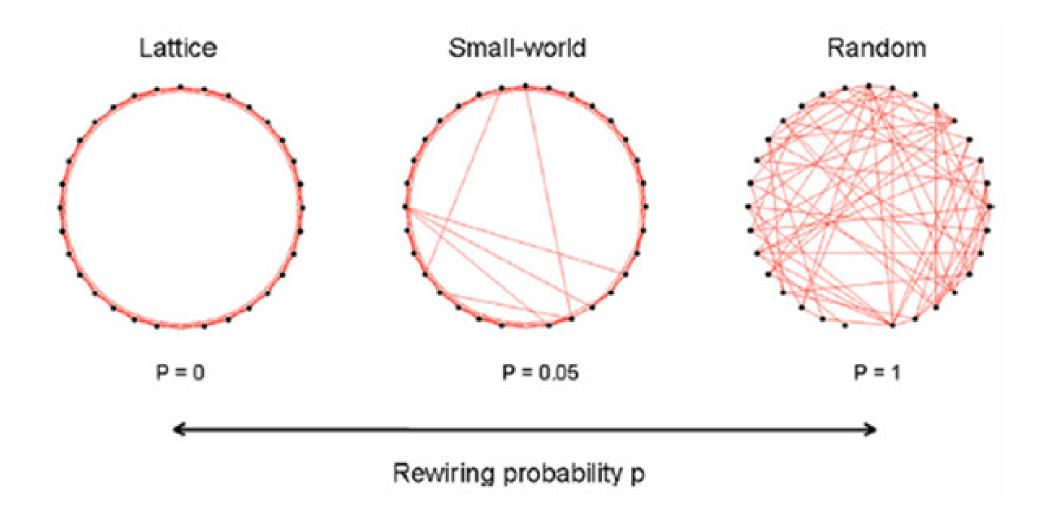
5- Modules are clusters of neurons with high density of nearest neighbors and are high degree nodes.

6- Hubs are regions that link distinct clusters or modules. Provincial hubs are hub regions that are highly connected within one module and connector hubs are hub regions that link multiple modules.

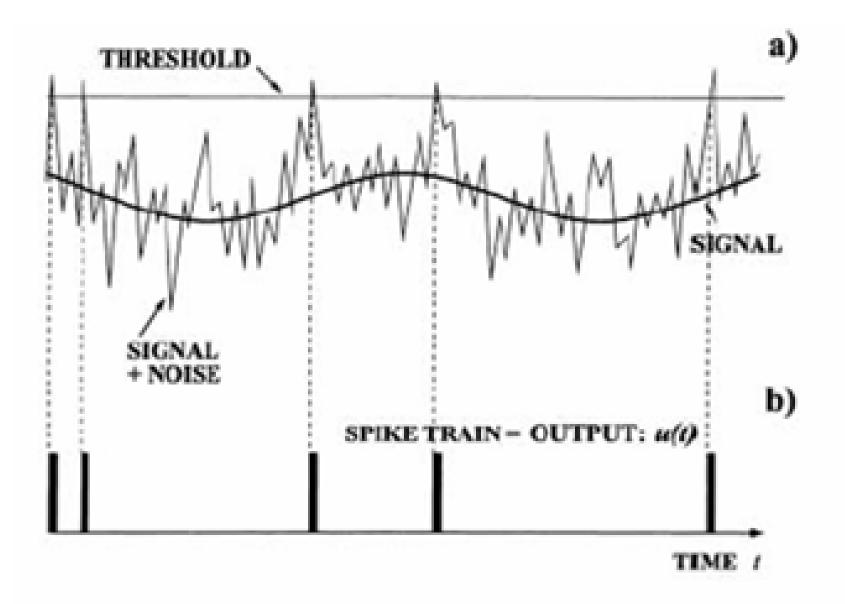
7- A scale-free network is where the distribution of node number follows a power law.

8- A specific pattern of links or connections defines the network's *Topology*.

Small world models emphasizes the intermediate position of total regularity and randomness where the small world model while containing random connections involves a small set of preferred long distance connections.



## Noisy Ionic Channels, Action Potentials and Stochastic Resonance



The 'Small-World' models are considered to be the best balance of these opposing factors.

**Benefit:** Increased brain size. Enlarging size by adding more neurons increases processing capacity.

**Trade-offs:** Neurons consume a lot of energy. And as brains get bigger the axons or "wires" that connect neurons have to become longer, which makes them slower.

**Benefit::** Increase interconnectedness. Adding more links between distant neurons enables brain parts to communicate better.

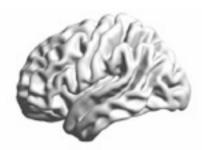
Trade-offs: The added wiring eats up-energy and takes up space.

Benefit:: Increase signaling speed is achieved by making axons thicker.

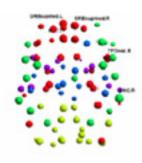
**Trade-offs**: Thicker axons consume more energy and take up more space than thinner ones do.

**Benefit:** Pack more neurons in the existing space. Achievable by shrinking neurons or axons or both.

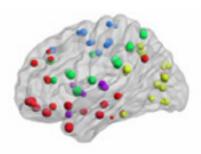
**Trade-offs:** If axons or neurons get too small, they tend to fire randomly (<u>stochastic</u> <u>resonance</u>).



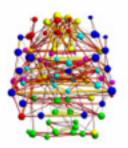
1) Brain Surface



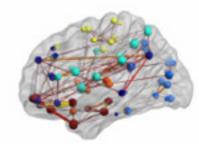
2) Nodes

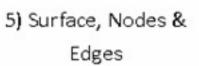


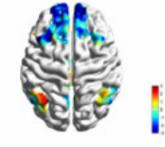
3) Surface & Nodes



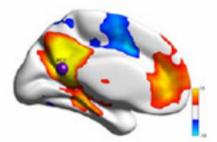
4) Nodes & Edges



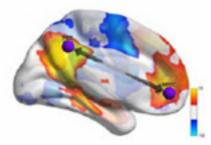




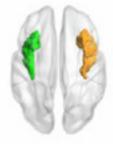
6) Surface mapping



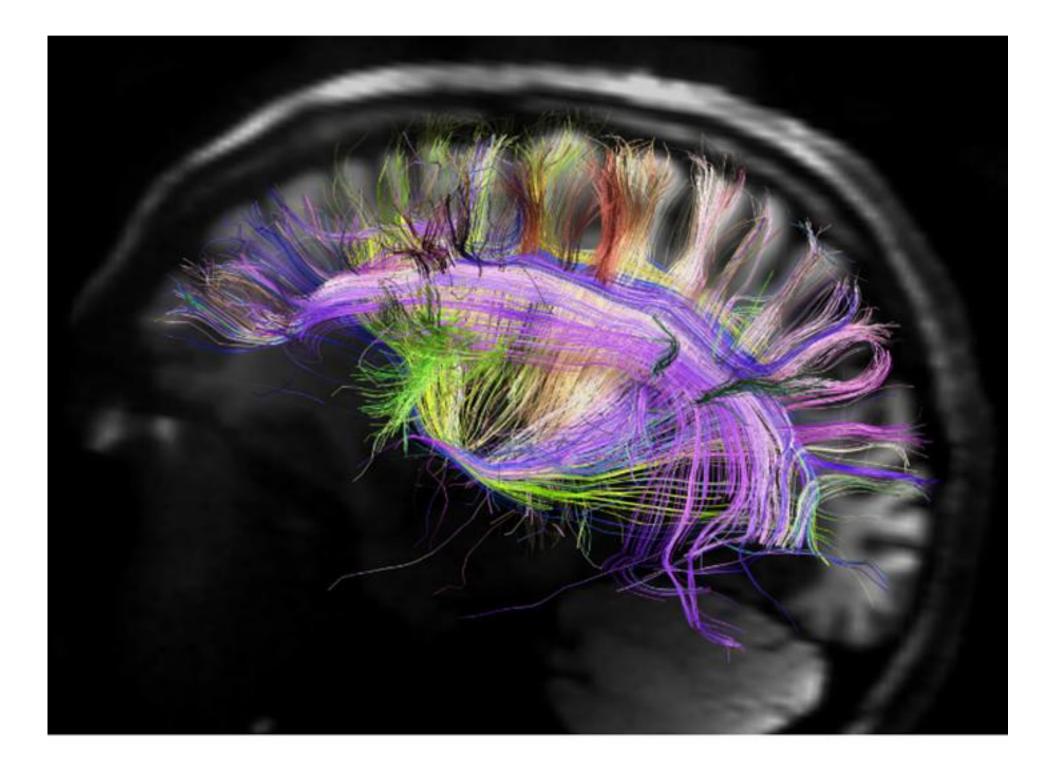
 Surface mapping & node

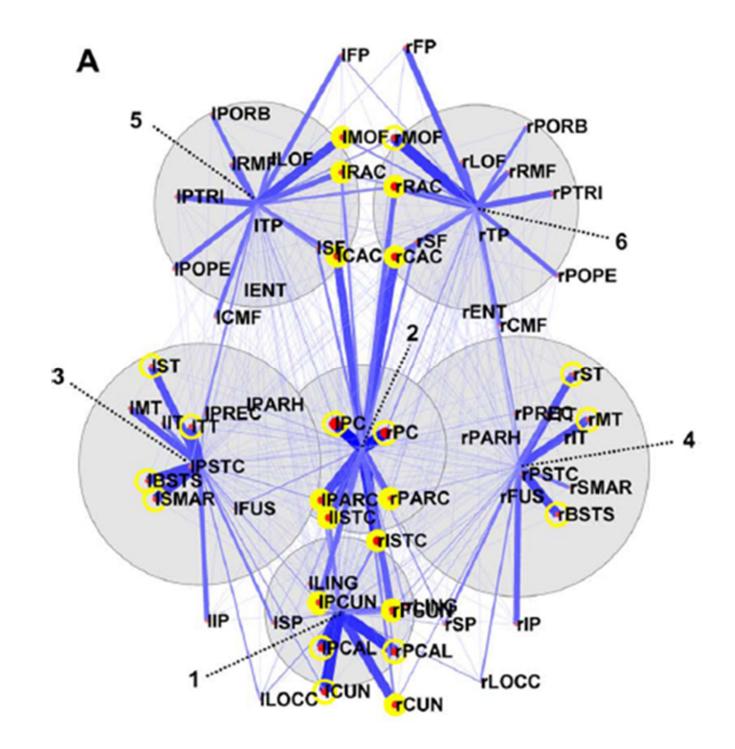


 Surface mapping with node & edge

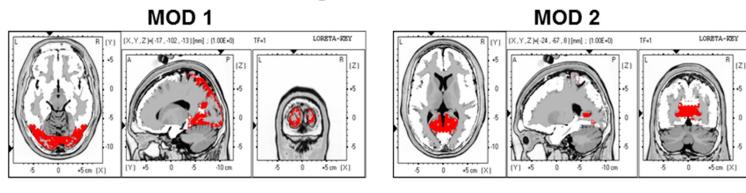


9) ROI in Volume





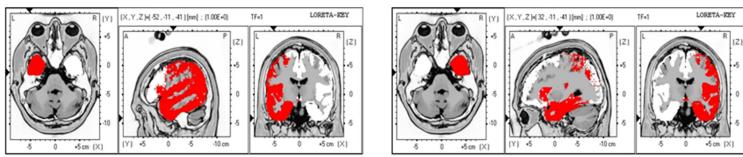
## **Correlations Between EEG Neuroimaging and Diffusion Spectral Imaging (DTI)**



