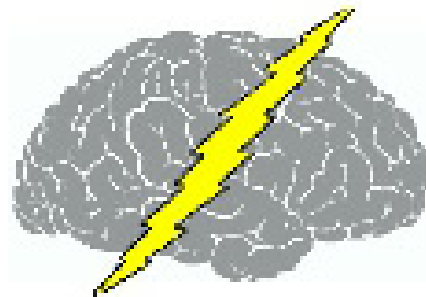


# NeuroGuide Help Manual

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**Applied Neuroscience, Inc.  
7985 113th Street  
Suite 210  
Seminole, FL 33772**

**Contact: [qeeg@appliedneuroscience.com](mailto:qeeg@appliedneuroscience.com)  
or Call 727-244-0240 for More Information**

**[www.appliedneuroscience.com](http://www.appliedneuroscience.com)**



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# Getting Started

## Manual and Tutorial

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# Part

[www.appliedneuroscience.com](http://www.appliedneuroscience.com)

(All EEG Selections and/or Sine Wave Segments are for Illustrative Purposes Only)



# Getting Started Manual & Tutorial

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## Introduction

NeuroGuide is an informative and comprehensive digital EEG and QEEG analysis system. NeuroGuide provides access to modern and simple to use Microsoft windows for automatic artifact rejection, Dynamic Lifespan Eyes Open and Eyes Closed Reference Normative Database, covering the age from 2 months to 82 years of age (N = 625). NeuroGuide includes Re-Montaging to Average Reference or the Laplacian for eyes open and eyes closed conditions.

NeuroGuide is designed for use with the LORETA Key Institute Source Localization software for registration with the Talairach MRI Atlas from the Montreal Neurological Institute. NeuroGudie provides tab delimited output files that can be imported into any statistical package or database management system.

Joint-Time-Frequency-Analyses (JTFA) are available to explore the details of time and frequency, including dynamic JTFA normative database analyses and instantaneous power, coherence and phase delays.

The NeuroGuide Discriminant Functions (DIS) add on includes a Mild Head Injury Discriminant Function and a Learning Disabilities Discriminant Function. The discriminant functions are not intended to provide a clinical diagnosis but are only an adjunct to other measures.

NeuroGuide Brain Performance Index (BPI) is an add on product and includes predictive correlations between EEG and Neuropsychological function such as Block Design, Digit Span and I.Q. and other cognitive measures. The Brain Performance Index is a correlative research tool and is not intended to diagnose or render clinical judgments.

NeuroStat (NS) is an add on program that computes Pre-Test vs. Post-Test EEG Comparisons, as well as, Statistical Group Comparisons.

NeuroBatch (NB) is an add on program that Automatically Processes Large Batches of Edited EEG and Organizes EEG Data for Purposes of Group Statistics.

LORETA Normative Reference Database (LOR) is an add on program that provides 3-Dimensional Z Scores from 2 months to 82 years of age launched from the NeuroGuide edit window using the Key Institute Explorer Viewer.

LORETA Normative Source Correlation Database (SC) is an add on program that provides 3-Dimensional Correlations between Regions of Interest from 2 months to 82 years of age.



**LORETA Normative Coherence and Phase Database (LCP)** is an add on program that provides 3-Dimensional Correlations between Regions of Interest from 2 months to 82 years of age.

**LORETA Phase Reset Normative Database (LPR)** is an add on product that provides 3-Dimensional Phase Shift Duration and Phase Lock Duration means and standard deviations between Regions of Interest from 2 months to 82 years of age.

**Connectivity Suite (CS)** includes the full 171 electrode combination topographic maps of Cross-Spectra, In-Phase Spectra, Out-of-Phase Spectra, correlation (comodulation), coherence, Phase and Phase Reset.

**Spindle or Burst Metrics** include number of spindles/sec, mean amplitude of spindles, mean duration of spindles and mean inter-spindle interval.

**Scalp Surface EEG Phase Reset** is part of the Connectivity Suite (CS) and is the first derivative of the time series of straightened phase differences and includes number of phase resets/sec, mean amplitude of phase resets, mean duration of phase resets, mean phase locking interval and average rate of change of phase differences.

**EEG Acquisition add on module (NC)** designed to record EEG from different amplifiers and is necessary for surface or LORETA Z Score neurofeedback.

**Surface 1-19 Channel Z Score Neurofeedback (NF1)** is a Symptom Check List based EEG biofeedback add on module. Allows for Neurofeedback of Average Reference and Laplacian and Linked Ears montages for absolute and relative power, power ratios, amplitude asymmetry, coherence, phase differences, phase shift duration and phase lock duration.

**LORETA Z Score Neurofeedback (NF2)** is a Symptom Check List based EEG biofeedback add on module. Allows for Neurofeedback of 88 different Brodmann areas for current density, amplitude asymmetry, coherence, phase differences, phase shift duration and phase lock duration.

**BrainSurfer (SURF)** is a Brain-Computer-Interface (BCI) method to operantly modify the current sources from Brodmann areas and connections between Brodmann areas (i.e., nodes and network connections) of the EEG. BCI is a type of EEG Biofeedback or Neurofeedback procedure in which particular EEG activity is detected and then subjects are trained to increase the probability of EEG activity linked to a device like a computer display or robot or prosthesis. BrainSurfer is the patient's own brain rendered by an MRI that provides real-time and continuous feedback about the stability of nodes and connections between nodes in networks of the brain linked to the patient's symptoms. A clinician can zoom inside of the 3-D rendered



brain to a specific node or a specific connection between nodes to increase specificity of instrumental learning in particular Brodmann areas or functional connections between Brodmann areas in real-time. One can view the 3-dimensional current sources inside of the MRI volume by rotating the volume and making the rendered surface transparent. BrainSurfer computes real-time sLORETA from the center voxel Brodmann Area Current Density, including Surface and/or Node views. BrainSurfer also computes real-time functional connectivity Z Scores of Coherence, Phase difference, Phase Lock Duration, Phase Shift Duration between Brodmann Areas.

Standalone Symptom Check List (SCL) is a neurofeedback protocol generator using a patient symptom check list to link symptoms to dysregulated nodes and connections between nodes linked to symptoms. One can print and save the protocol in tab delimited format.

NeuroGuide Signal Generator is a free educational tool distributed in the Demo at [www.appliedneuroscience.com](http://www.appliedneuroscience.com) by which basic digital signal processing of EEG can be learned and LORETA and NeuroGuide and other programs can be tested.

NeuroGuide provides tools as analytical resources and as an EEG reference based on peer reviewed scientific publications. NeuroGuide does not diagnose nor render any clinical decisions and it is designed for use by trained and competent individuals. Any clinical use must be by qualified medical or clinical professionals restricted to the visual and statistical evaluation of the human electroencephalogram (EEG). EEG artifact can invalidate analyses and improper positioning of electrodes or significant deviations from accepted standards of electroencephalographic recording methodology can invalidate EEG recordings or erroneous storage of data and falsification of data, improper manipulation of data or unlawful uses of NeuroGuide including violations of copyright law and other improper uses of NeuroGuide are all contra indicated.

Visit [www.appliedneuroscience.com](http://www.appliedneuroscience.com) to learn more about NeuroGuide



## Intended Use

For clinical purposes the NeuroGuide Analysis system is to be used by qualified medical or clinical professionals for the statistical evaluation of the human electroencephalogram (EEG). For research and education NeuroGuide is intended to be used by competent and ethical students and professionals for the statistical evaluation of the human electroencephalogram (EEG).

## Installations

### How to Install NeuroGuide:

Before you proceed make sure to make a backup copy of zip folder that contains the NeuroGuide installation files and keep it in a safe place, in case you need to reinstall this version of NeuroGuide.

Unzip or Extract the NeuroGuide installation files from the .zip folder and save all the installation files to the same folder and note the location of that folder (be sure that all the installation files are in the same folder). To install NeuroGuide open the folder with all the installation files, then open the Volume folder and double click on the setup.exe file.

If you have installed an earlier version of NeuroGuide then uninstall will run first and then automatically proceed with the install.

After installation, depending on which version of Window you are currently using, Click the Start button, select All Programs, select the NeuroGuide Folder, then select NeuroGuide to launch NeuroGuide or Click on the NeuroGuide icon located on your Desktop or in your Task Bar. We advise that one always use the default directory of c:/program files for the installation directory. If you shift installation to a different directory after receiving a Key B based on the initial directory then your initial Key B will no longer work. If this happens, please contact us by phone 727-244-0240 or at [geeg@appliedneuroscience.com](mailto:geeg@appliedneuroscience.com).

### Download the Tutorial Files:

To download the other EEG Tutorial Files available to help you learn NeuroGuide, go to: [www.anipublishing.com/Downloads](http://www.anipublishing.com/Downloads). The link is near the bottom of the Downloads page, before the Download Form. Save the .zip file in the NeuroGuide Folder on your hard drive. Then Extract or Unzip and save the TUTORIAL\_FILES folder that contains the tutorial files in the NeuroGuide folder for later use.





## How to Install the Add-On Normative Databases:

The Bi-Spectral Normative Database and the LORETA Source Correlation Normative Database are large files that need to be downloaded separately. Go to: [www.appliedneuroscience.com/AddonDatabases.htm](http://www.appliedneuroscience.com/AddonDatabases.htm) to download the Add-on Normative Databases. Save the .zip file in a folder on your hard drive then right mouse click and select unzip or Extract and save the installation files in the same folder. Then double click the Setup.exe to install the large normative database add-ons. These databases are accessible only if one has purchased the BiSpectrum add on and/or the LORETA Source Correlation normative database add on. See [http://www.appliedneuroscience.com/Price\\_List.htm](http://www.appliedneuroscience.com/Price_List.htm) for price details.

## How to Install the Key Institute's LORETA software:

Go to: [www.unizh.ch/keyinst/NewLORETA/Software/Software.htm](http://www.unizh.ch/keyinst/NewLORETA/Software/Software.htm) and after reading the available information before you download the free software package, then:

Download the LORETA-KEY® software package; and

Request the Password ( necessary for installation & may take 2-3 days to arrive).

If you are interested:

Download Brodmann Area information for LORETA Voxels (use the LORETA-KEY software password to Extract the files from the .zip folder).



## Key A and Key B to Activate NeuroGuide

The first time that NeuroGuide is launched a Copyright Agreement appears. Click yes to accept the Terms of the Agreement, otherwise the program will terminate. The next window is a NeuroGuide Security Key window that contains a Key A. Once your payment for NeuroGuide has processed then a Key B will be issued that will unlock the full power of NeuroGuide including the ability to import EEG files. Highlight and Copy (Ctrl-C) the Security Key A and then Paste (Ctrl-V) the Security Key A into an email addressed to [geeg@appliedneuroscience.com](mailto:geeg@appliedneuroscience.com). To facilitate this process, click Create Key A File to automatically launch Notepad, which you then attach to an email to [geeg@appliedneuroscience.com](mailto:geeg@appliedneuroscience.com). Note on some systems a blank Send\_Key\_A.txt WordPad document will open, you can then Copy and Paste the Key A in the blank WordPad document, select Save as under the File menu, and save the document to some other location on your computer. Go to [www.appliedneuroscience.com/Order.htm](http://www.appliedneuroscience.com/Order.htm) to purchase NeuroGuide, any of the many NeuroGuide Add-ons or to view the prices.



NeuroGuide Security Keys

NeuroGuide Security Key A

38ZI UE7A CYIA F5B9 AZHY MY39

38ZIVE7ACYIAF5B9AZHYMY39

NeuroGuide Security Key B

NeuroGuide Security Key C

Create Key A File

OK Cancel

After your payment for NeuroGuide has processed and you have received your Key B by email, Copy (Ctrl-C) and Paste (Ctrl-V) the Key B into the NeuroGuide Security Key B area and click OK. The Security Key B uses the Computer ID numbers that are unique to the single computer and single user license that you use to register your software. The security key C is issued only if one purchases the NC acquisition module (Click Collection > Hardware Selection to view the amplifiers that NeuroGuide can collect EEG from). A second but renewable license will be issued at no extra cost to individuals who have a laptop at work and/or a desktop computer at home, etc. It is important to note that a single user's license is all that is allowed and separate licenses must be purchased if users other than the single user intends to use the software (see Copyright License Agreement which is saved on your computer when you launch NeuroGuide).



NeuroGuide Security Keys

NeuroGuide Security Key A

Q O U 7 8 Q 7 N 1 O U B H X P P 9 A 8 W E O R B

QOU78Q7N1OUBHXPP9A8WEORB

NeuroGuide Security Key B

U D U Z 0 O M 8 9 I 4 R L L 6 G E K J D 7 6 7 I

UDUZOOM89I4RLL6GEKJD767I

NeuroGuide Security Key C

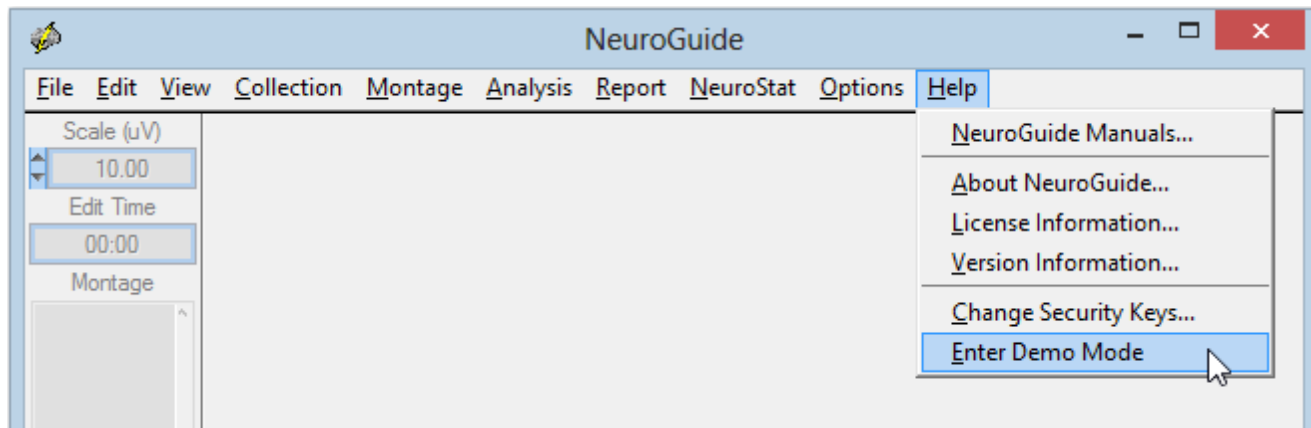
Create Key A File

OK Cancel



## Demo Mode

The Demo mode is activated clicking Help, and then selecting Enter Demo Mode. In the Demo mode the user is still bound by the terms of the single user copyright agreement, however, users are limited to using the exemplar files inside of NeuroGuide and demo users will not be able to import their own data.



Even after one has activated NeuroGuide the user can Enter the Demo Mode at any time. This allows users to explore Add Ons that they may want to purchase in the future.