### Hagmann et al. Moduless

MOD 3



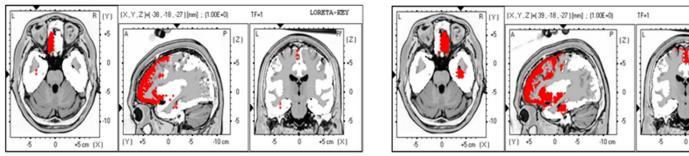






LORETA-KEY

+5 cm [X]



EC\_LEFT

0.9

0.8

0.7

0.6

0.5

0.4

0.3

0.2

0.9

8.0

0.7

0.6

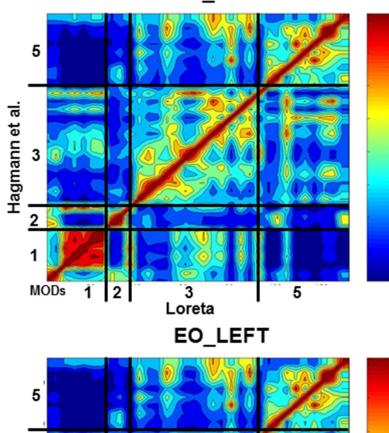
0.5

0.4

0.3

0.2

5



3 Loreta

Hagmann et al.

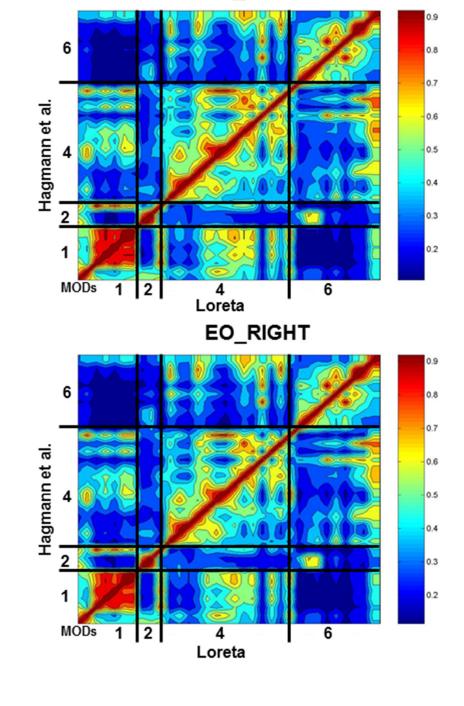
3

2

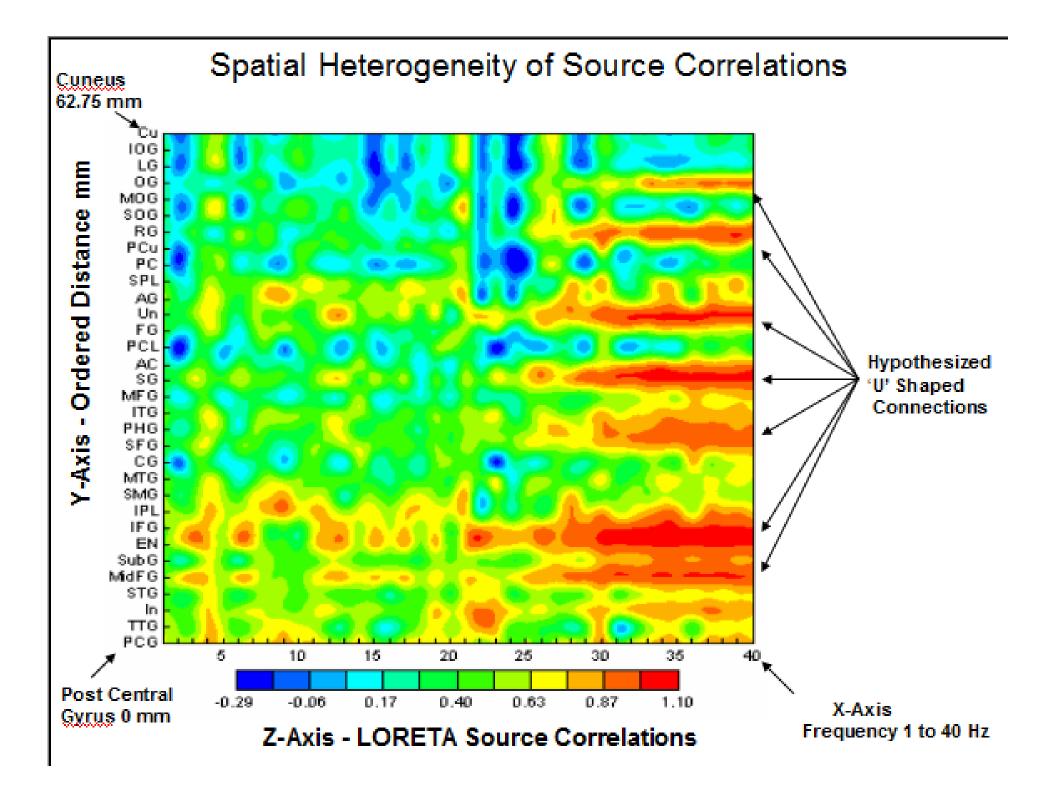
1

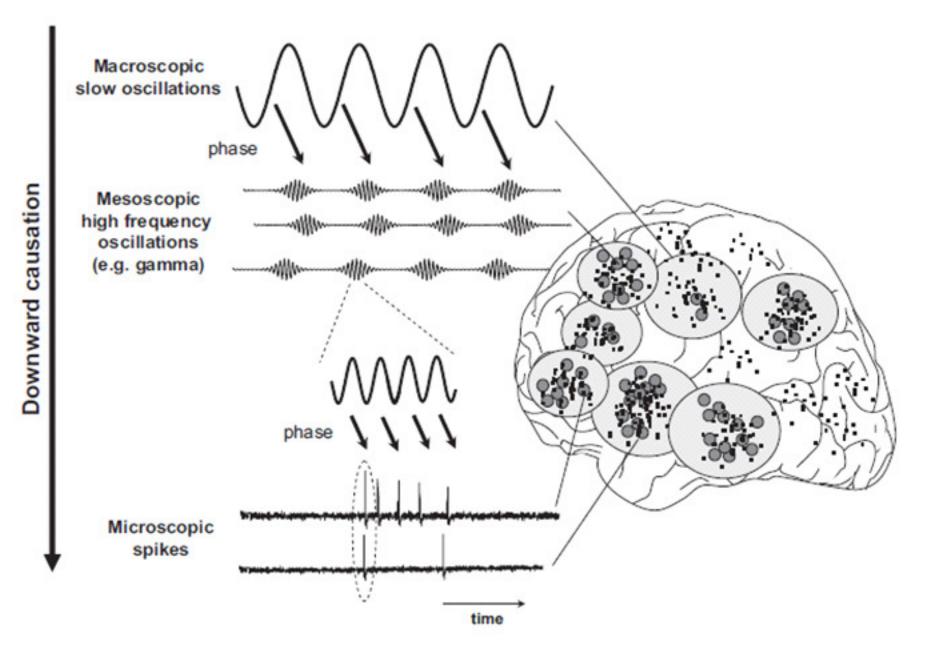
MODs

1 2

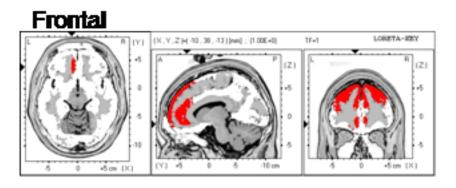


EC\_RIGHT

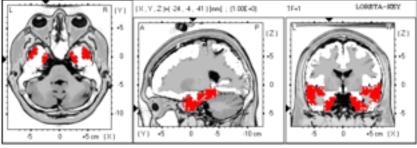




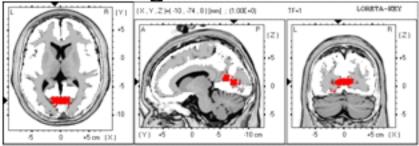
# **Loreta Default Brain Network**



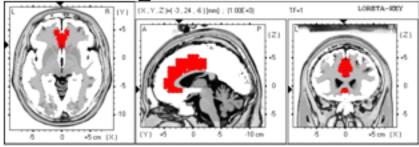
## Temporal



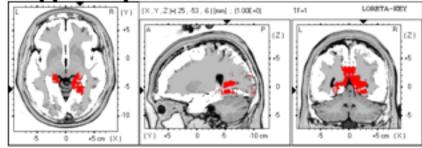
## **Posterior Cingulate**



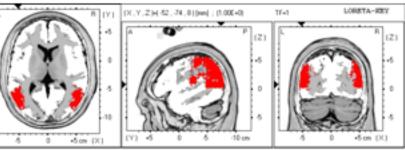
## Anterior Cingulate

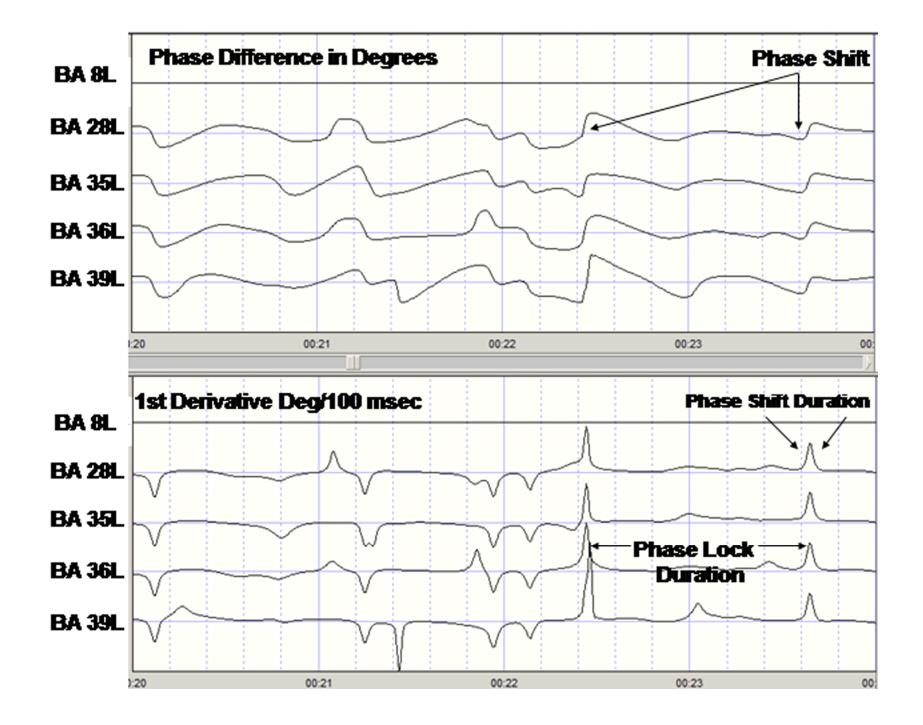


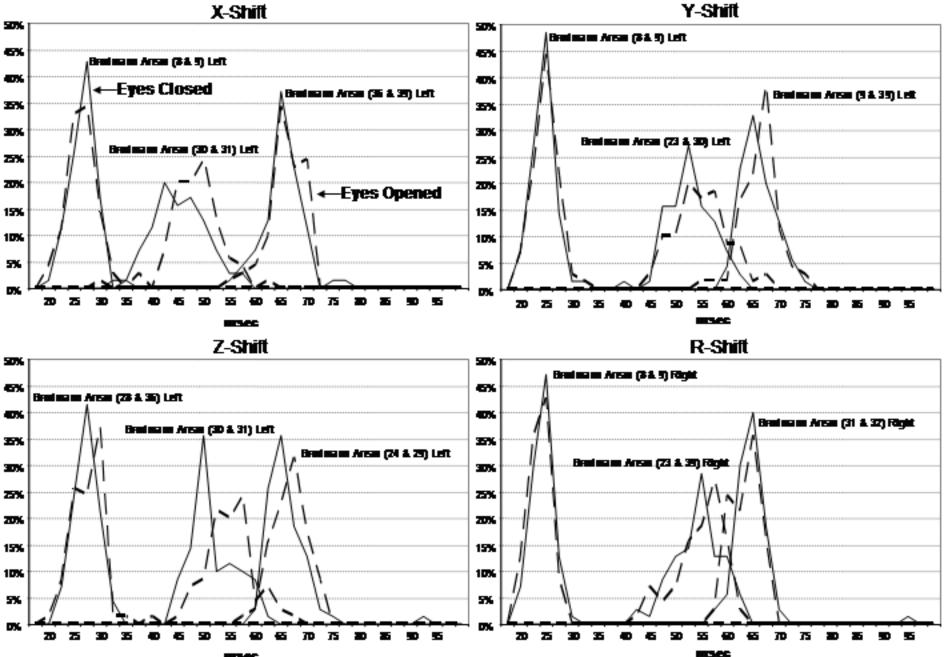
## Hippocampus



Parietal

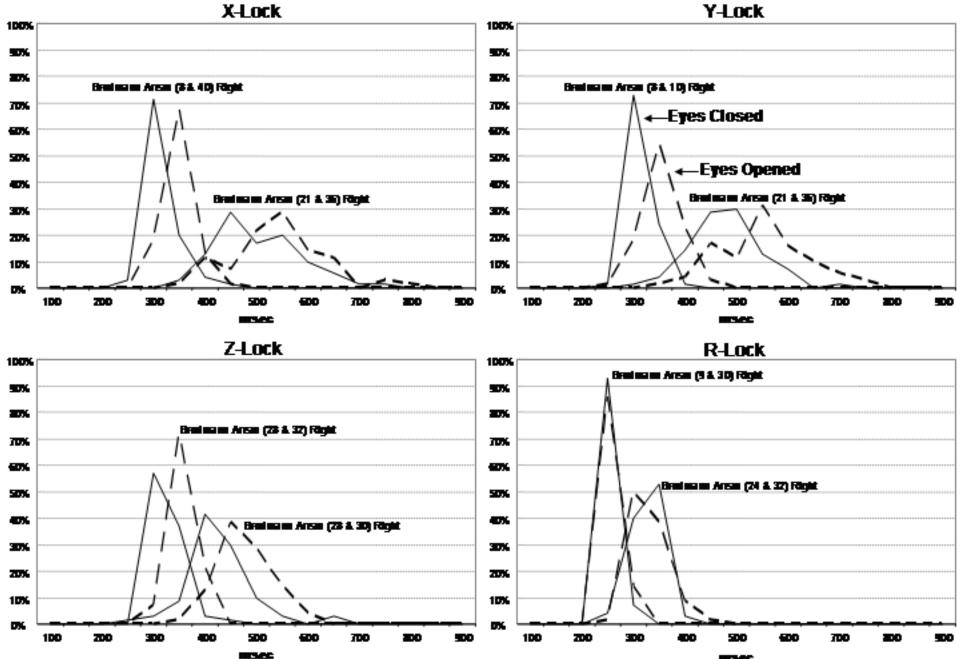






#### Phase Reset Shift Duration LORETA Default Brain Brodmann Area Pairs

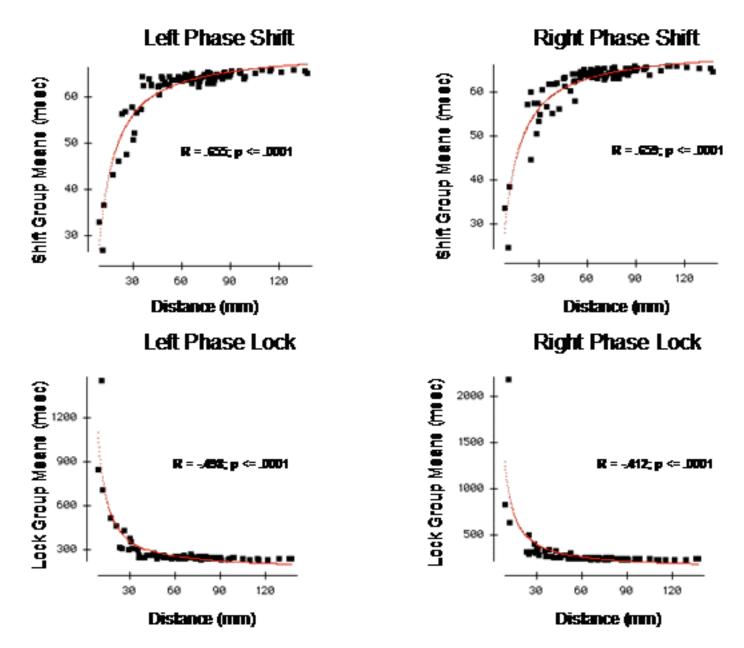
**INCOME** 



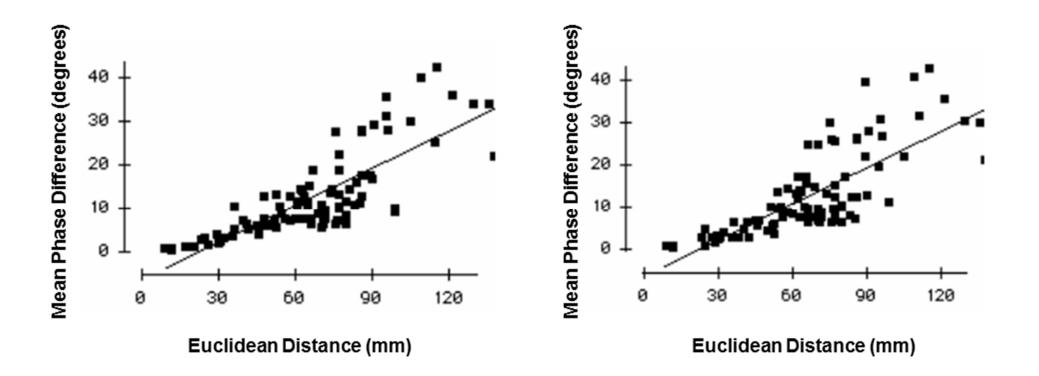
#### Phase Reset Lock Duration LORETA Default Brain Brodmann Area Pairs

**INCOME** 

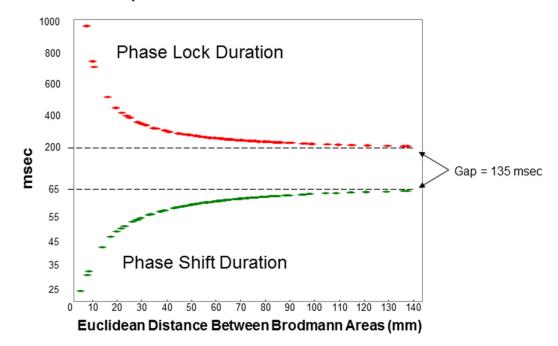
#### Relations Between Phase Reset Shift & Lock Means and the Euclidean Distance Between Voxels



#### **Correlations of Default Brain Phase Difference with Euclidean Difference Distances**



Non-Linear Exponential Brodmann Area Distances: Shift vs Lock

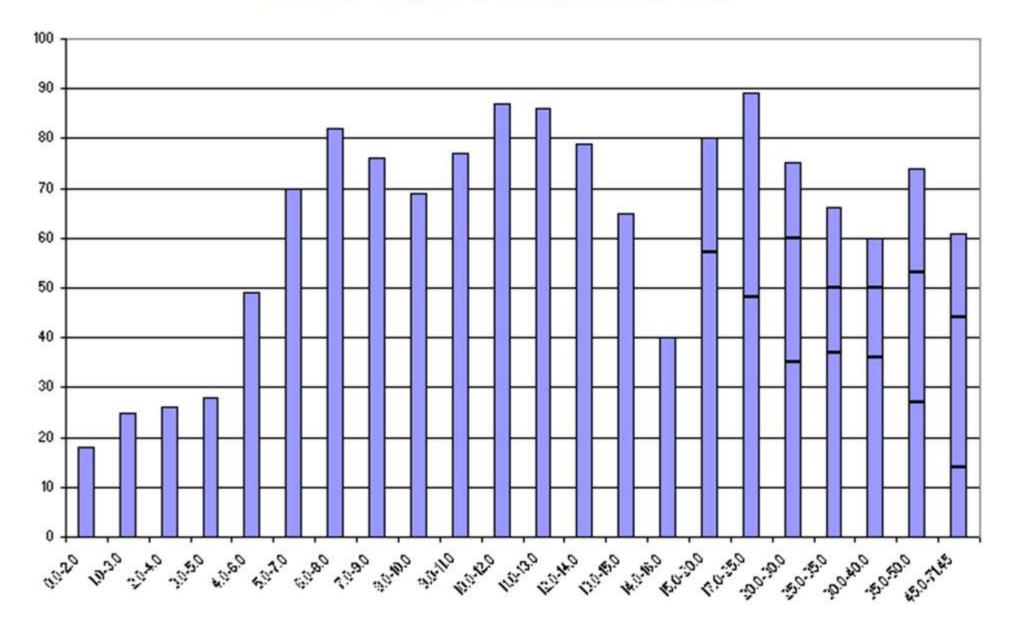


Published as a chapter in "Introduction to QEEG and Neurofeedback: Advanced Theory and Applications" Thomas Budzinsky, H. Budzinski, J. Evans and A. Abarbanel editors, Academic Press, San Diego, Calif, 2008.