## Support and Upgrades

Support is available from 9am to 5pm Monday to Friday. You may contact us by email or phone at [http://www.appliedneuroscience.com/contact\\_us.htm](http://www.appliedneuroscience.com/contact_us.htm). We are constantly updating the program with new features and new EEG file formats.

One year of free upgrades from the date of first purchase are included with each purchase of NeuroGuide. After one year of free updates, there is a fee for a one year update subscription if one wants to continue to have access to future updates ([www.appliedneuroscience.com/Update\\_Subscription.htm](http://www.appliedneuroscience.com/Update_Subscription.htm)). The Key B issued prior to expiration of free updates will continue to operate for all NeuroGuide versions that were made available prior to expiration of the free service condition.

You will be invited to join the NeuroGuide users group at yahoo.com where open discussion is encouraged and new upgrades are announced. Once you purchase NeuroGuide please join this group and check for the release of new updates of NeuroGuide. To view the most recent updates and the history of updates go to: <http://www.appliedneuroscience.com/whatsnew.htm>

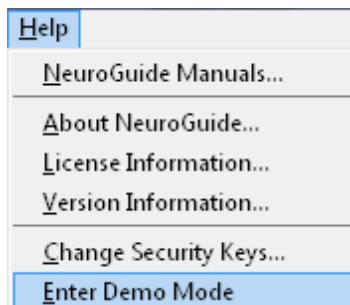


## Supported Formats

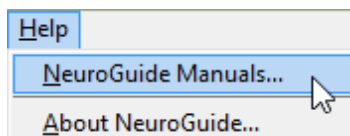
New File formats and features are constantly being added to NeuroGuide. Visit our website at [www.appliedneuroscience.com](http://www.appliedneuroscience.com) > [Why NeuroGuide](#) > [EEG Imports](#) for the most up-to-date list of supported formats. To equate the amplifier characteristics of different EEG machines to the amplifier characteristics of the normative reference database micro-volt calibration sine waves are input into the different EEG machines and equilibrated to the amplifier characteristics of the normative amplifiers. The Universal physics metric of the EEG is the Volt defined as joules/coulomb.

## Help Menu

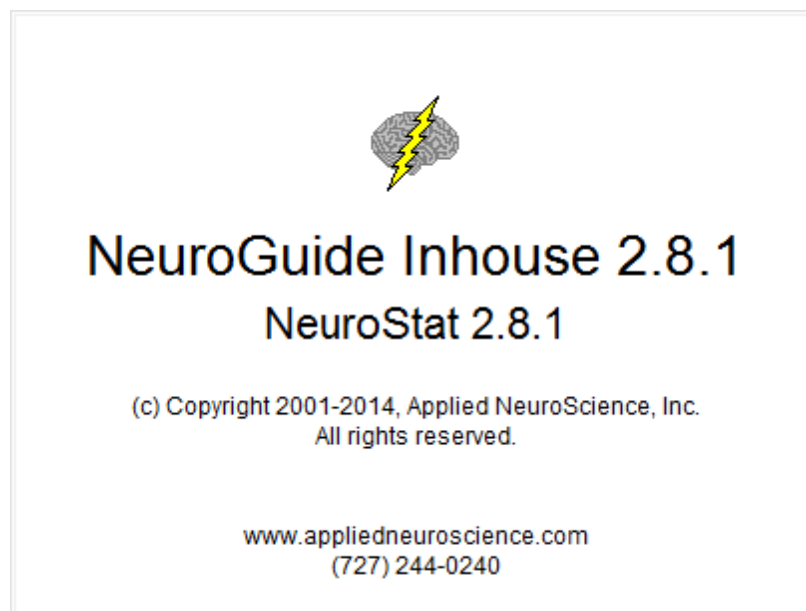
The Help Menu contains important options. Click Help and view the options below:



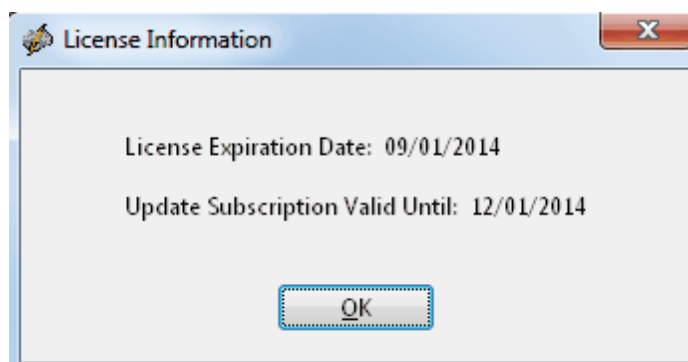
Click Help > NeuroGuide Manuals to Open the Manuals...



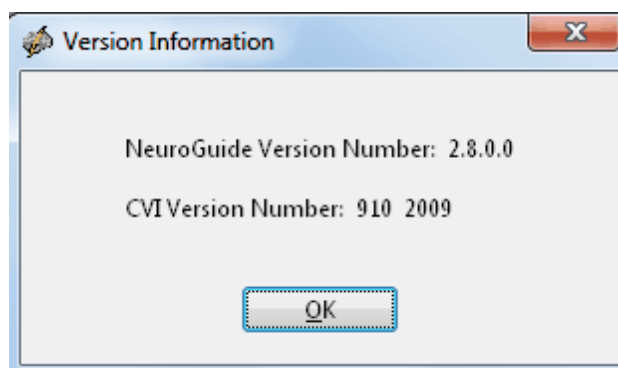
Click Help > About NeuroGuide...



Click **Help > License Information...** to determine the **Expiration Date** if a **Renewable** or **Temporary License** is active and the **Date of Expiration** of the one year update subscription after which access to future updates will not be permitted.



Click **Help > Version Information...** to determine the exact release number of **NeuroGuide** and the **CVI** version number that was used to create **NeuroGuide**

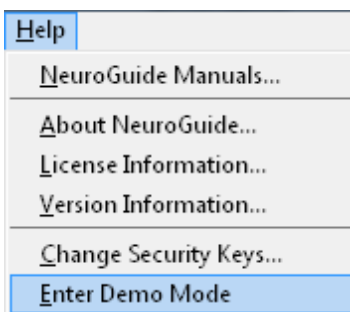




Click Help > Change Security Keys... in order to gain access to your Key A. Key B & C will be blank and this window is important to send to Applied Neuroscience, Inc., if there was an expiration or if new add ons are purchased.

The screenshot shows the 'NeuroGuide Security Keys' dialog box. It has a title bar with a close button (X). The dialog is divided into three sections for 'NeuroGuide Security Key A', 'NeuroGuide Security Key B', and 'NeuroGuide Security Key C'. Key A is pre-filled with six boxes containing '4S4U', 'KJOJ', 'J4X6', 'WI4E', 'EW3Y', and 'EUJH', with a summary box below showing '4S4UKJOJJ4X6WI4EEW3YEUVJH'. Key B and Key C each have six empty boxes and a summary box below them. At the bottom, there are three buttons: 'Create Key A File', 'OK', and 'Cancel'.

To Enter the Demo Mode Click Help > Enter Demo Mode







## Tutorials

[Conventional EEG Tutorial Steps](#) <sup>22</sup>

[QEEG Tutorial Steps](#) <sup>23</sup>

[EEG Collection Tutorial Steps](#) <sup>24</sup>

[EEG Surface Neurofeedback Tutorial Steps](#) <sup>25</sup>

[LORETA Neurofeedback Tutorial Steps](#) <sup>26</sup>

[Brain Surfer Brain-Computer-Interface \(BCI\) Tutorial Steps](#) <sup>27</sup>



## Conventional EEG Tutorial Steps

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- Step 2 [Import EEG](#) <sup>101</sup>
- Step 3 [Change Polarity & Colors](#) <sup>198</sup>
- Step 4 [Create Montages](#) <sup>162</sup>
- Step 5 [Remontage to Bipolar, Common Reference, Average & Laplacian](#) <sup>199</sup>
- Step 6 [Visually Examine & Mark Events](#) <sup>94</sup>
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## QEEG Tutorial Steps

- Step 1      **Symptoms & Hypothesis Formation Prior to Recording EEG**
- Step 2      [Import EEG](#) <sup>101</sup>
- Step 3      [Visual Examination and Artifact Free Selections](#) <sup>31</sup>
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- Step 7      **Test Hypothesis Linkage of Symptoms using LORETA Frequency Domain**
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- Step 9      **Generate, Save & Print Report**
- Step 10     **Save & Export EEG**



## EEG Collection Tutorial Steps

Step 1 [Amplifier Selection](#) <sup>89</sup>

Step 2 [Setup & Monitor](#) <sup>89</sup>

Step 3 [Record, Pause & Stop](#) <sup>94</sup>

Step 4 **Save the Recording**



## EEG Surface Neurofeedback Tutorial Steps

- Step 1** Hypothesis Formation of Likely Networks Linked to Symptoms
- Step 2** Start EEG Collection & Monitor Traces
- Step 3** Click Collection > Neurofeedback > Surface EEG Neurofeedback
- Step 4** [Symptom Check List to link symptoms to dysregulated brain systems](#)<sup>171</sup>
- Step 5** Protocol Generation
- Step 6** [Set Number of Rounds and Duration of Rounds](#)<sup>175</sup>
- Step 7** Start Neurofeedback and [View the Progress Chart to Achieve 25-30 rewards/minute](#)<sup>177</sup>
- Step 8** Adjust Z Score threshold toward Z = 0 and maintain 25-30 rewards/minute



## LORETA Neurofeedback Tutorial Steps

- Step 1 Hypothesis Formation of Likely Networks Linked to Symptoms
- Step 2 Start EEG Collection & Monitor Traces
- Step 3 Click Collection > Neurofeedback > LORETA Neurofeedback
- Step 4 [Symptom Check List to link symptoms to dysregulated nodes and connections between nodes](#) <sup>184</sup>
- Step 5 Protocol Generation
- Step 6 [Set Number of Rounds and Duration of Rounds](#) <sup>189</sup>
- Step 7 Start Neurofeedback and [View the Progress Chart to Achieve 25-30 rewards/minute](#) <sup>193</sup>
- Step 8 Adjust Z Score threshold toward Z = 0 and maintain 25-30 rewards/minute



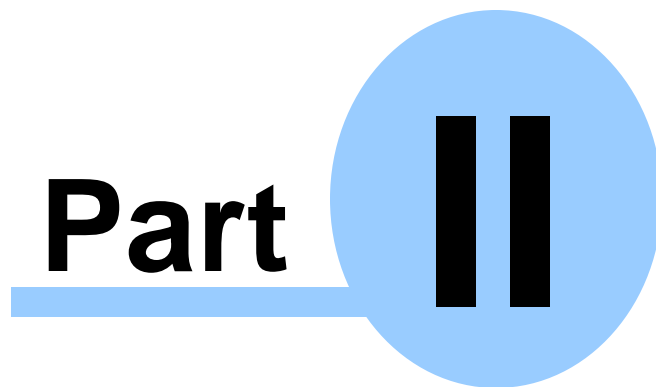
## Brain Surfer Brain-Computer-Interface (BCI) Tutorial Steps

- Step 1** Hypothesis Formation of Likely Networks Linked to Symptoms
- Step 2** Start EEG Collection & Monitor Traces
- Step 3** Click Collection > BrainSurfer
- Step 4** [Symptom Check List to link symptoms to dysregulated brain systems](#)<sup>65</sup>
- Step 5** Protocol Generation
- Step 6** [Set Number of Rounds and Duration of Rounds](#)<sup>67</sup>
- Step 7** Start BrainSurfer and view the Progress Chart to Achieve 80-90 percent of metrics/minute
- Step 8** Adjust Z Score threshold toward  $Z = 0$  and maintain 80-90 percent metrics/minute

# NeuroGuide

## Manual and Tutorial

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(All EEG Selections and/or Sine Wave Segments are for Illustrative Purposes Only)