# HISTORY OF THE SCIENTIFIC STANDARDS OF QEEG NORMATIVE DATABASES

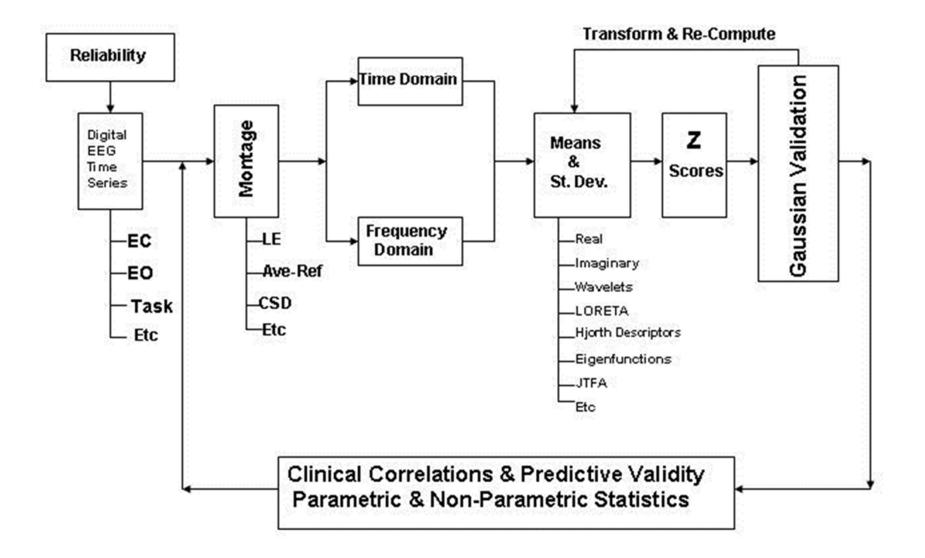
Thatcher, R.W. 1,2 and Lubar, J.F.3

Department of Neurology, University of South Florida College of Medicine, Tampa, Fl.<sup>1</sup> and EEG and NeuroImaging Laboratory, Applied Neuroscience, Inc., St. Petersburg, Fl<sup>2</sup>, Brain Research and Neuropsychology Lab, University of Tennessee, Knoxville, TN<sup>3</sup>.



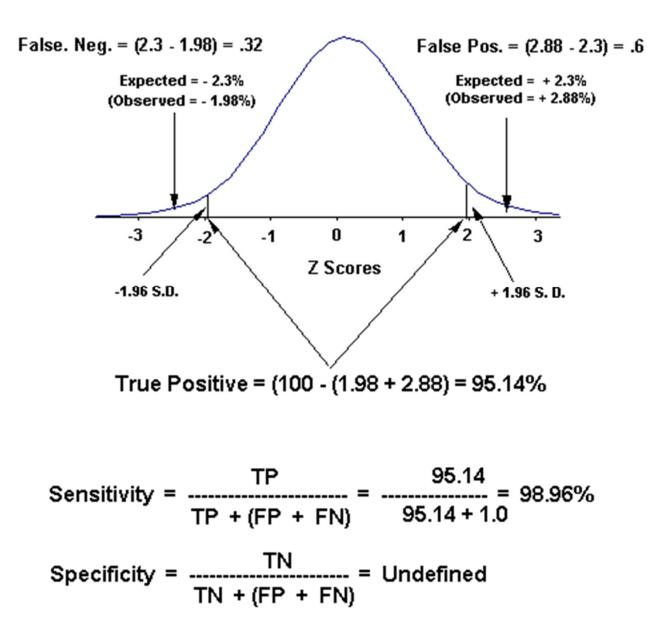
#### NORMATIVE DATABASE N = 727 Subjects as of 8/24/2011

# Normative Database Validation Steps

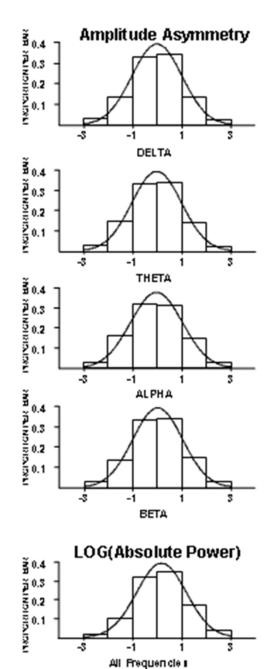


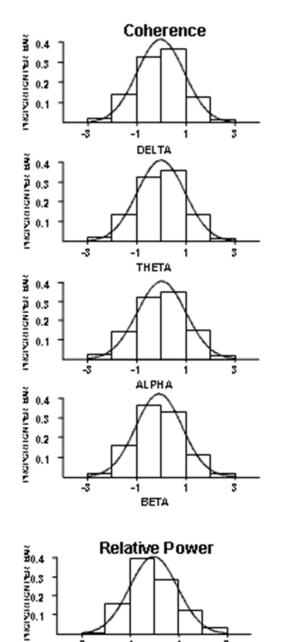
### Sensitivity Based on Deviation from Gaussian

Cross-Validation Accuracy N = 625 Subjects



# **Cross-Validation Birth to 82 Year EEG Normative Database**



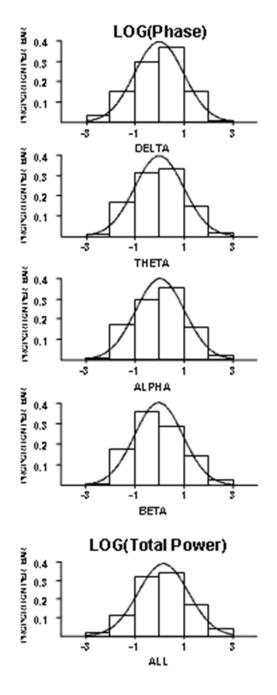


-3

-1

All Frequencie :

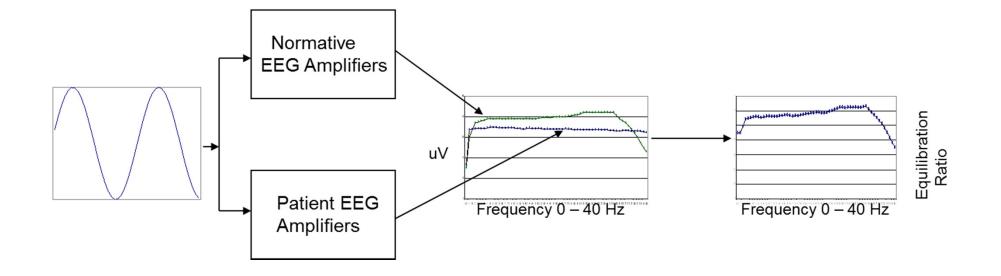
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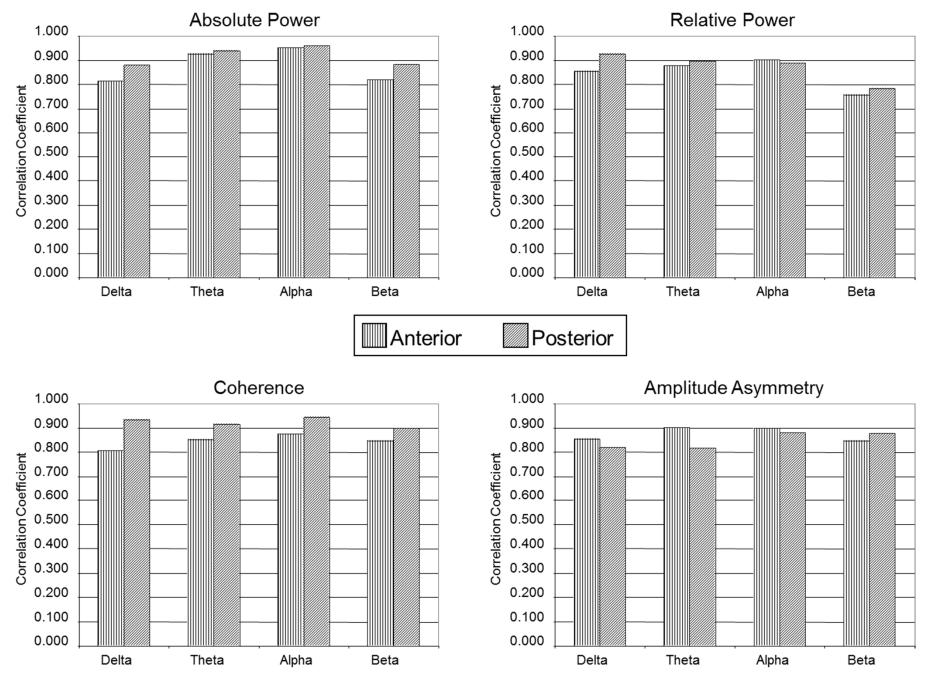
## **FFT Normative Database Sensitivities**

2 STDEVs	CALC SENSITIVITY:	FP=TP/(TP+FP) or FN=TP/(TP+FN)		
AGES	(+/- 2 SD)	(>= 2 SD)	(<= -2 SD)	
0-5.99	0.95448265	0.9771774	0.97730526	
6-9.99	0.95440363	0.9772031	0.97720054	+/- 2 Std. Dev.
10-12.99	0.9543997	0.97724346	0.97715624	
13-15.99	0.95440512	0.97723601	0.97716911	
16-ADULT	0.9543945	0.97718143	0.97721307	
ALL	0.95442375	0.97720714	0.97721661	
3 STDEVs	CALC SENSITIVITY:	FP=TP/(TP+FP) or FN=TP/(TP+FN)		
AGES	(+/- 3 SD)	(>= 3 SD)	(<= -3 SD)	
0-5.99	0.99743898	0.99871123	0.99872774	
6-9.99	0.99744112	0.99871611	0.99872501	+/- 3 Std. Dev.
10-12.99	0.99744688	0.99873171	0.99871518	
13-15.99	0.99743186	0.99871951	0.99871234	
16-ADULT	0.99743835	0.99870216	0.99873619	
ALL	0.99744002	0.99871716	0.99872286	

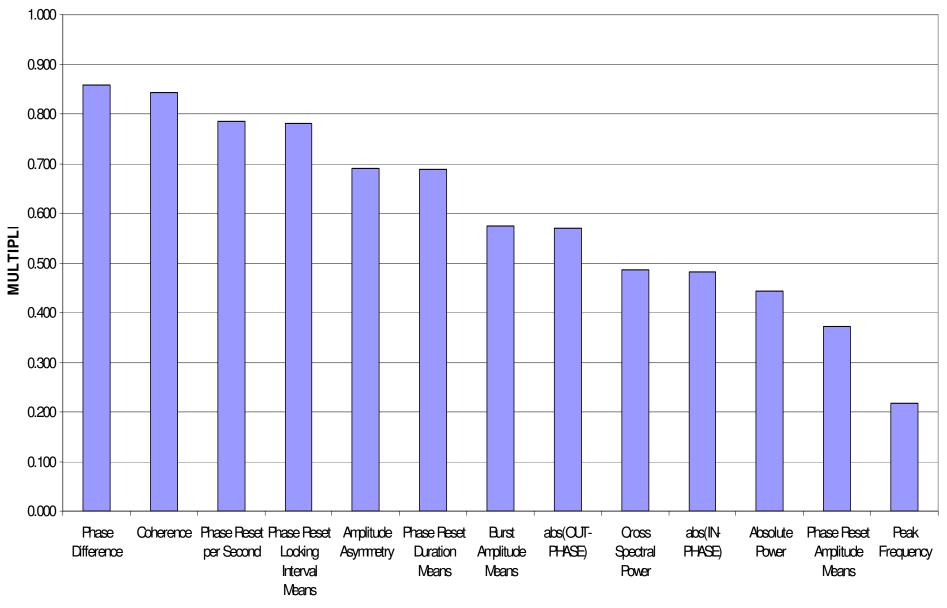
Normative Database Amplifier Matching – Microvolt Sine Waves 0 to 40 Hz Equilibration Ratios to Match Frequency Responses



## **Cross-Validation of NeuroGuide vs NxLink**



#### Multiple Regressions of QEEG with FULL IQ



**QEEG MEASURE** 

## Table IV List of "Gold Standards" by which to judge QEEG Normative databases

	Standards	Yes	No
1	Peer reviewed publications		
2	Amplifier Matching		
3	Artifact Rejection		
4	Test Re-Test Reliability		
5	Inclusion/exclusion criteria		
6	Adequate Sample size per age group		
7	Approximation to a Gaussian		
8	Cross-Validation		
9	Clinical Correlation		
10	FDA Registered		

Some Relevant Items and Questions

Loops in the Brain and Why Homeostasis and Equilibrium are Critical for Brain Function

The EEG is Produced Exclusively by Summated Synaptic Potentials

How does EEG Biofeedback Change the EEG?

How does EEG Biofeedback Change Synaptic Potentials?

What are the Mechanisms of Modification of Synapses by Operant Conditioning of EEG at the Molecular Level? (nu. Accumbens & reinforcement)

Eric Kandel "In Search of Memory" Norton & Co., 2006 – Nobel Prize 2000 Gyorgy Buzsaki "Rhythms of the Brain", Oxford Univ. Press, 2006 **Essentials of Operant Conditioning** 

1- There must be a 'real' & 'valid' neural event to be reinforced

- 2- The 'Reinforcement' must be distinct and clear
- 3- The interval of time between the spontaneous 'emitted event' & the 'reinforcement' can not be too short, approx. < 250 msec? or too long approx. > 20 sec
- 4- The Schedule of Reinforcement is Important with two General Types "Continuous' vs 'Partial' Reinforcement - Continuous is good at the beginning but not as resistent to extinction as is Partial Reinforcement

# A General Theory of EEG Operant Conditioning and Z Score Biofeedback

#### Definitions

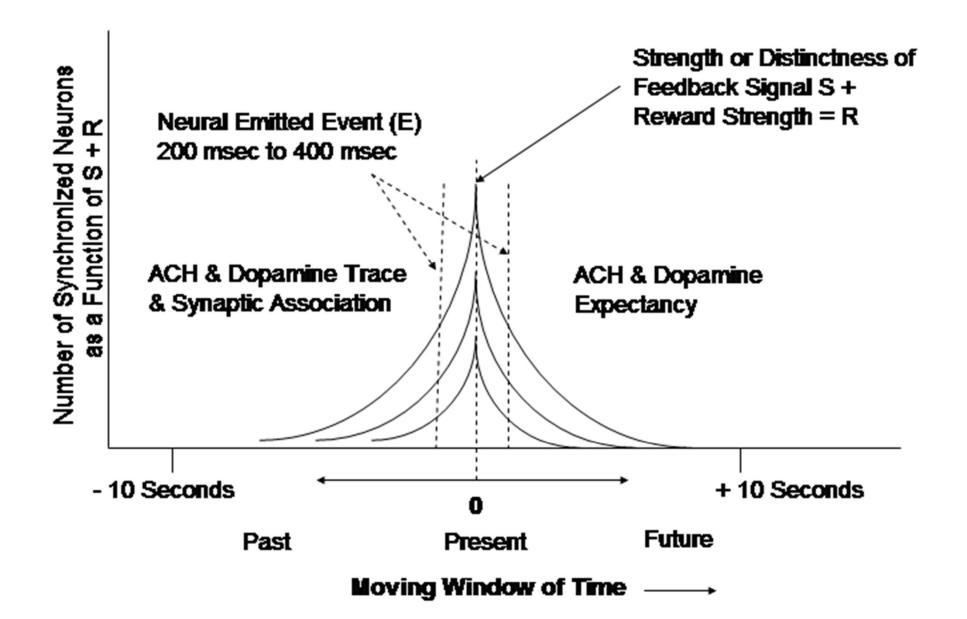
- 1- Duration of Spontaneous EEG Event (E) = Neural State Interval (I)
- 2- Contiguity Window (C) = Time period preceding and following a E
- 3- Reward Signal (S) = Feedback signal time locked to E
- 4- Reward Strength (R) = Value of the reward if N successes occur in an interval of time, e.g., toys, candy, cookies, money, etc.

#### Category

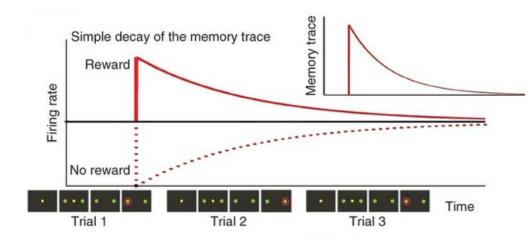
#### Measurement

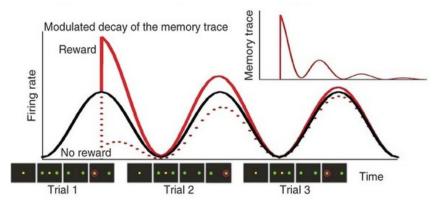
Duration of Spontaneous EEG Event (E)	Neural State Interval (I) (msec)
Contiguity Window (C)	Time preceding/following E (msec – sec)
Reward Signal (S)	Feedback signal time locked to E (msec)
Reward Strength (R)	Ordinal or Nominal measure

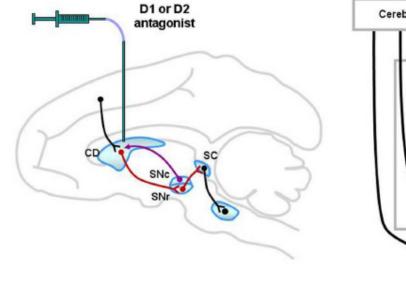
## **Contiguity Window**

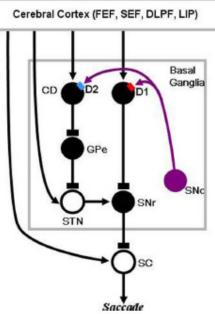


# **EEG Neurofeedback**

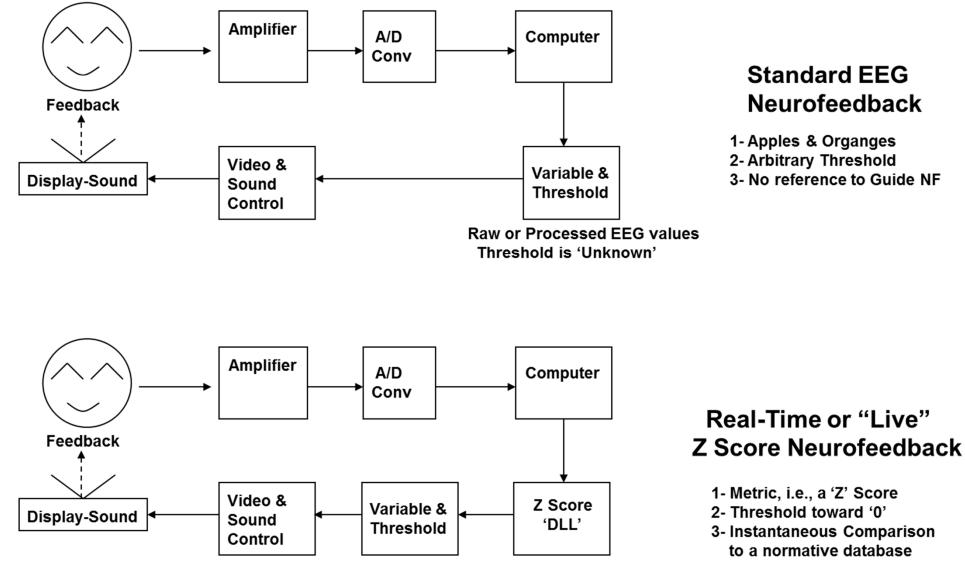






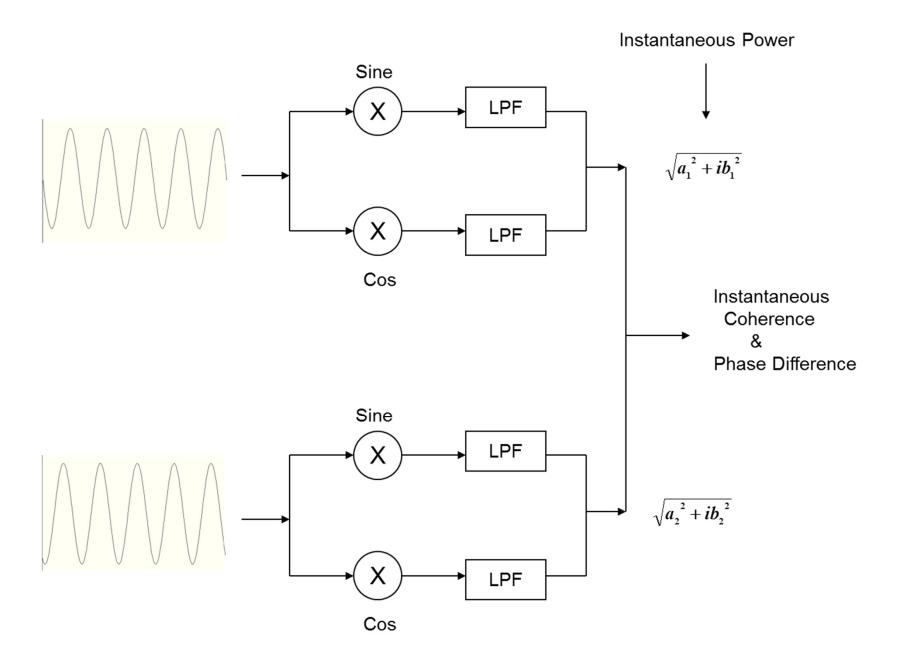


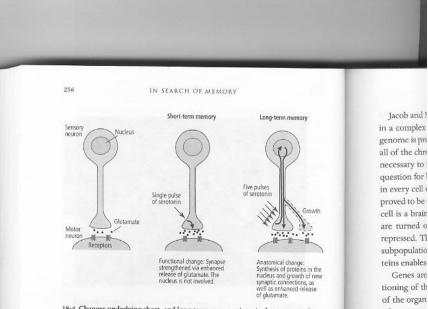
### Difference Between Standard Neurofeedback vs Z Score Neurofeedback