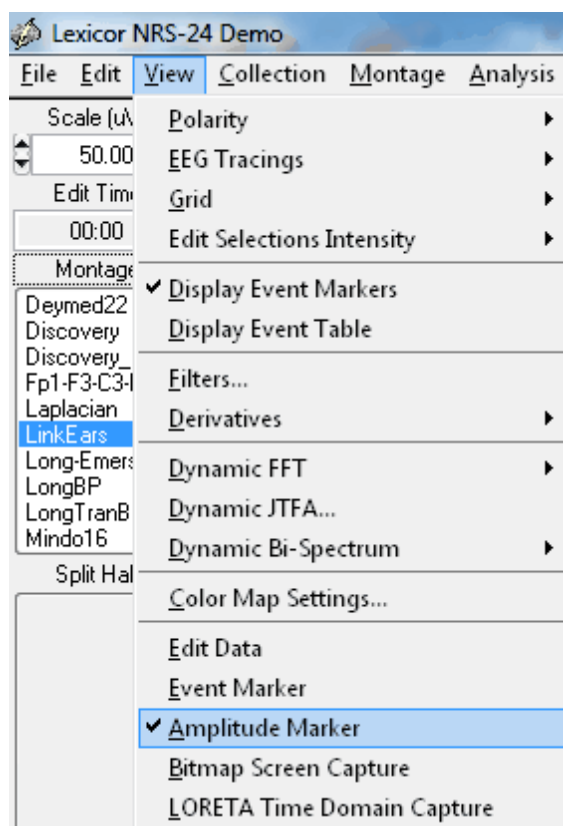


## NeuroGuide Manual & Tutorial

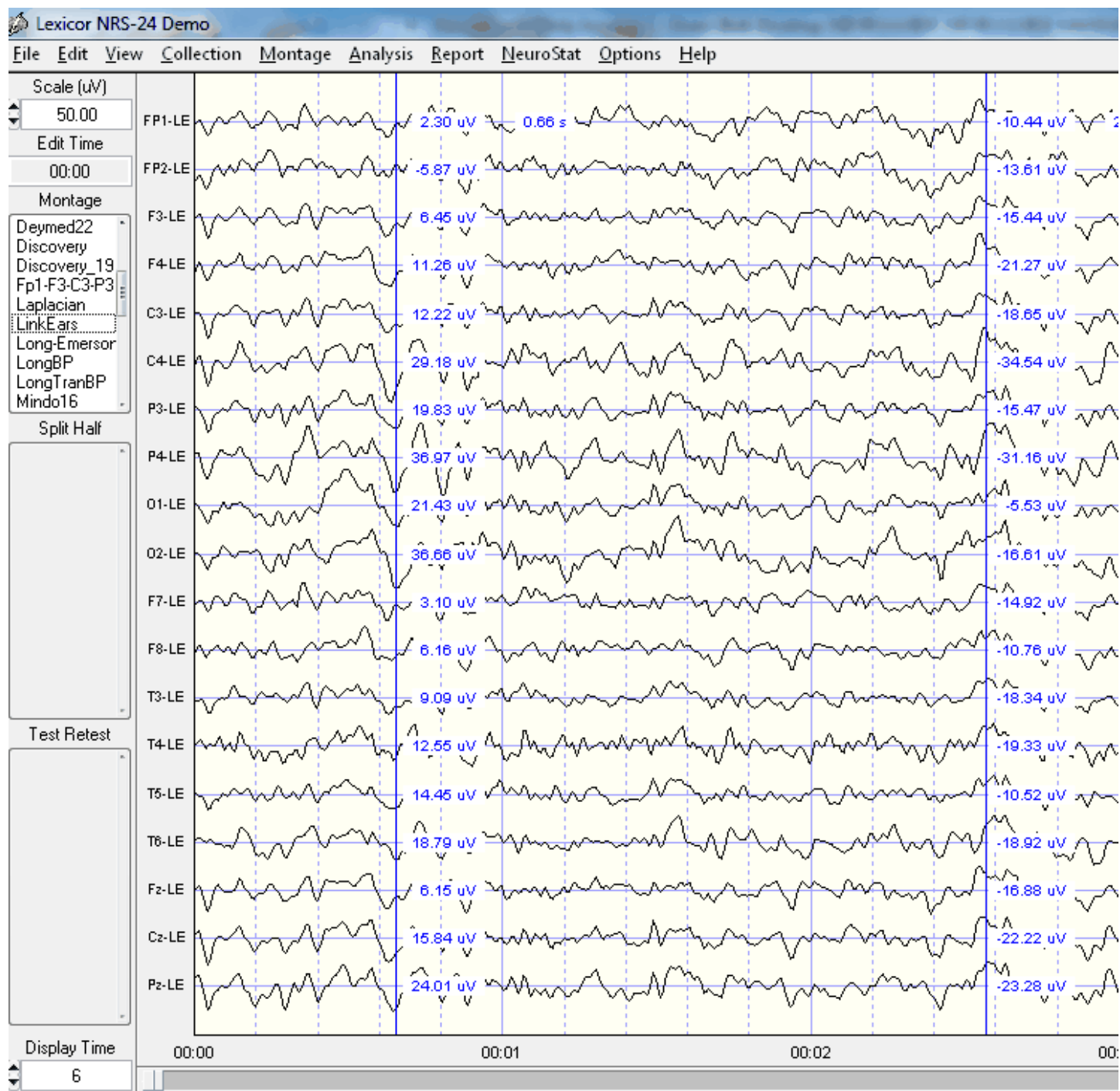
The NeuroGuide Manual is a guide with a brief tutorial with step by step procedure designed to help users to learn the basics of conventional EEG and qEEG. qEEG builds on the foundations of artifact free selections and uses computers to spectral analyze the frequency, power, phase differences, coherence and source localization of the surface EEG.

### Annotation Tool

Use Annotate Tool to Examine peak-to-peak features of the EEG such as amplitude in microvolts ( $\mu\text{V}$ ) and time



Press the left mouse button and drag over the EEG segments of interest and read the instantaneous microvolt values ( $\mu\text{V}$ ) or microamperes ( $\mu\text{A}$ ) in the CSD montage. To Erase the annotations, press the right mouse button and drag over the annotations to be erased.





## Artifact Free Manual and Automatic EEG Selections

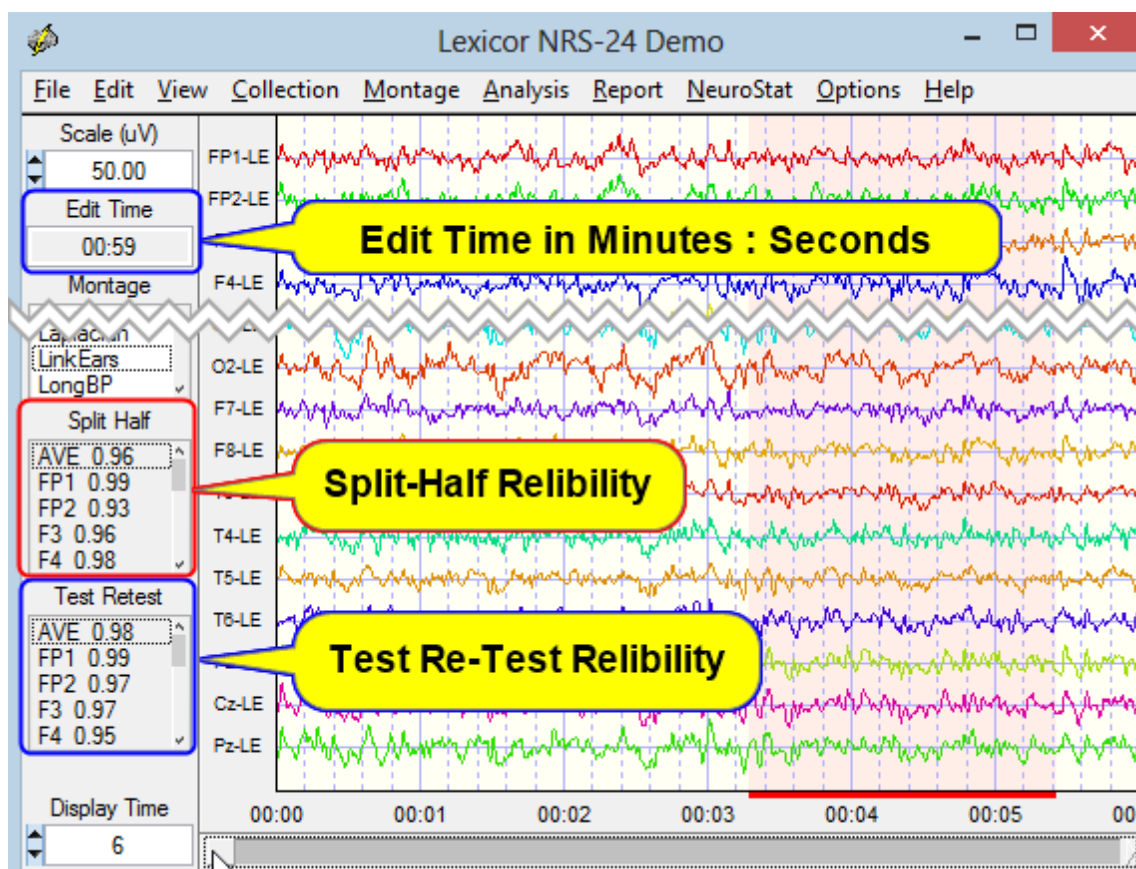
The complete entire EEG record must be viewed by clicking end and page down and page up and home and by arrow keys and by moving the wiper at the bottom of the screen. Conduct a careful visual examination of the EEG record to detect epilepsy and gross pathology as well as to identify artifacts. The goal is to avoid selecting any artifact and instead to only select artifact free segments of EEG. There are three methods of obtaining Artifact Free Selections:

1. Manual Selections are obtained by pressing the left mouse button and dragging to select, press right mouse button and drag to erase;
2. Artifact Free Template Matching; and
3. Z Score Artifact Free Selections.

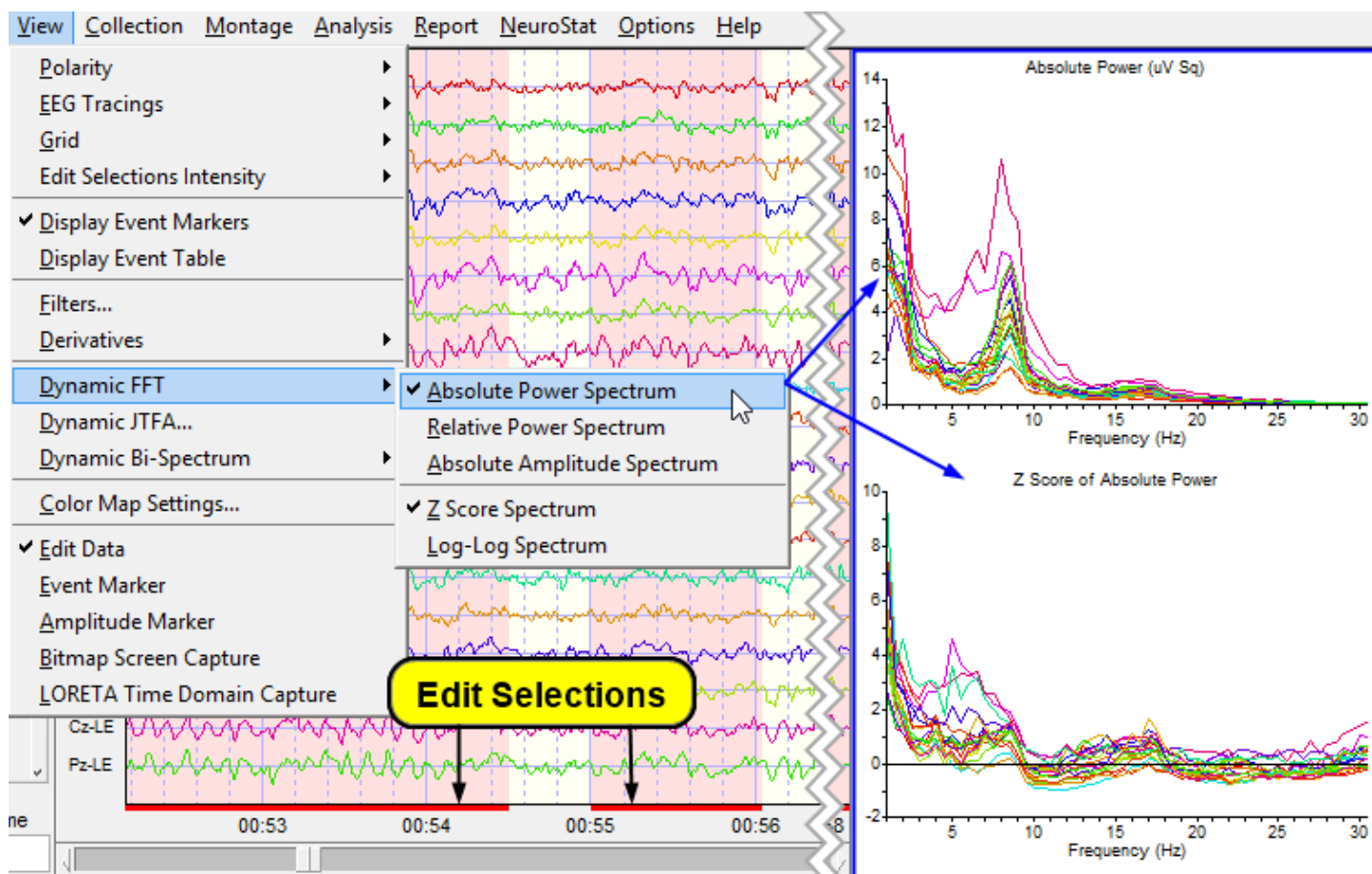
All three methods can be used and manual selection takes priority over all methods of artifact free selection. That is, left and right mouse button dragging will override all other methods. View the Length of EEG Selections in seconds and View the dynamic Reliability Measures of the EEG Selections.

### Manual Selections of Artifact Free EEG

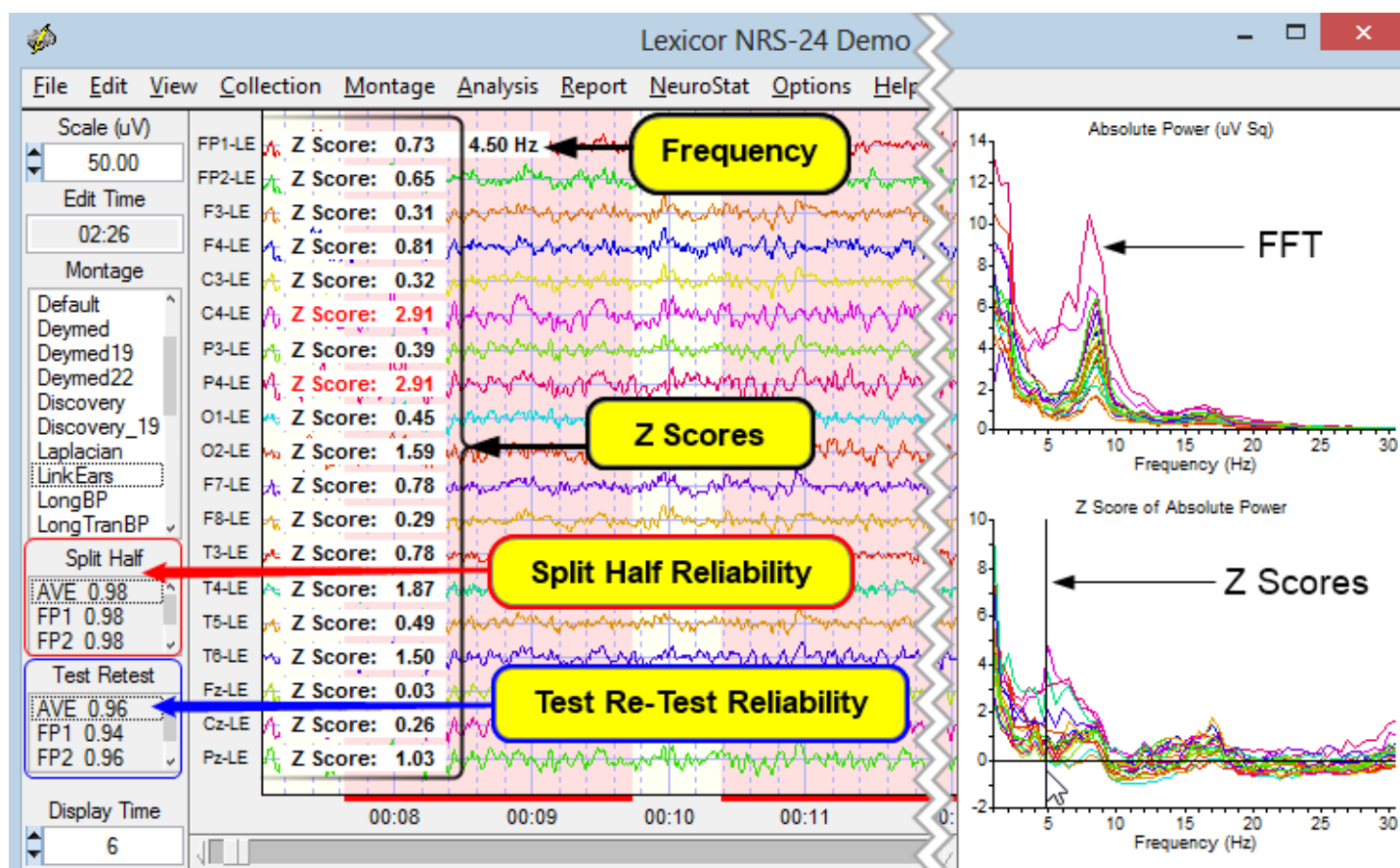
Depress the left mouse button and drag it over the sections of EEG that do not contain eye movement or muscle or drowsiness or head movement or any other type of artifact. Select at least 60 seconds of artifact free EEG data as shown in the Edit Time counter (upper left of screen). If a mistake is made, then right mouse click and drag over the EEG traces to erase a selection. View the test re-test reliability which must be at least 0.90. Scan the EEG record and select real and valid EEG and avoid selecting artifact.



Then click View > Dynamic FFT > Absolute Power and depress the left mouse button and drag over the power spectrum at the top right of the screen and do the same to the lower right screen.

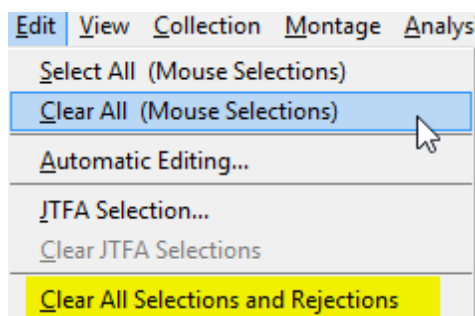


**Split-Half reliability** is the ratio of variance between the even and odd seconds of the time series of selected digital EEG (variance = sum of the square of the deviation of each time point from the mean of the time points). Examine the average reliability and the reliability of each channel as you increase the length of the sample and manually select different segments. Selection of artifact free EEG should have a reliability > 0.95 and a sample length of edited EEG > 60 seconds.



Test re-test reliability is the ratio of variance between the first half vs. the second half of the selected EEG segments (variance = sum of the square of the deviation of each time point from the mean of the time points). Test re-test reliability > 0.90 and a sample length of edited EEG > 60 seconds is commonly published in the scientific literature. Test re-test reliability is an excellent statistic to compare Brain state changes such as drowsiness as well as the consistency of a measure independent of changes in brain state.

One can clear all the manual EEG Edit Selections by Clicking Edit > Clear All (Mouse Selections) or by Clicking Edit > Clear All Selections and Rejections.

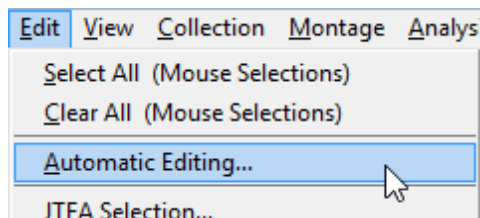


or



## Automatic Editing Tools

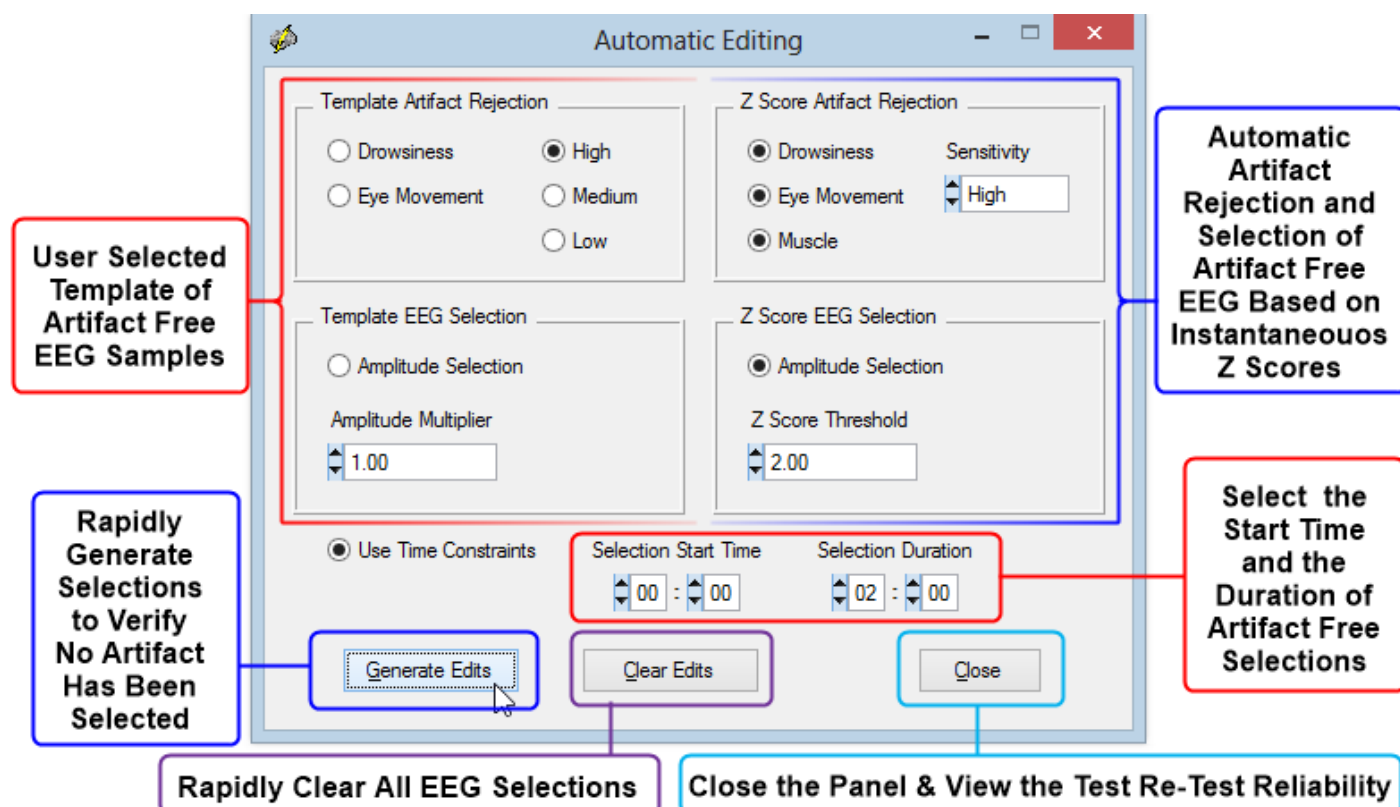
To Activate the Automatic Editing Tools.... Click **Edit > Automatic Editing**



## Automatic Edit Selection - Z Score Artifact Free Selections

Deselect all of the Template items on the left side of the panel, i.e., Template Artifact Rejection and Template EEG Selection. Retain all of the default Z Score Artifact Rejection selections on the right side of the panel and click Generate Edits to make artifact free selections. Default for eye movement and drowsiness selection is 'High' which is the most sensitive setting and 1.5 standard deviation threshold for the Amplitude Multiplier. The Z Score of 1.5 standard deviations means that if at least one second of successive instantaneous Z Scores are equal to or less than 1.5 standard deviations then a selection is made. Visually examine the EEG selections and test re-test reliability and the Edit Time. Save the edits by clicking Edit > Save Edit File. Then click 'Clear Edits' and experiment by changing the sensitivity and/or amplitude multiplier and click 'Generate Edits' and re-examine the EEG selections to verify that no artifact has been selected and that representative samples are made. Select a different start time and duration and save the edits by clicking Edit > Save Edit File and compare the clinical interpretation and stability of selections by clicking Edit > Open Edit File. Visually verify that no artifact was selected and that the clinical interpretation is the same no matter what selections one makes as long as the arousal state is the same (e.g., no drowsiness or sleep, etc.). The goal is to make multiple artifact free selections (2 to 3) and verify that no matter what artifact free selections are made the same clinical conclusions are obtained. This is another form of test re-test reliability. For example, if probabilities of 0.01 (i.e., 2 st. dev.) are obtained by three independent selections then the probability of finding this is  $0.01 \times 0.01 \times 0.01 = 0.000001$





If one wants to use the template method of automatic artifact free EEG selections then deselect all of the Z Score items on the right side of the panel, i.e., Z Score Artifact Rejection and Z Score EEG Selection. The select the template Artifact Rejection selections and click Generate Edits to make artifact free selections. Default for eye movement and drowsiness selection is 'High' which is the most sensitive setting and 1.00 for the Amplitude Multiplier. The amplitude Multiplier of 1.00 means that the template is match one-to-one to the RMS amplitude of the EEG recording. If the RMS amplitude is equal to or less than the RMS value of the template then a selection is made. Visually examine the EEG selections and test re-test reliability and the Edit Time. Save the edits by clicking Edit > Save Edit File. Then click 'Clear Edits' and experiment by changing the sensitivity and/or amplitude multiplier and click 'Generate Edits' and re-examine the EEG selections to verify that no artifact has been selected and that representative samples are made. Save the edits by clicking Edit > Save Edit File and compare the clinical interpretation and stability of selections by clicking Edit > Open Edit File. The goal is to make multiple artifact free selections (2 to 3) and verify that no matter what artifact free selections are made the same clinical conclusions are obtained. This is another form of test re-test reliability. For example, if probabilities of 0.01 (i.e., 2 st. dev.) are obtained by three independent selections then the probability of finding this is  $0.01 \times 0.01 \times 0.01 = 0.000001$

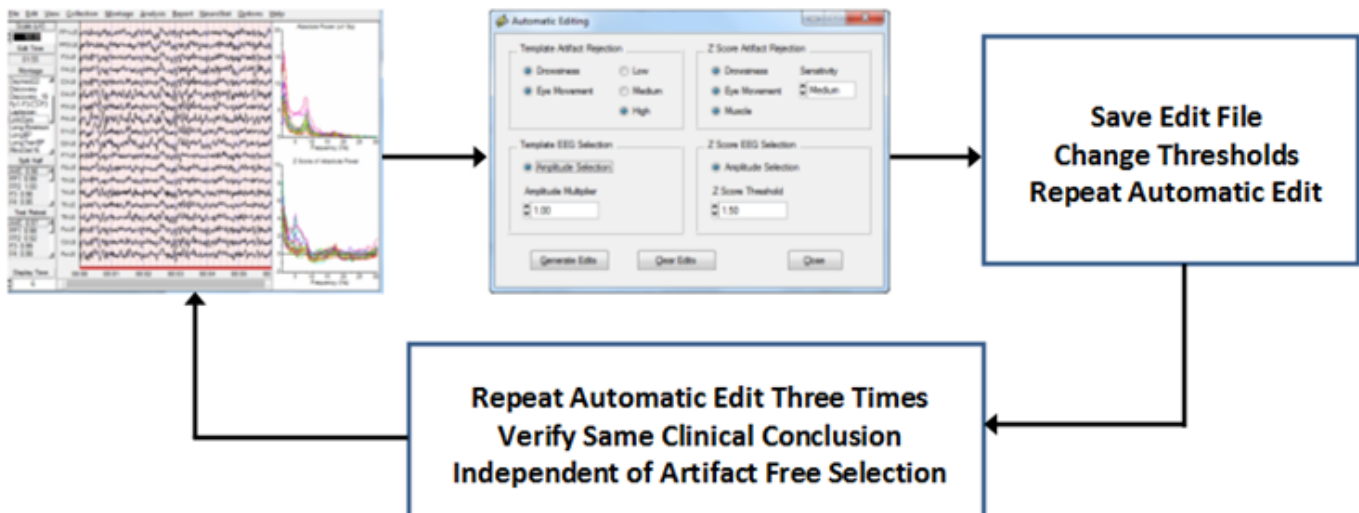
Both Template and Z Score Methods can be used simultaneously. To test and to create a different selection of artifact free EEG to further verify high test re-test reliability click Close and then re-open the Automatic Editing panel (click Edit > Automatic Edit) and click 'Generate





Edits'. Then save these edits and compare to the Template alone and the Z Score alone methods of selecting artifact free EEG data. Repeat artifact free selections two or three times with different thresholds and/or settings and verify that the deviant Z Scores linked to a patient's symptoms are the same. Repeated selections can occur in a few seconds and thereby create a high degree of statistical reliability. For example, three repetitions at  $P < .05 = 0.000125$  and at  $P < 0.01 = 0.000001$ . Read the next section on how to create Dynamic FFT Z Scores and how to link patient symptoms to functional networks in the brain.

**Repeat Artifact Free Selections three times and verify that the your clinical conclusions based on deviant Z scores and brain locations do not change and therefore achieve high test Re-Test reliability. For Example with three repetitions the probability =  $P < 0.05^3 = 0.000125$**





## Bi-Spectral Analyses

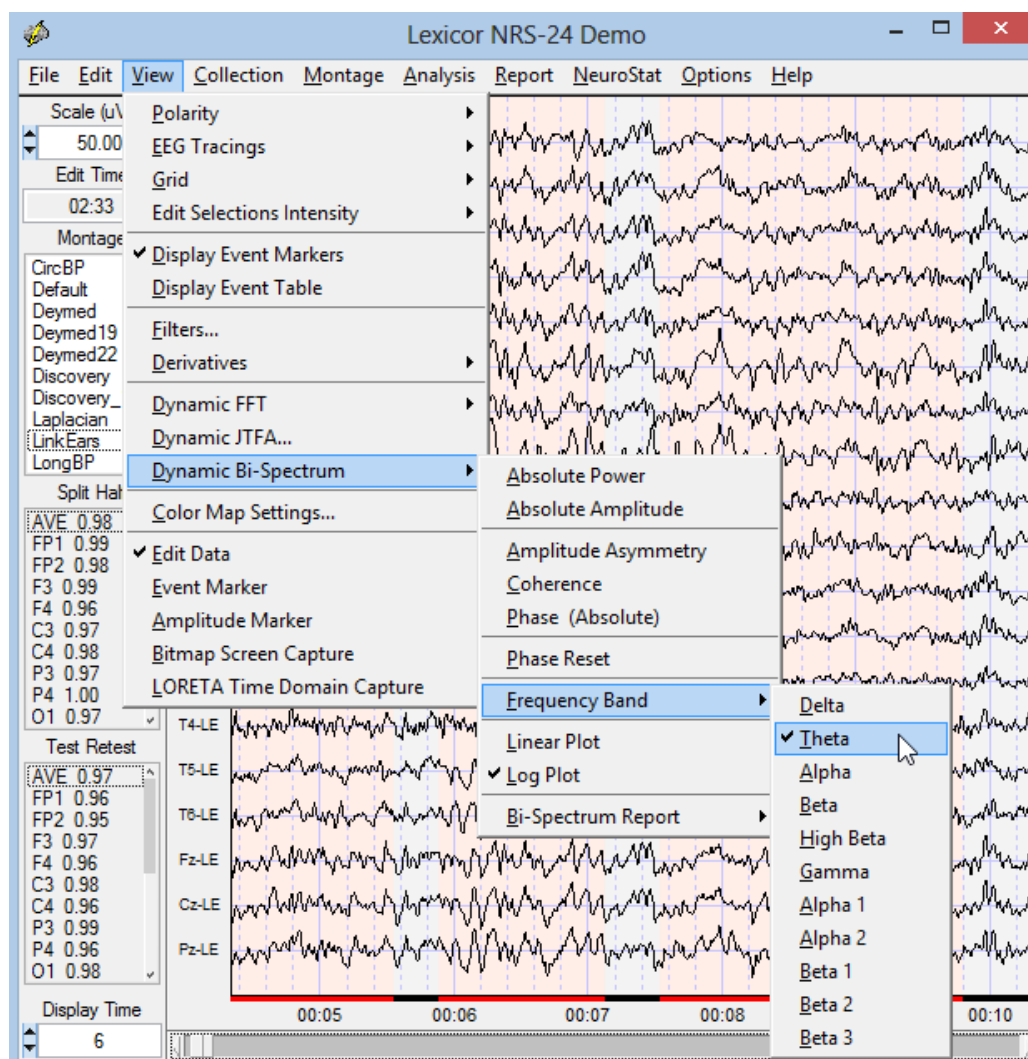
The NeuroGuide Bi-Spectrum Normative Database is an add on product that only works with NeuroGuide version 2.5.4 or later. The Bi-Spectrum Normative Database must be [downloaded](#) and installed separately. See [How to Install the Add-On Normative Databases](#)<sup>13</sup> located in the [Installations](#)<sup>12</sup> section of the [Getting Started](#)<sup>8</sup> part of this Manual, before attempting to view Bi-Spectrum Z Scores.