Move Z toward 0

## **Complex Demodulation**



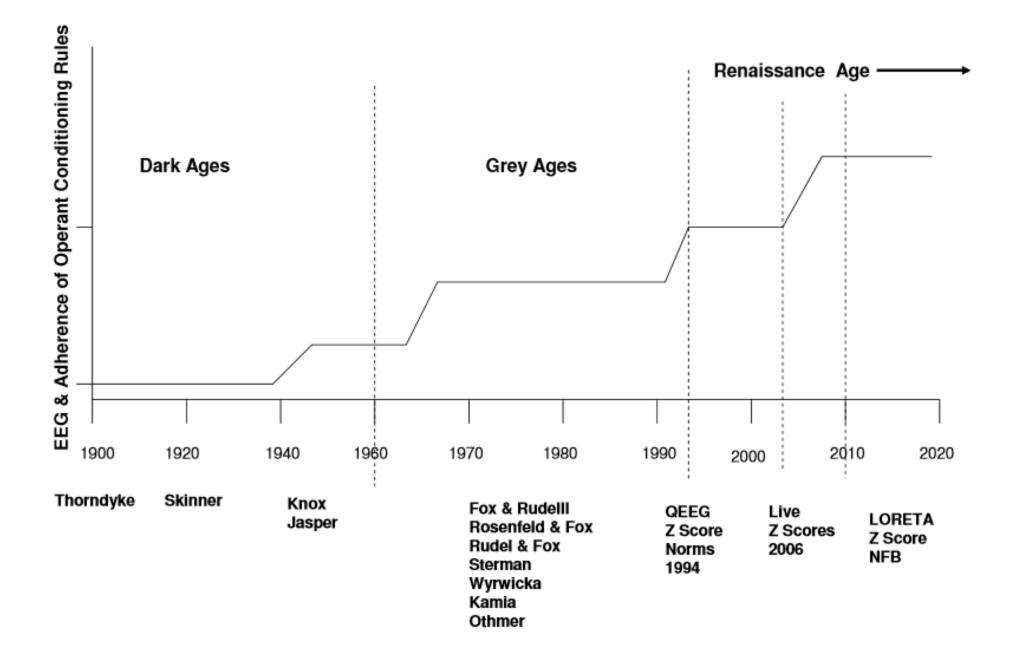


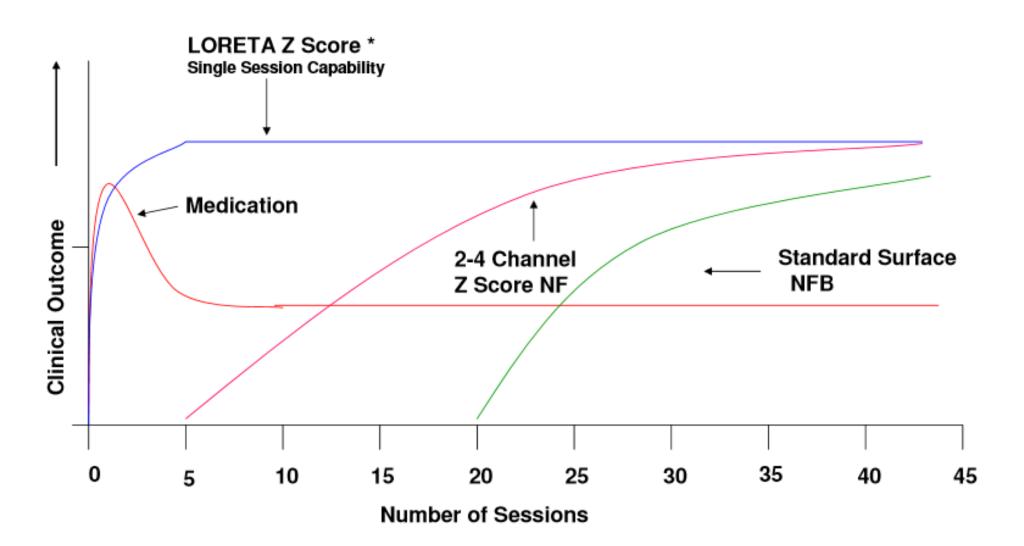
18-4 Changes underlying short- and long-term memory in a single sensory and motor neuron.

days and led to the growth of new synaptic connections, an anatomical change that did involve the synthesis of new protein (figure 18-4). This showed us that we could initiate new synaptic growth in the sensory neuron in tissue culture, but we still needed to find out what proteins are important for long-term memory.

My career in neurobiology now intersected with one of the great intellectual adventures of modern biology: the unraveling of the molecular machinery for regulating genes, the coded hereditary information at the heart of every life form on earth.

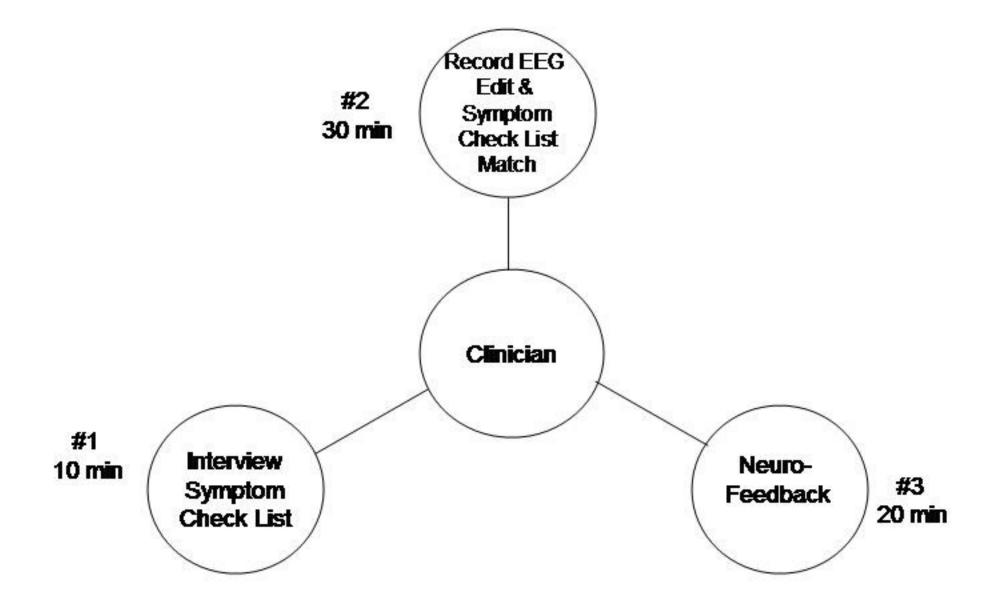
THIS ADVENTURE BEGAN IN 1961 WHEN FRANÇOIS JACOB AND Jacques Monod of the Institut Pasteur in Paris published a paper entitled "Genetic Regulatory Mechanisms in the Synthesis of Protein." Using bacteria as a model system, they made the remarkable discovery that genes can be regulated—that is, they can be switched on and off like a water faucet. in a complex genome is pre all of the chro necessary to question for in every cell proved to be cell is a brain are turned o repressed. Th subpopulatio teins enables Genes are tioning of th of the organ of energy, at essential for only at cert response to This set of night: What ment, with or patterns of What sor genes turne genes are sv guish betwe encode effe mediate spe called gene off. Jacob ar tory genes a tor gene ha particular p as the prom



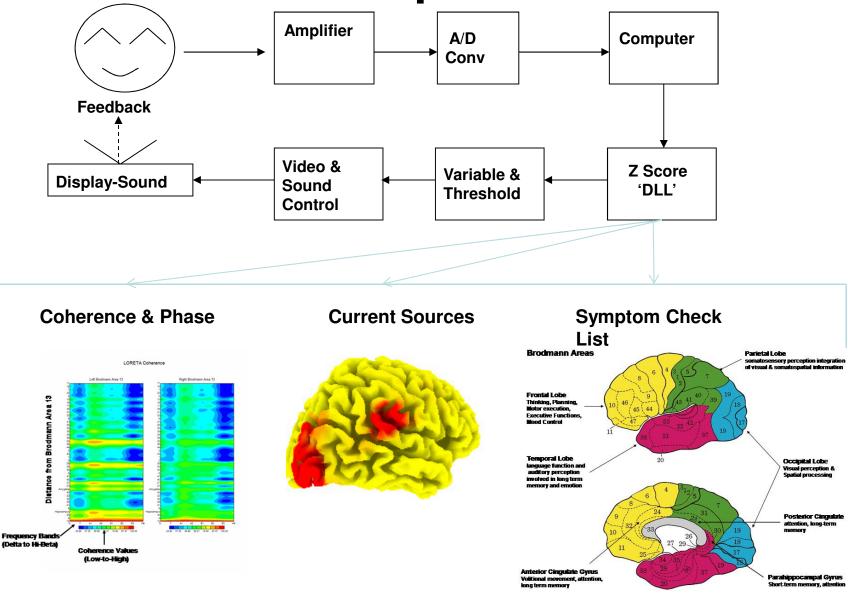


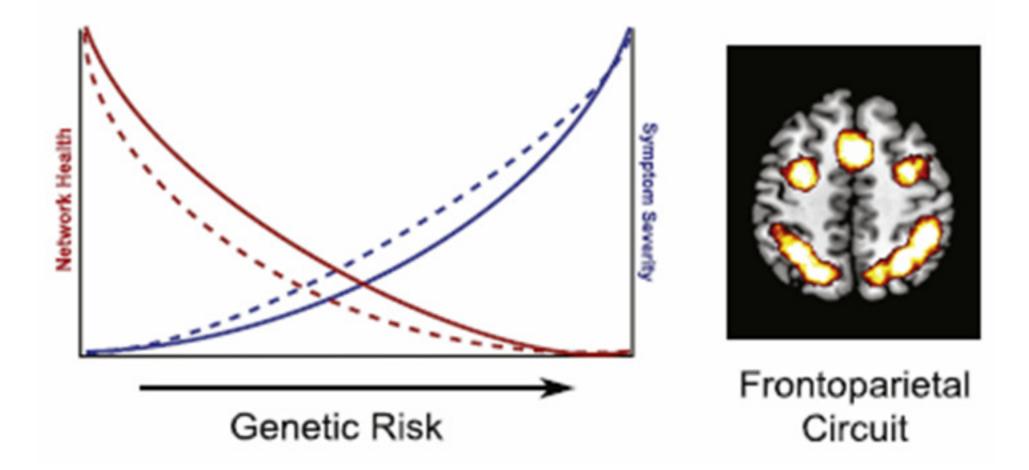
\* Combine with Neurofield in cases to reset or "unstick" the brain

### Seamless QEEG and Neurofeedback – approx. 50 – 60 minutes for a single Session in four Steps from Clinical Interview to QEEG to Neurotherapy



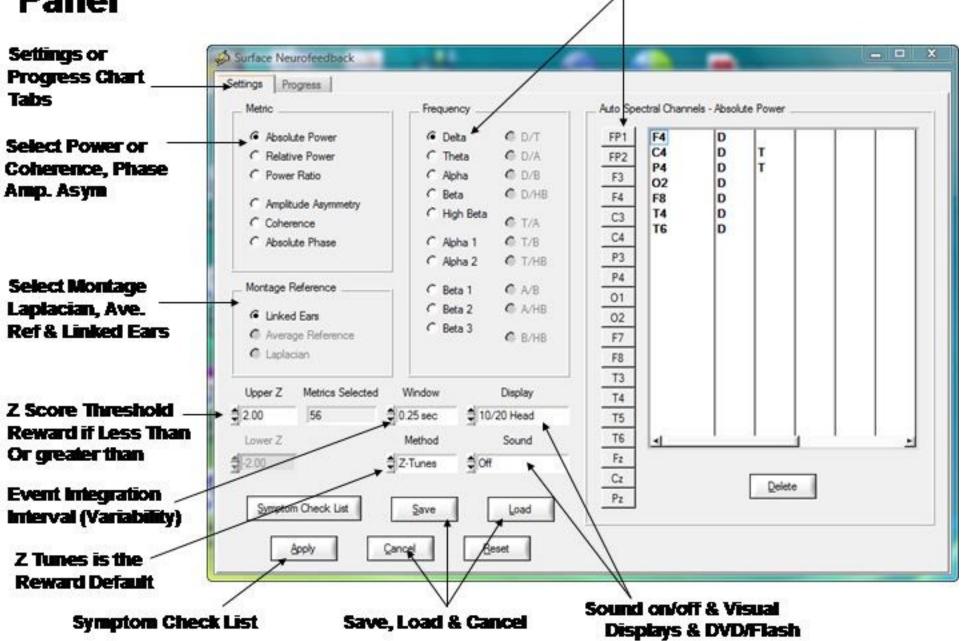
# Neuroimaging Neurofeedback – Fort Campbell



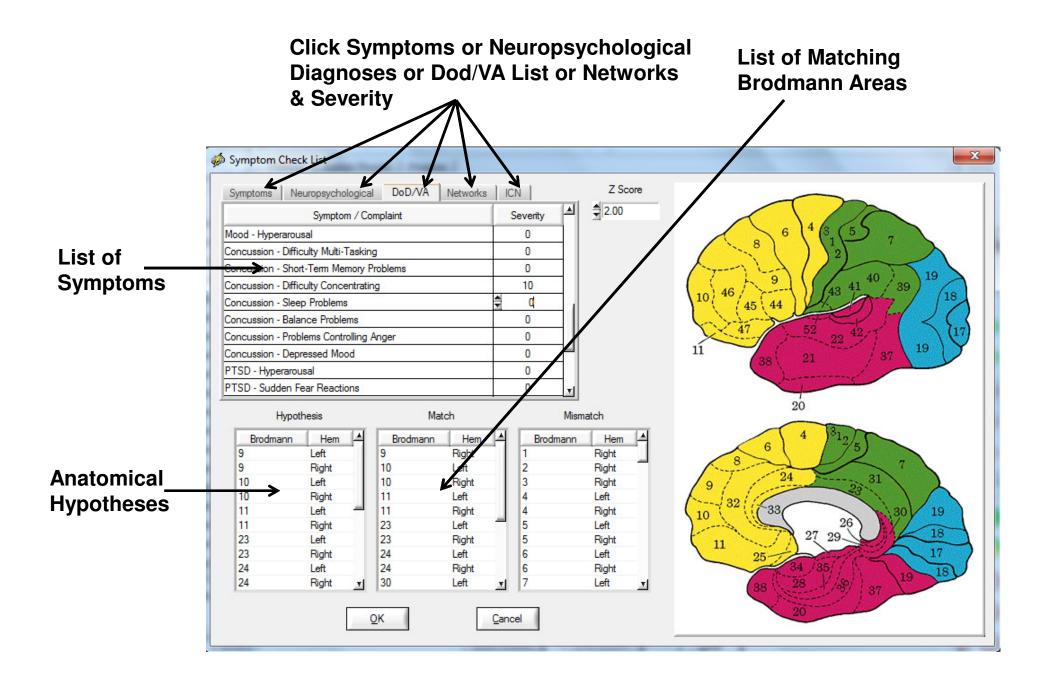


# Z Score Neurofeedback Panel

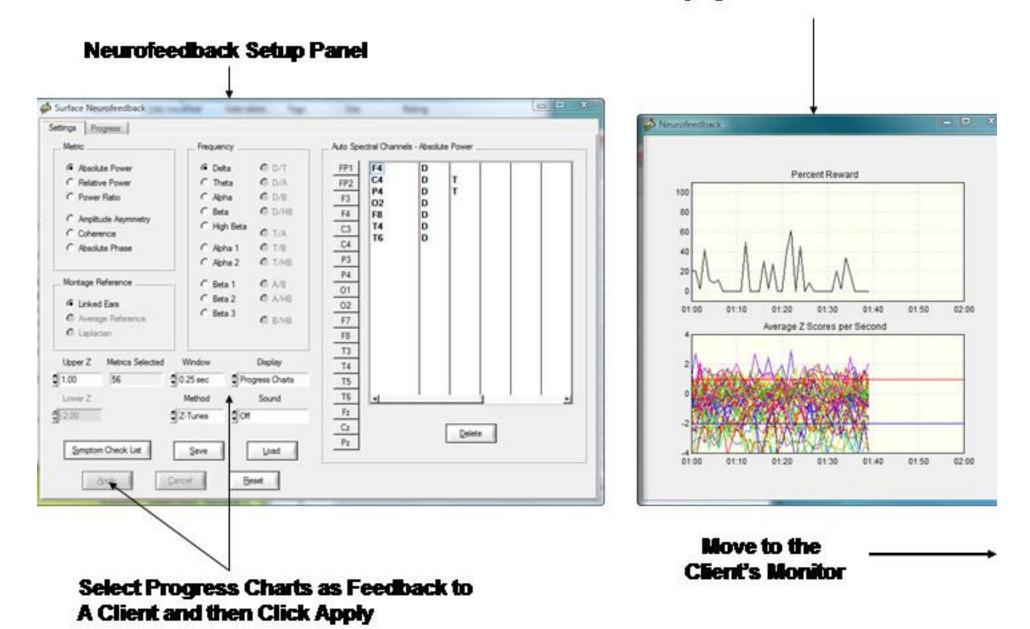
#### Select Frequency Bands & 1 to 19 Channels & Combinations of Channels for Cross-Spectra



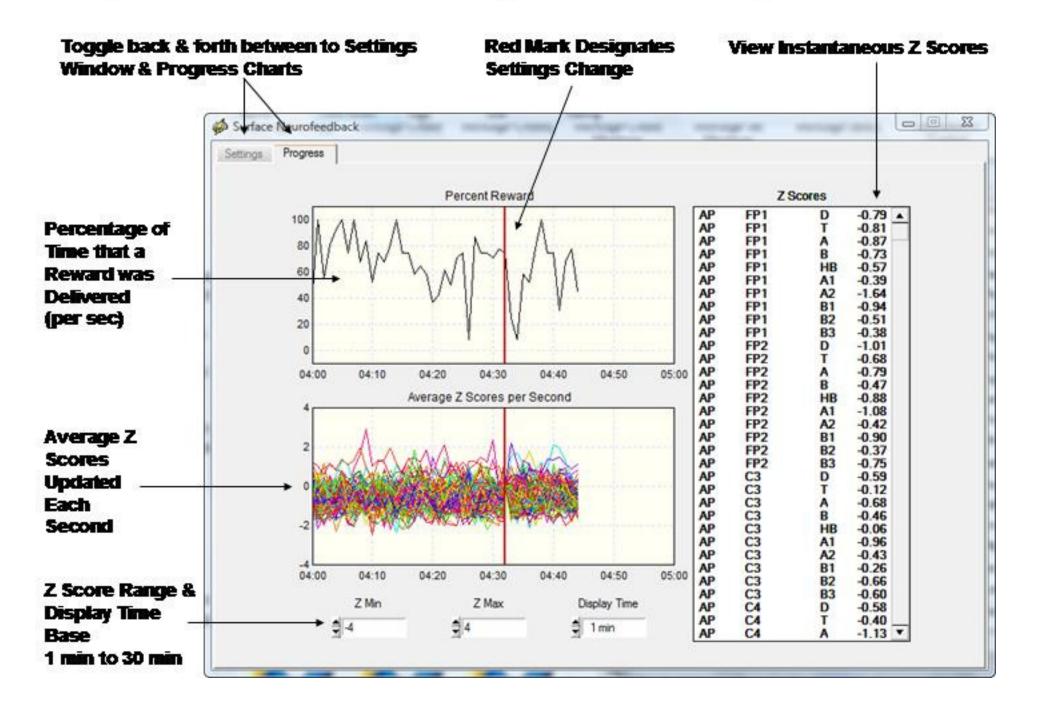
# **Neuroimaging Neurofeedback Symptom Check List**



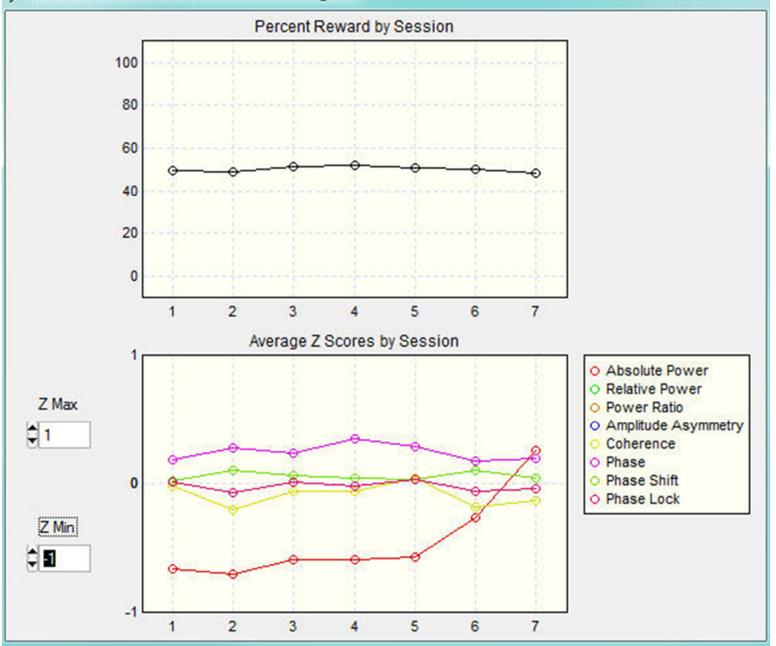
#### Use the Progress Chart as a Feedback Display and Move the Display to the Client's Monitor