The Bi-Spectrum is made of up two parts.

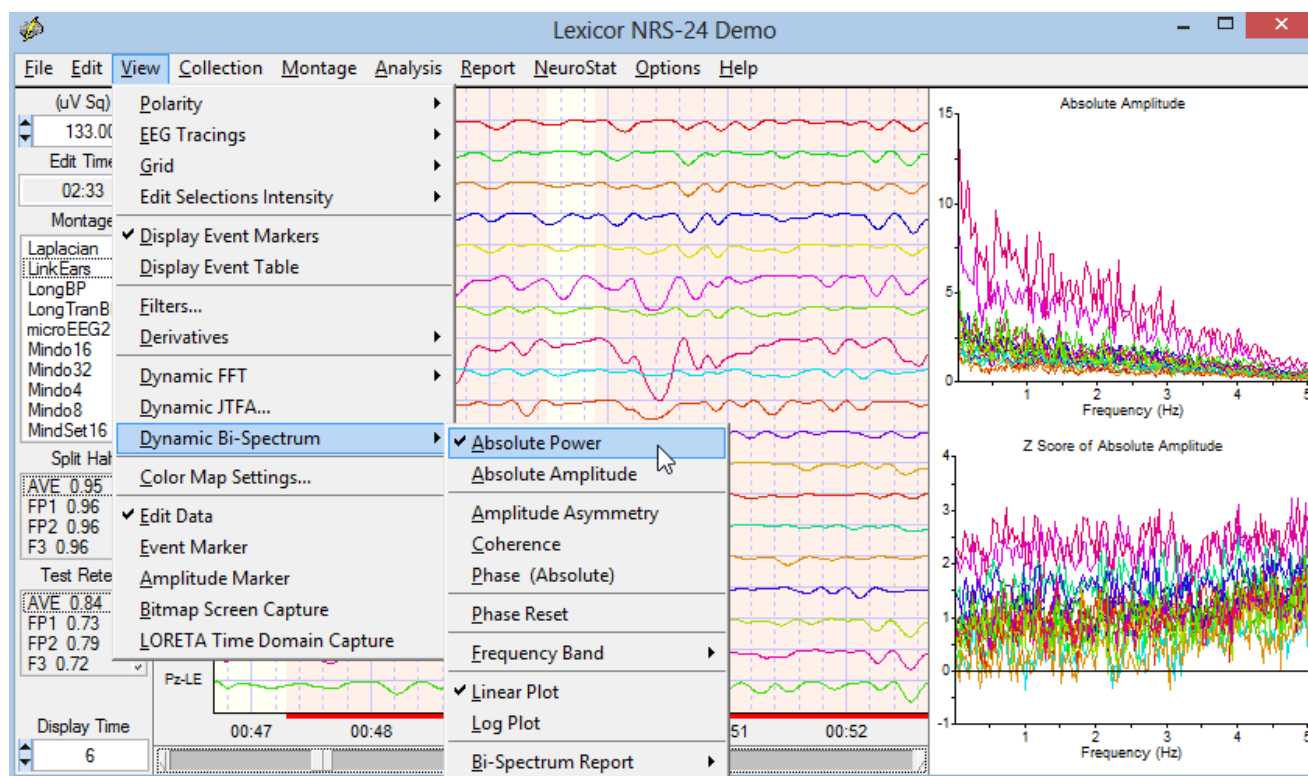
One is the Bi-Spectrum of the instantaneous time series of absolute power, relative power, amplitude asymmetry, coherence, phase differences and phase reset (1st derivative of straightened phase) is accessed by clicking View > Dynamic Bi-Spectrum. The Bi-Spectrum of the instantaneous time series provides information about the frequency of bursts and the frequency of changes in coherence and phase and phase reset over long intervals of time. The frequency range is from the Infra-Slow 0.03 Hz to 5.0 Hz and a log-log plot or a simple linear plot option is available.

A second part of the Bi-Spectral analyses is obtained by clicking Analysis > Bi-Spectrum which provides the Cross-Frequency Bi-Spectrum using the correlation function of power over time and by using the 2nd derivative of the phase synchrony across frequencies or cross-frequency phase synchrony or n:m phase synchrony. The cross-frequency phase synchrony is measured in terms of the duration of phase locking and the duration of phase shift.

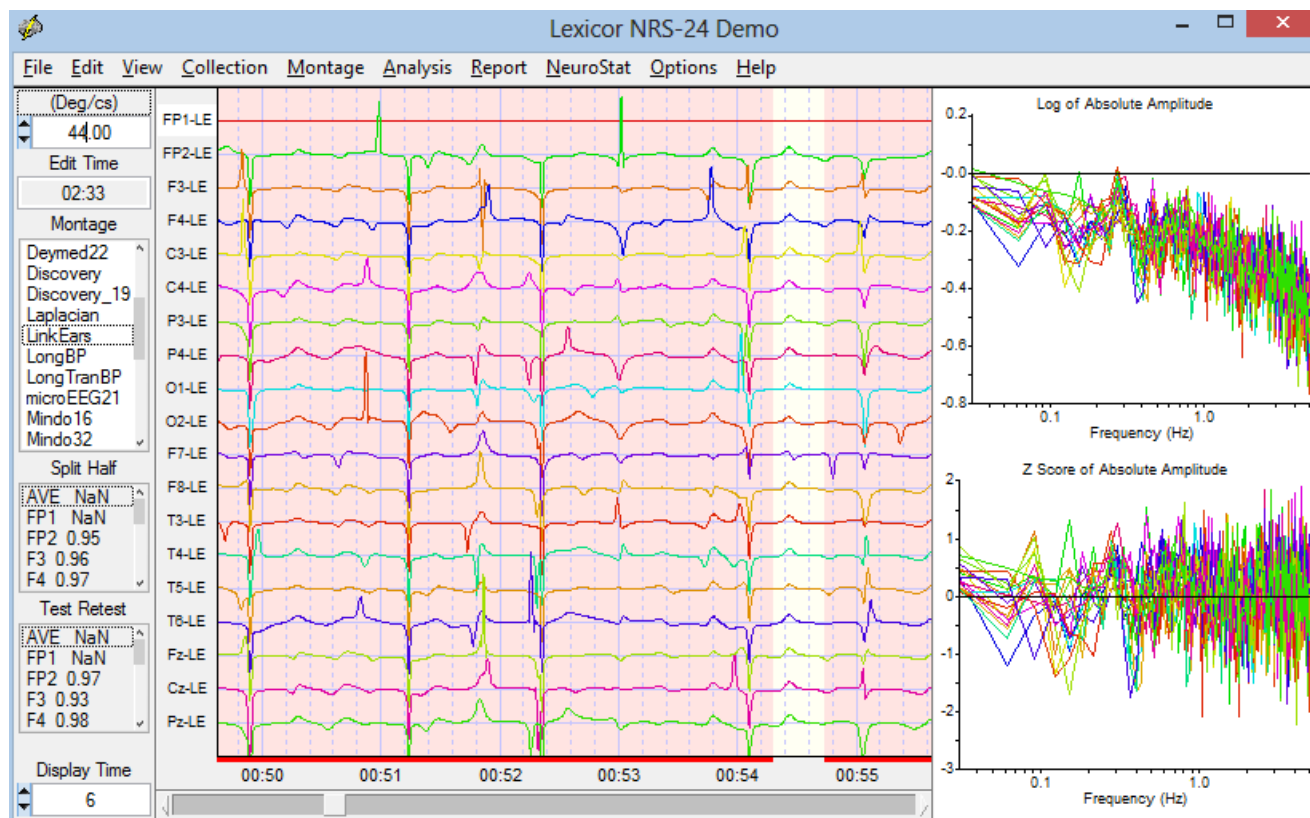
To view the Bi-Spectrum of the instantaneous time series, Click View > Dynamic Bi-Spectrum > Frequency Band and then select a desired Frequency from the list.



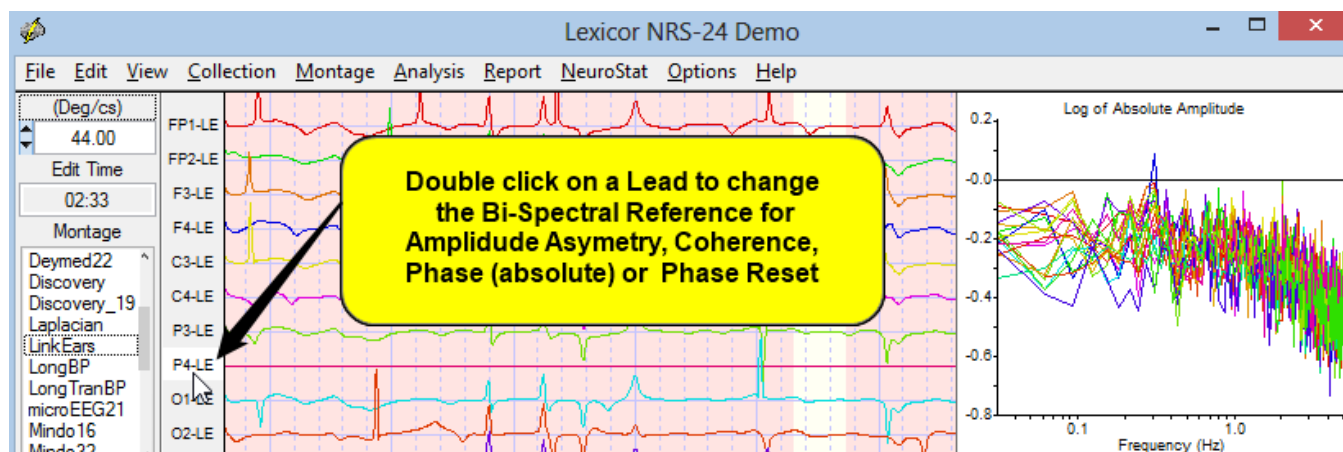
**Example of Bi-Spectrum of Instantaneous Absolute Power Time Series of the Theta Frequency Band - 0.03 Hz to 5 Hz with the FFT Spectrum Plot on the Top Right of the Screen and Z Scores on the Bottom Right .**



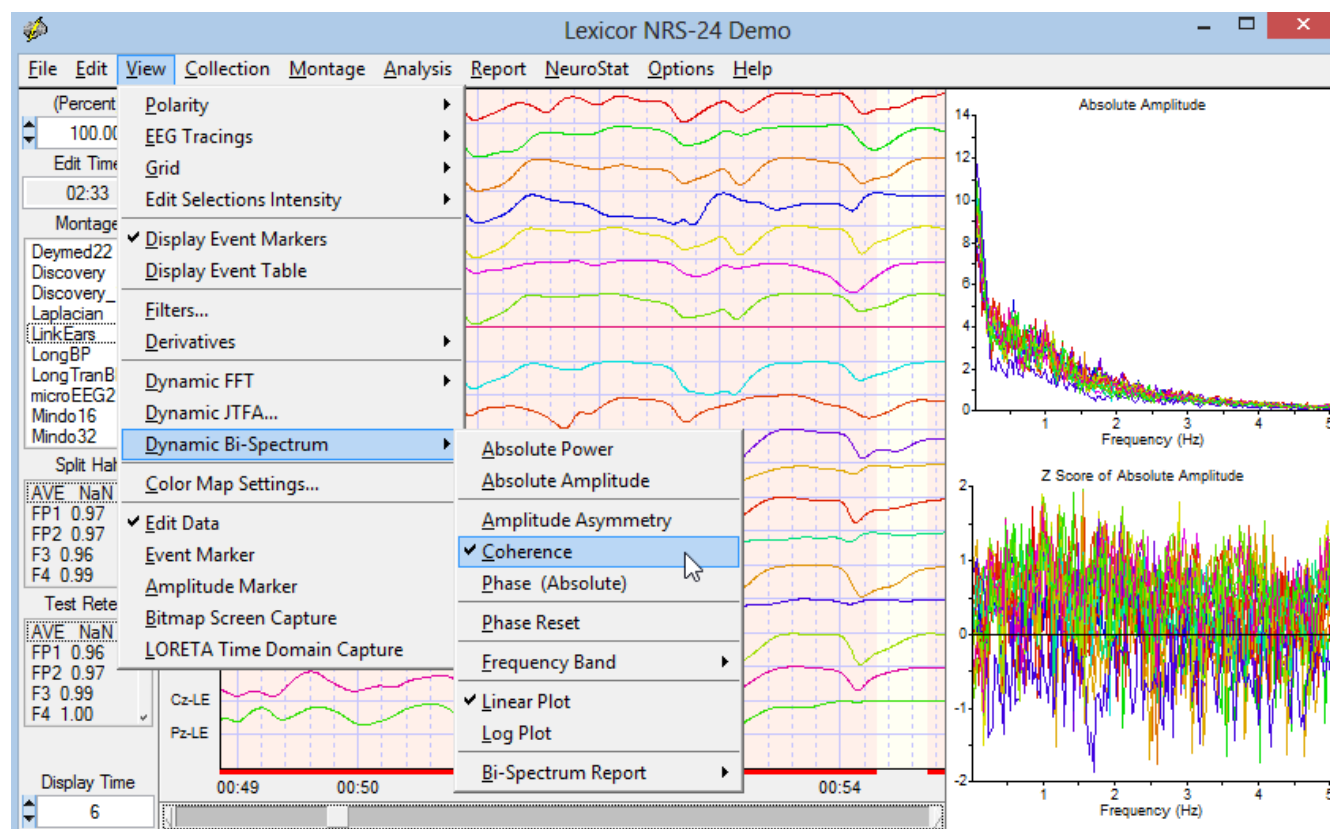
**To view the Bi-Spectrum of Instantaneous Time Series of Phase Reset - Delta Frequency Band with Log Plots. Click on View > Dynamic Bi-Spectrum > Phase Reset then Click on View > Dynamic Bi-Spectrum > Frequency Band > Delta then Click on View > Dynamic Bi-Spectrum > Log Plots**



Note, in the image above or on your screen that FP1-LE is flat and Background of the Lead name is White, that is the reference lead...double click on the name P4-LE or another lead to change the reference. Note the Instantaneous Time Series display in the middle and the FFT Spectrum & Z Score Plots on the Right change.

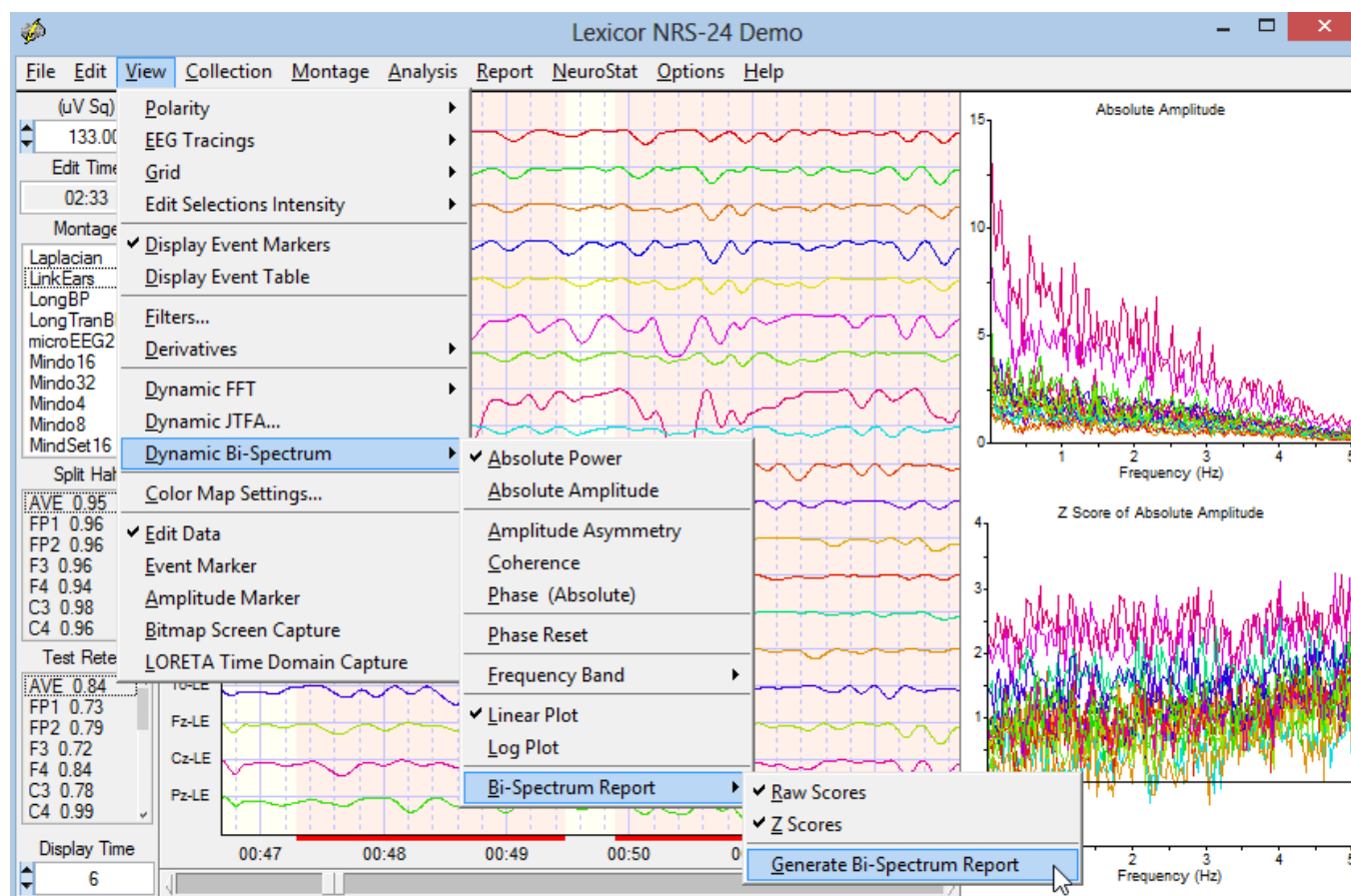


Example of Bi-Spectrum of Instantaneous Time Series of Coherence - Delta Frequency Band



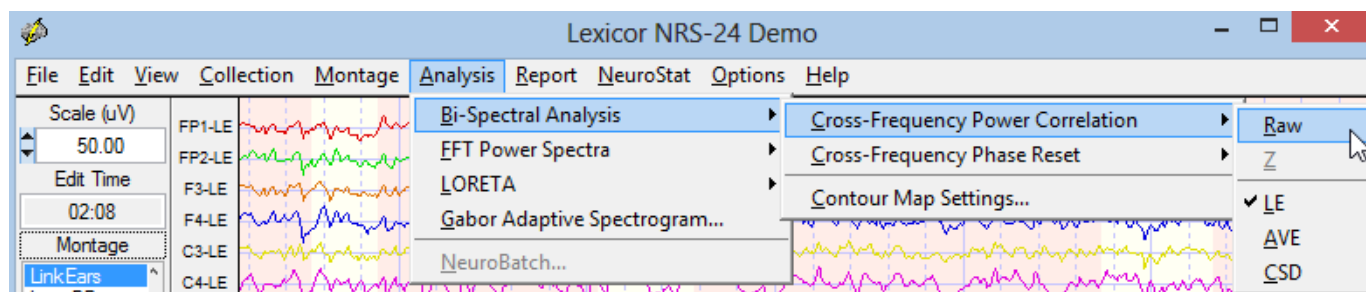
**To Generate a Bi-Spectrum Report of the Instantaneous Time Series with Topographic Color Maps and Tab Delimited Output. First click View > Dynamic Bi-Spectrum > Bi-Spectrum Report and select either Raw Scores, Z Scores or both. Then click View > Dynamic Bi-Spectrum > Bi-Spectrum Report > Generate Bi-Spectrum Report**



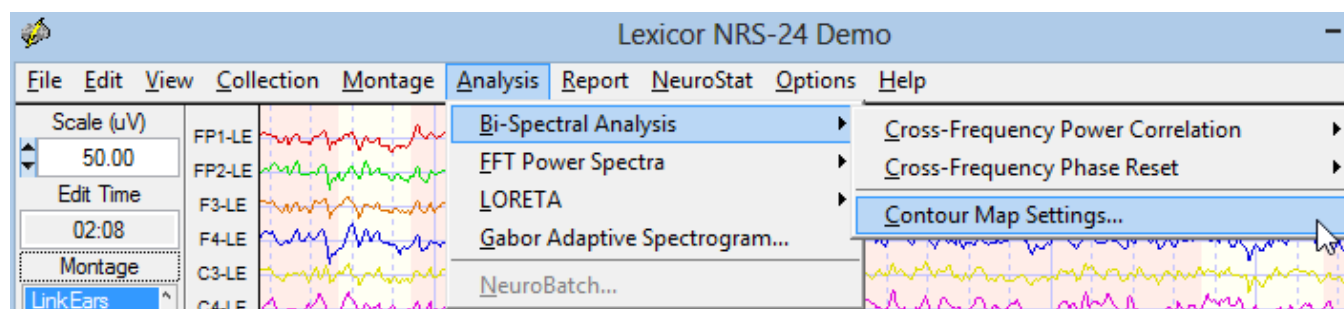


## Bi-Spectrum of the Cross-Frequency Power Correlation

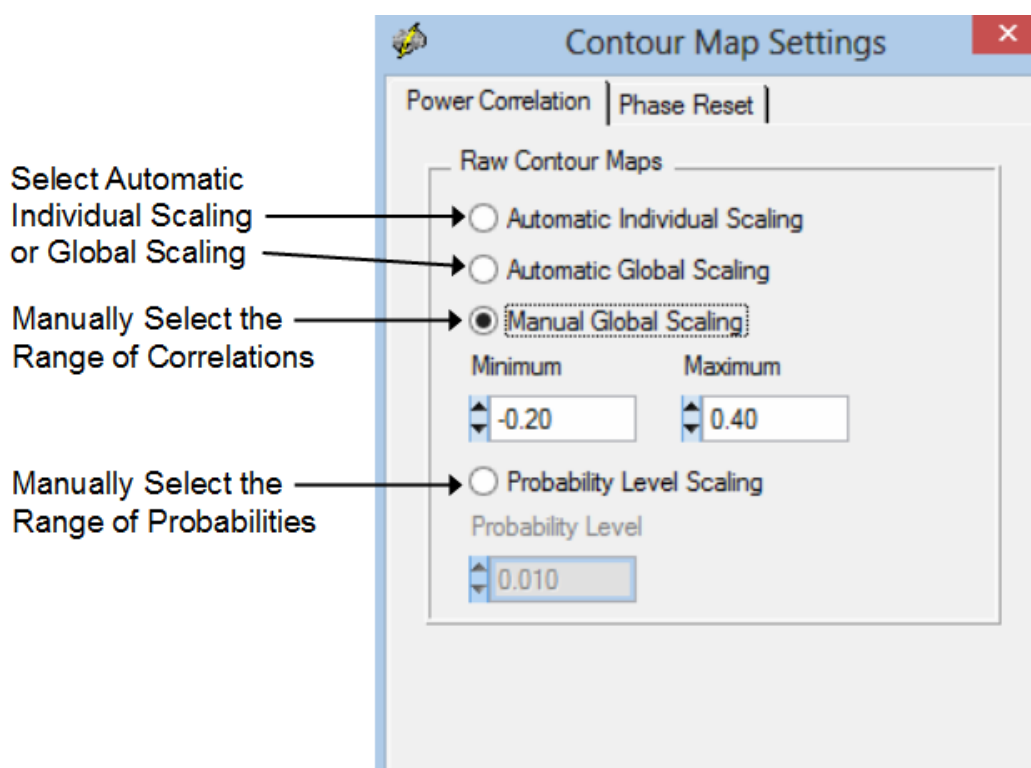
Click Analysis > Bi-Spectral Analysis > Cross-Frequency Power Correlation



Select the Contour Map Settings by Clicking Analysis > Bi-Spectral Analysis > Contour Map Settings



**To Set or Change the Cross-Frequency Power Correlation Contour Map Settings select the Power Correlation Tab**



**Examples of the output from the Bi-Spectral Cross-Frequency Power Correlation. In the Analysis Output Window Click Save > Bitmap Graphics Files to save the bitmap images and Click Save > Tab Delimited Text to save the text data.**



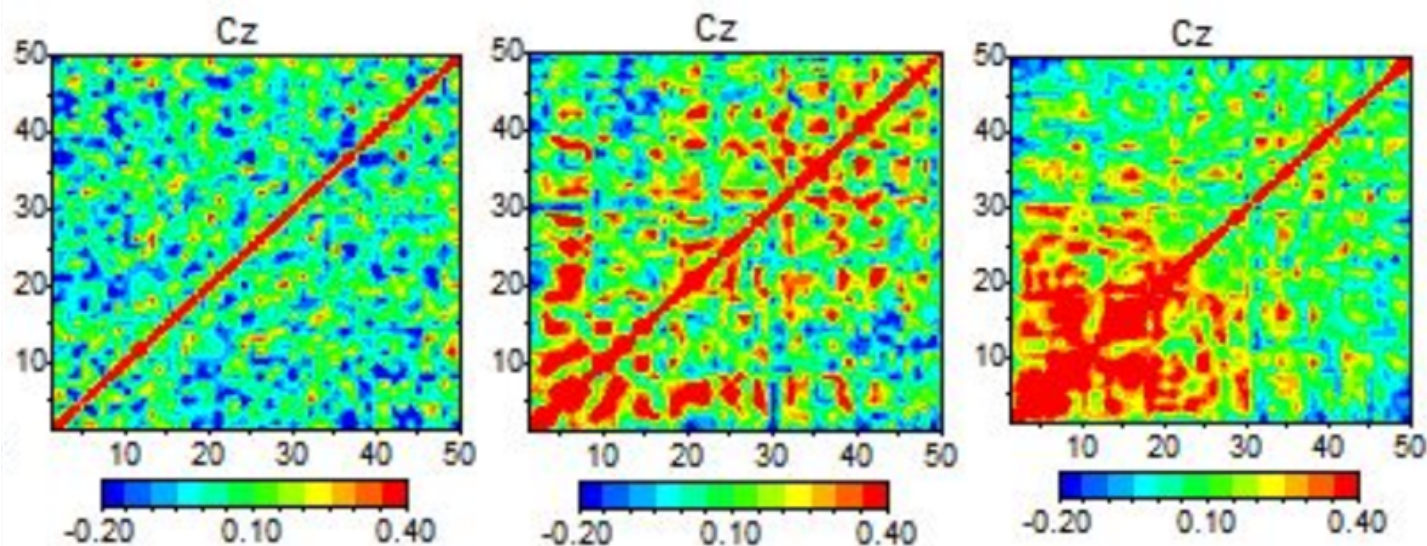


## CROSS-FREQUENCY ANALYSES OF BRAIN STATE

AWAKE

DROWSY

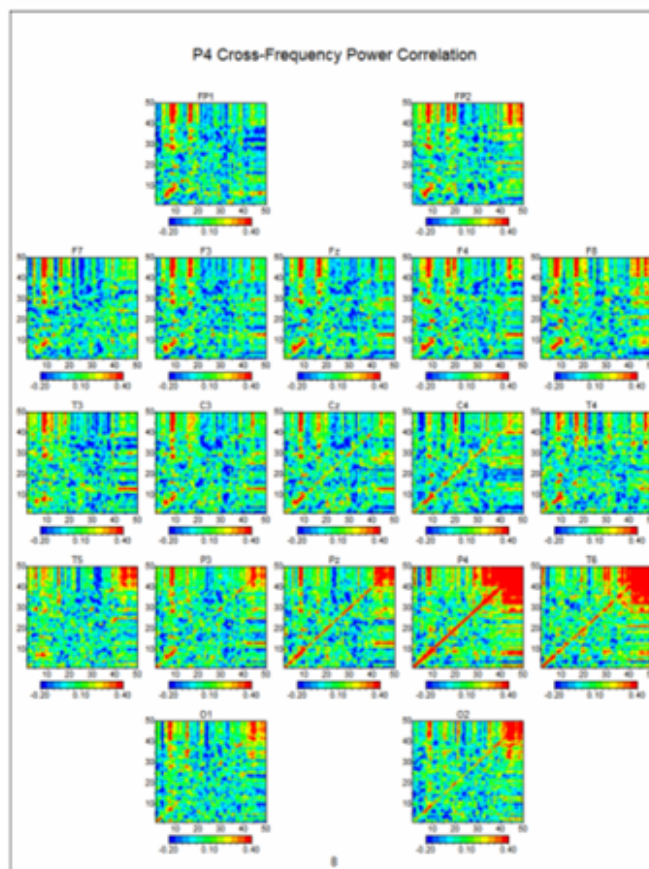
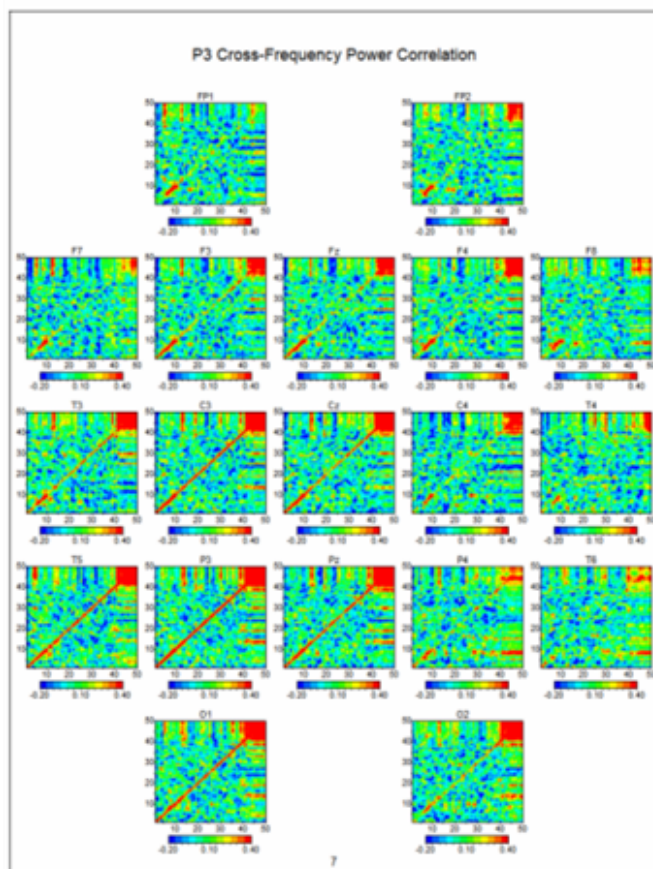
SLEEP – STAGE 1