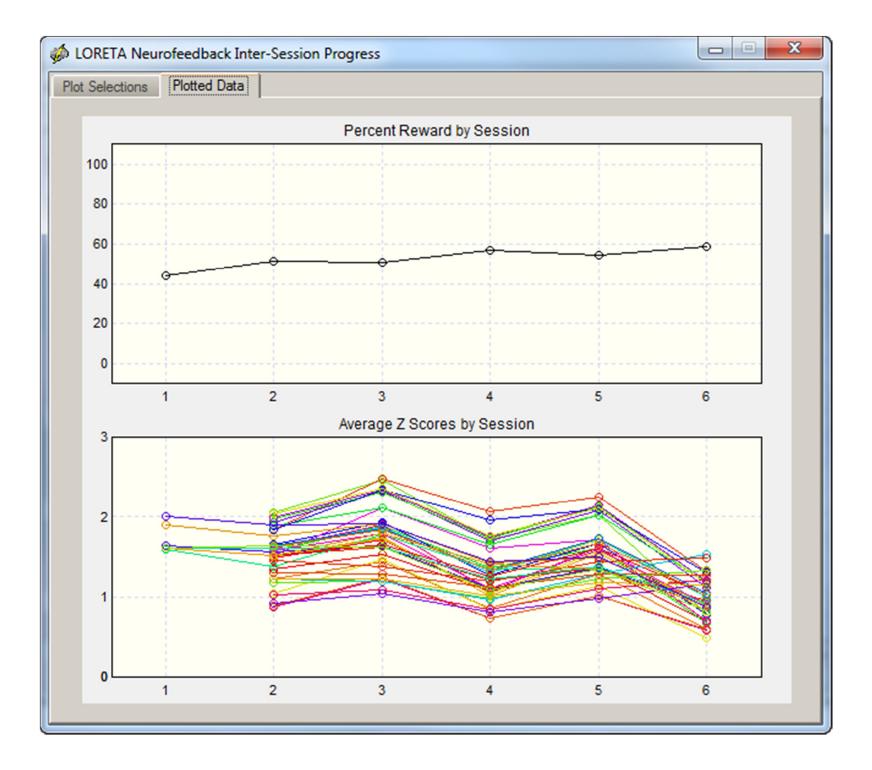
## Progress Charts to be Monitored by the Clinician During Neurofeedback

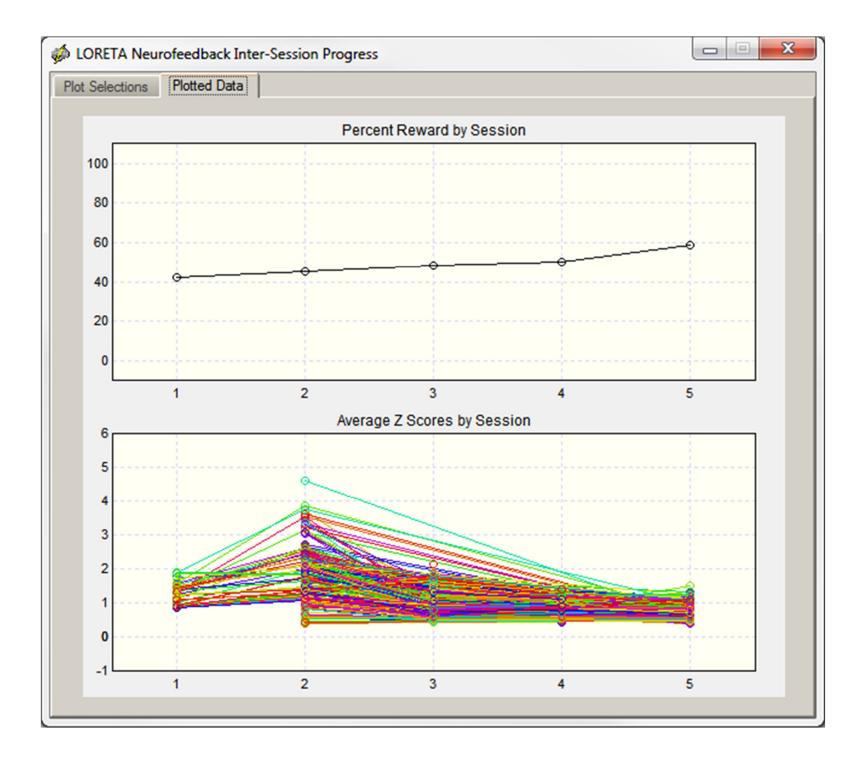


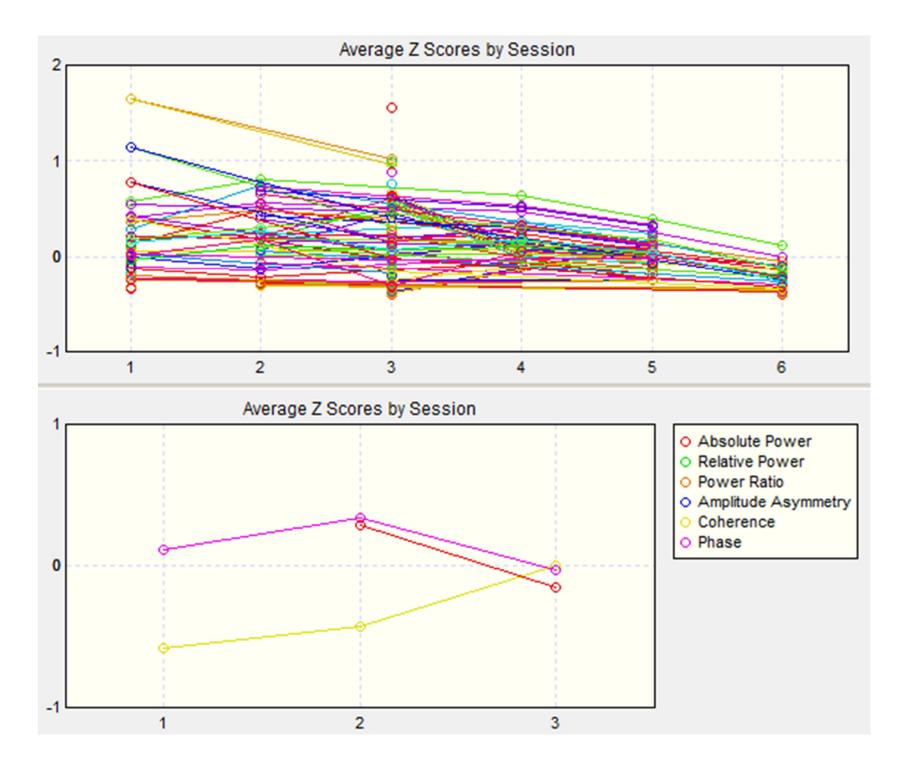
#### Surface Neurofeedback Inter-Session Progress



X



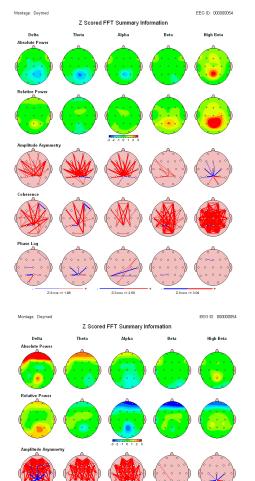




## **Examples of Surface EEG Changes After EEG Neurofeedback**

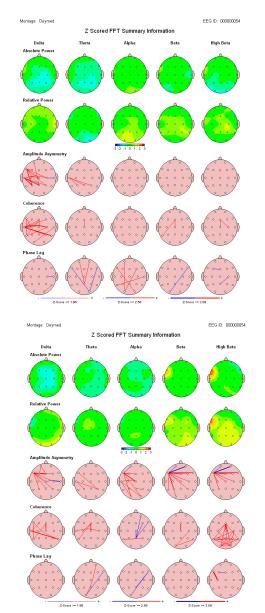
TBI Subject #1





**Pre-Treatment** 

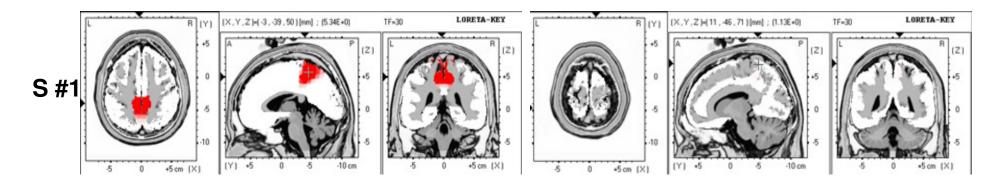
#### Post – 10 Treatments

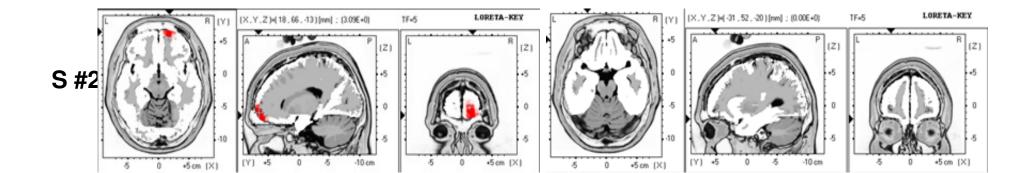


# **Examples of Electrical Neuroimaging After Neurofeedback**

### **Pre-Treatment**

## Post – 10 Treatments





## Select a Network, Frequency and Metric

Addiction Network	*
Anxiety Network	
Attention-Dorsal Network	
Attention-Ventral Network	
Attention-Emotional Network	=
Default Mode Network	
Mood Network	
Pain Network	
Pleasure Network	ш
Schizophrenia Network	
Working Memory Network	
ICN 1 (Limbic and Medial)	
ICN 2 (Subgenual ACC and OFC)	
ICN 3 (Bilateral BG and Thalamus)	*
ICN 4 (Anterior Insula, Orbital Frontal & Ant. Cingulate)	
ICN 6 (Superior and Middle Frontal Gyri)	
ICN 7 (Middle Frontal Gyri, Prefrontal & Parietal Gyri)	
ICN 8 (Ventral Precentral Gyri, Central Sulci, Postcentral Gyri)	
ICN 9 (Superior & Posterior Parietal Lobule)	
ICN 10 (Middle and Inferior Temporal Gyri)	
ICN 11, 12 (Lateral and Medial Posterior Occipital Cortices)	n
ICN 13 (Medial Prefrontal, Posterior Cingulate/Precuneus)	
ICN 15 (Right-Lateralized Fronto-Parietal Regions)	
Hagmann Module 1 (Vision)	
Hagmann Module 2 (Attention, Working Memory)	月
Hagmann Module 3 (Auditory, Language, Memory)	
Hagmann Module 4 (Auditory, Language, Memory)	
Hagmann Module 5 (Executive, Sequential Planning)	
Hagmann Module 6 (Executive, Social Skills)	+