## CROSS-FREQUENCY POWER CORRELATION

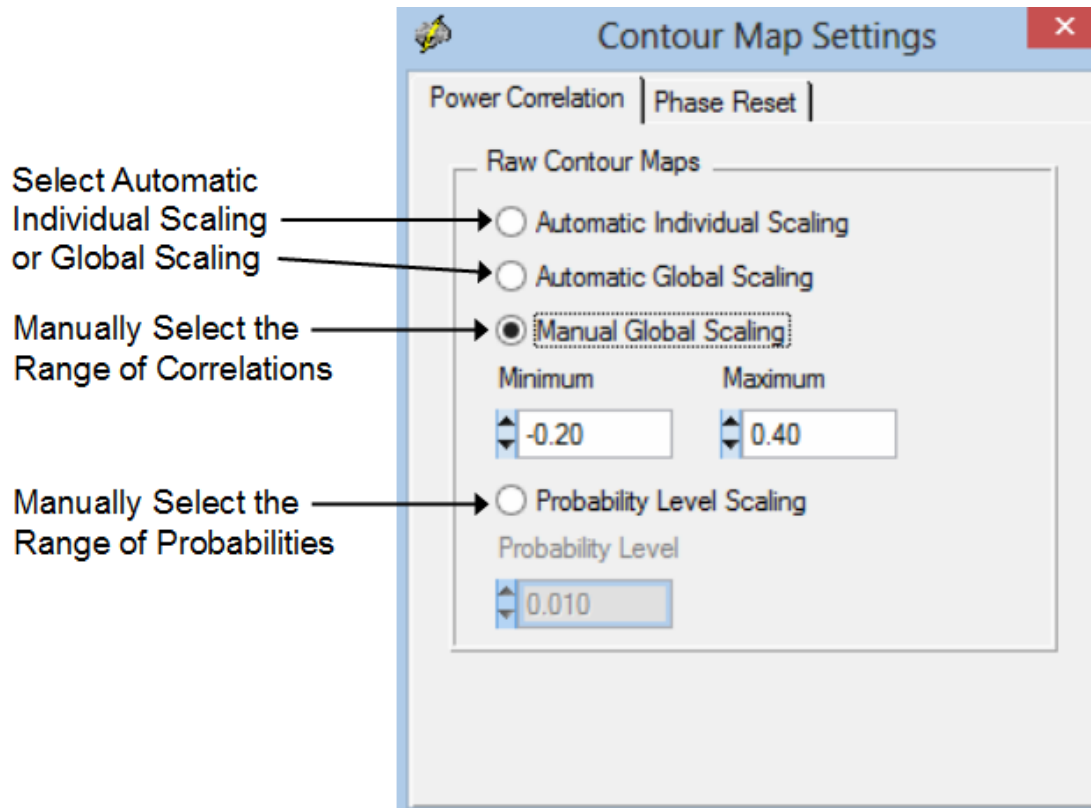
LEFT PARIETAL – P3

RIGHT PARIETAL – P4

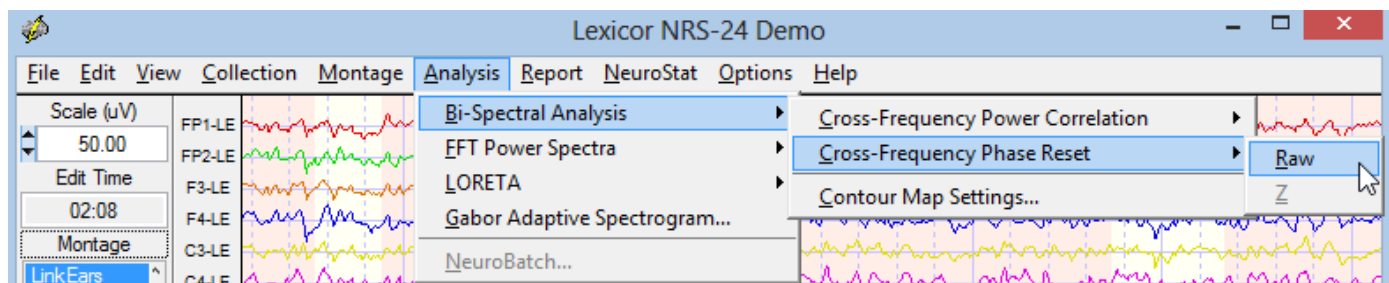




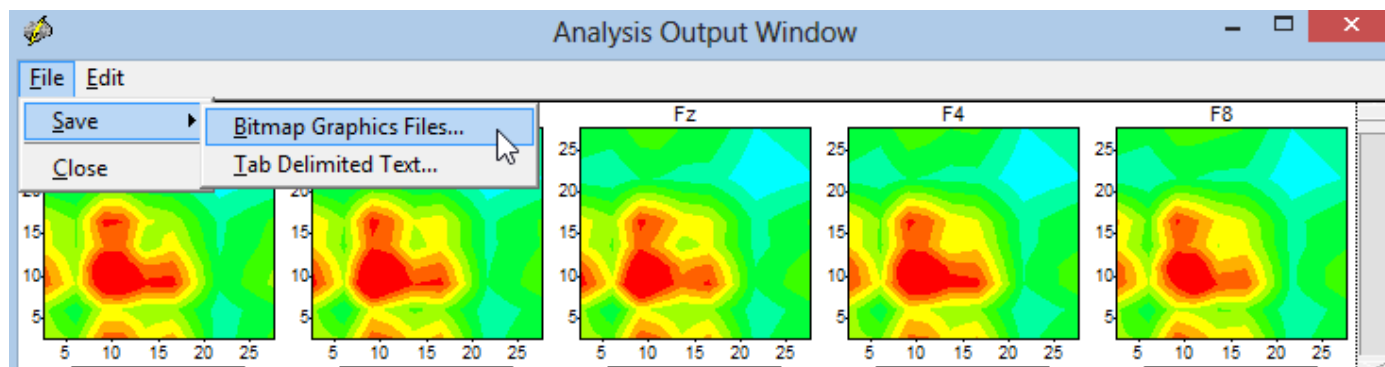
**Bi-Spectral Cross-Frequency Phase Reset (cross-frequency phase shift duration and cross-frequency phase lock duration). Click Analysis > Bi-Spectral Analysis > Cross-Frequency Phase Reset > Raw (or select Z Scores in the future)**



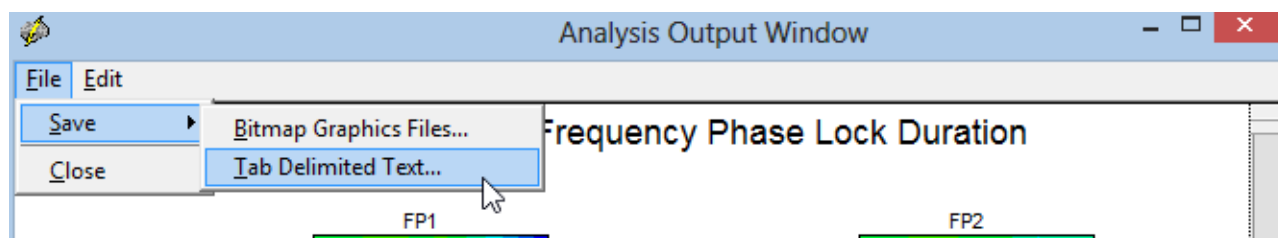
**To Compute Cross-Frequency Phase Shift Duration and Phase Lock Duration... Click Analysis > Bi-Spectral Analysis > Cross-Frequency Phase Reset > Raw**

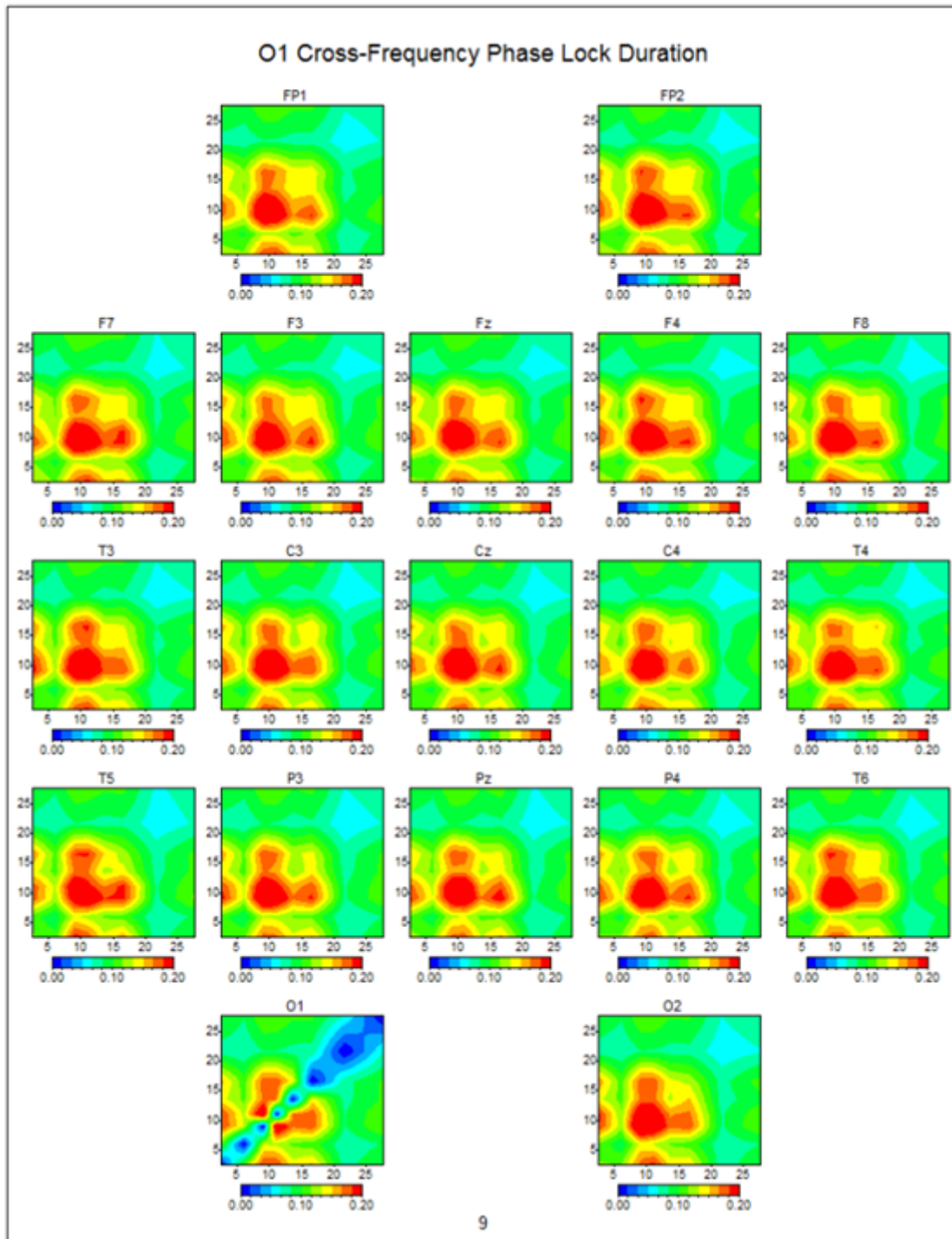


**In the Analysis Output window Click File > Save > Bitmap Graphic Files... then provide a File Name and save the Bitmaps in a sub-folder inside of the Patient's and/or Subject's folder.**

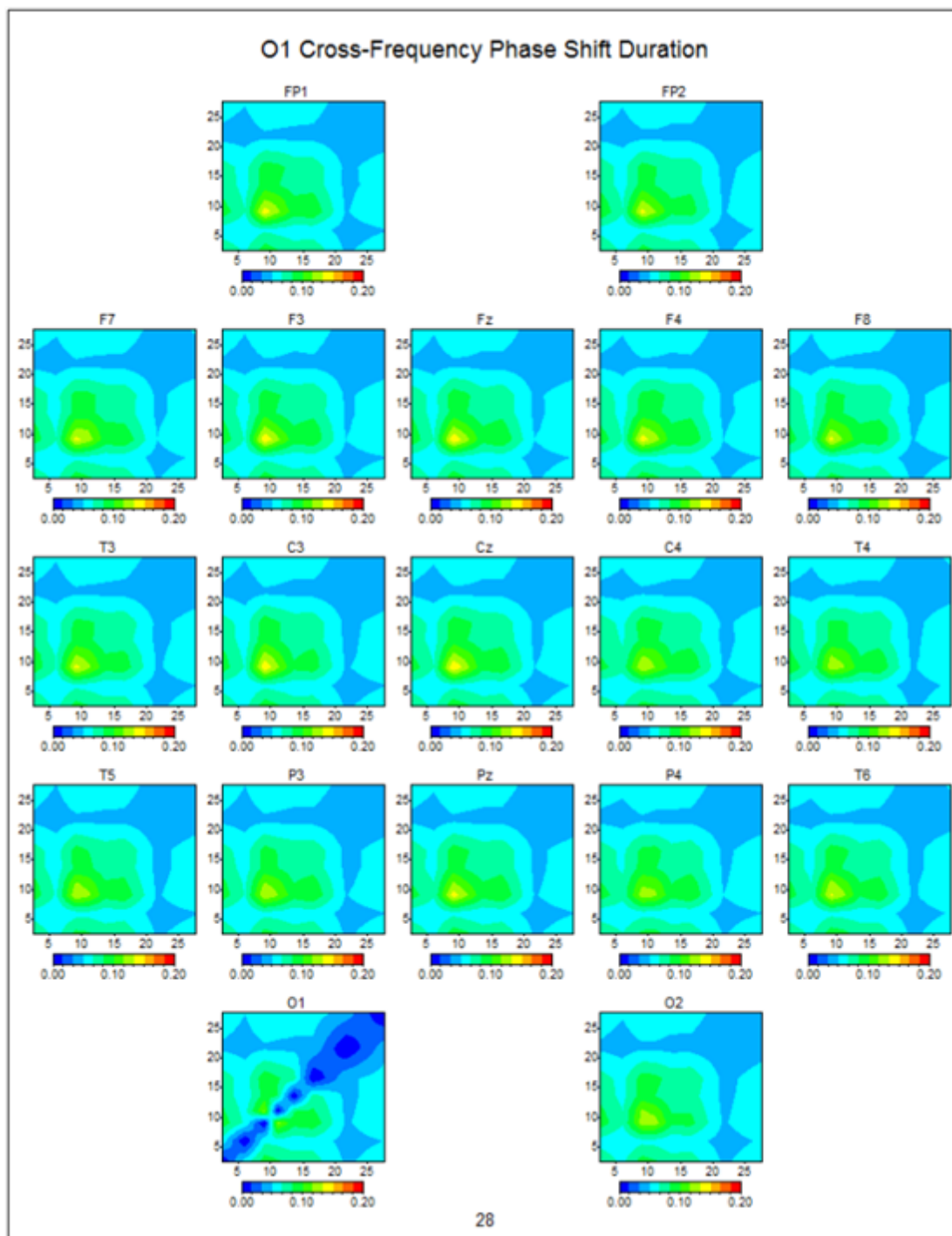


Also save the Tab Delimited raw values in the Patient/Subject's folder by Clicking File > Save > Tab Delimited Text ...then provide a File Name.



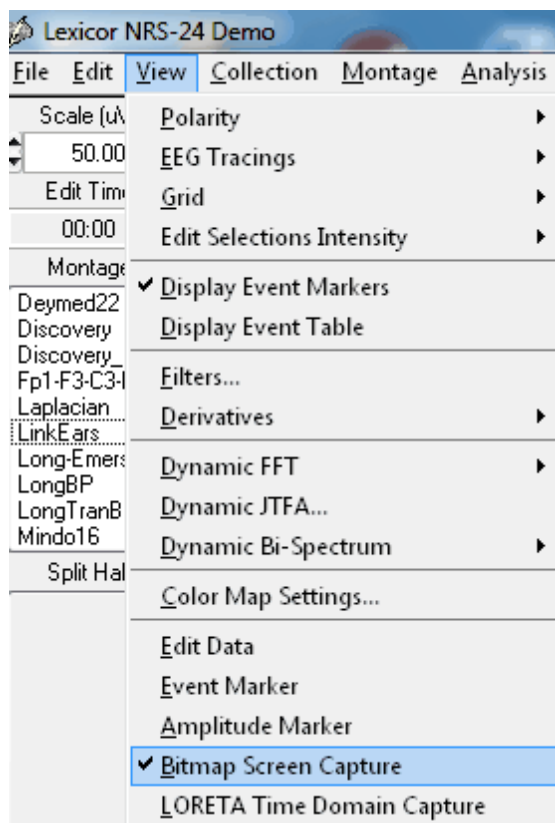




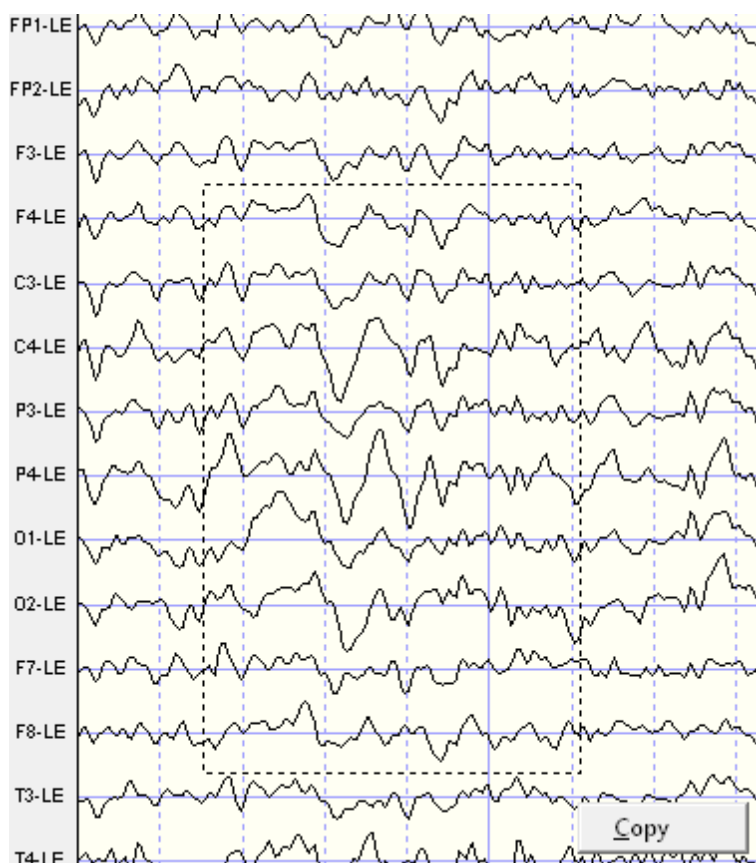


## Bitmap Screen Capture

Use the Bitmap Screen Capture tool to screen capture events and features in the EEG record. For example, gross pathology, epileptic spikes, phase reversals, delta or theta waves, etc. Open a Word document or clinical report and then paste into the report.

**Click View > Bitmap Screen Capture**

Depress the left mouse button and drag over the event of interest and note the dashed lines that represent the boundary of the screen capture.



Right mouse click to open the Copy button and then click the copy button to save the screen capture to the clipboard. Paste the clipboard screen capture in a Word document or clinical report to highlight and illustrate events of interest.

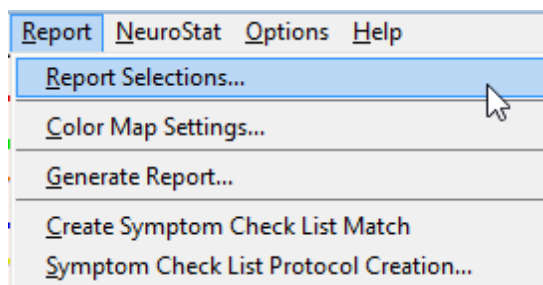
## Brain Performance Index

The Brain Performance Index (BPI) is based on EEG discriminant analyses of 442 subjects primarily age 5 to 18 a grouped based on I.Q. scores that ranged from < 90 I.Q. (low group) and > 120 I.Q. (high group). The intermediate group was used to cross-validate the discriminant functions. A multivariate regression equation was developed based on the best EEG predictors of I.Q. scores and correlated 0.57 with full performance I.Q.

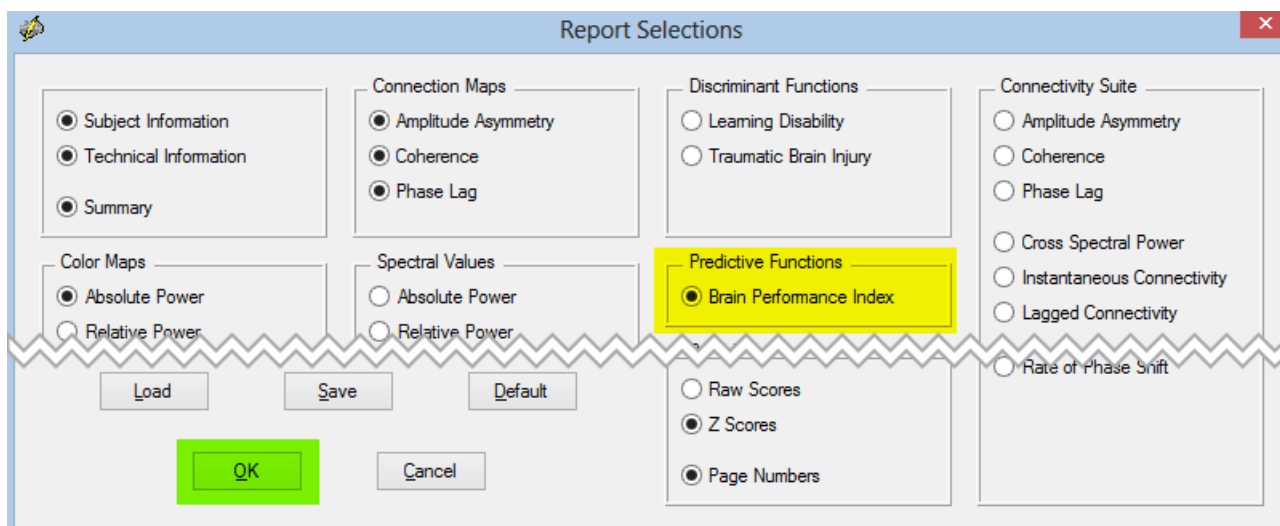
The BPI is a measure of the efficiency of neural resource allocation and is not a substitute for a neuropsychological examination. It is an adjunct to standard neuropsychological evaluations and is useful for individuals with a history of academic problems and a non-significant learning disability discriminant score but with possible focal or spatially localized dysregulation in nodes and connections in the brain. The BPI provides information about both general and specific learning disabilities by estimating the efficiency of information processing. Go to [www.appliedneuroscience.com/Articles.htm](http://www.appliedneuroscience.com/Articles.htm) and Download the study that the BPI is based on: [EEG and Intelligence: Relations Between EEG Coherence, EEG Phase Delay and Power](#)



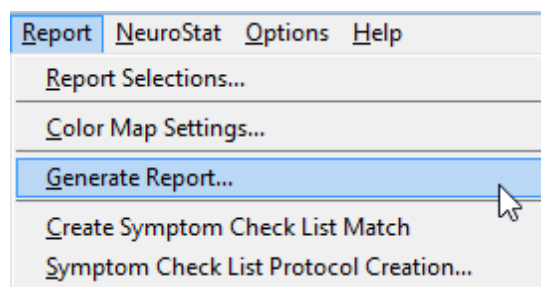
To activate the Brain Performance Index (BPI), Click Report > Report Selection



Select Brain Performance Index under Predictive Functions of the Report Selections Panel. After you have finished Click **OK** to close the Panel.



In order to Generate a Report that includes the Brain Performance Index the Subject/Patient must be between 5 to 18 years of age, else you will receive an message and the Report will not contain the BPI Analysis Outputs. To Generate a Report that includes the BPI Click Report > Generate Report

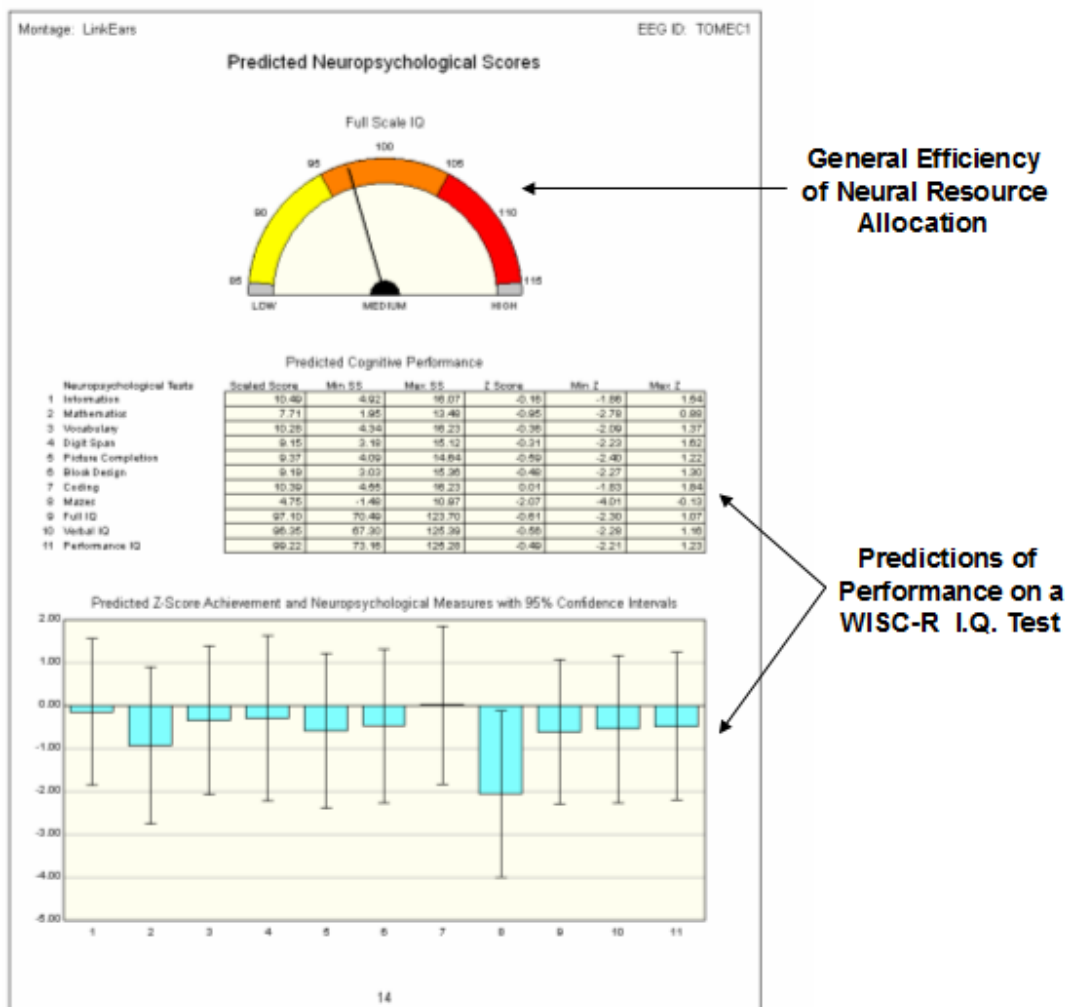


Here is an example of the BPI analysis output panel

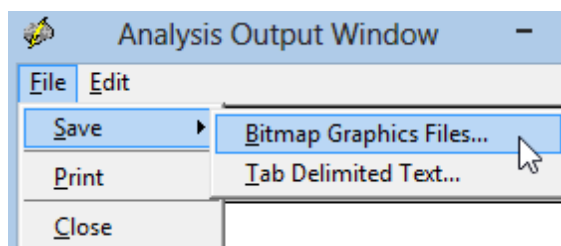




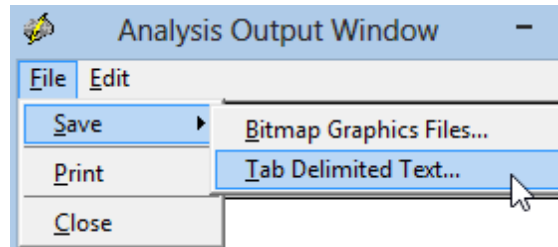
## Brain Performance Index (BPI) Analysis Output



Click **File > Save > Bitmap Graphics Files...** and Save the Report Analysis Outputs as Bitmaps in a sub-folder in the Patient/Subject's Folder.



Click **File > Save > Tab Delimited Text...** and Save the Report Analysis Outputs as Tab Delimited Text File in the Patient/Subject's Folder.



## BrainSurfer

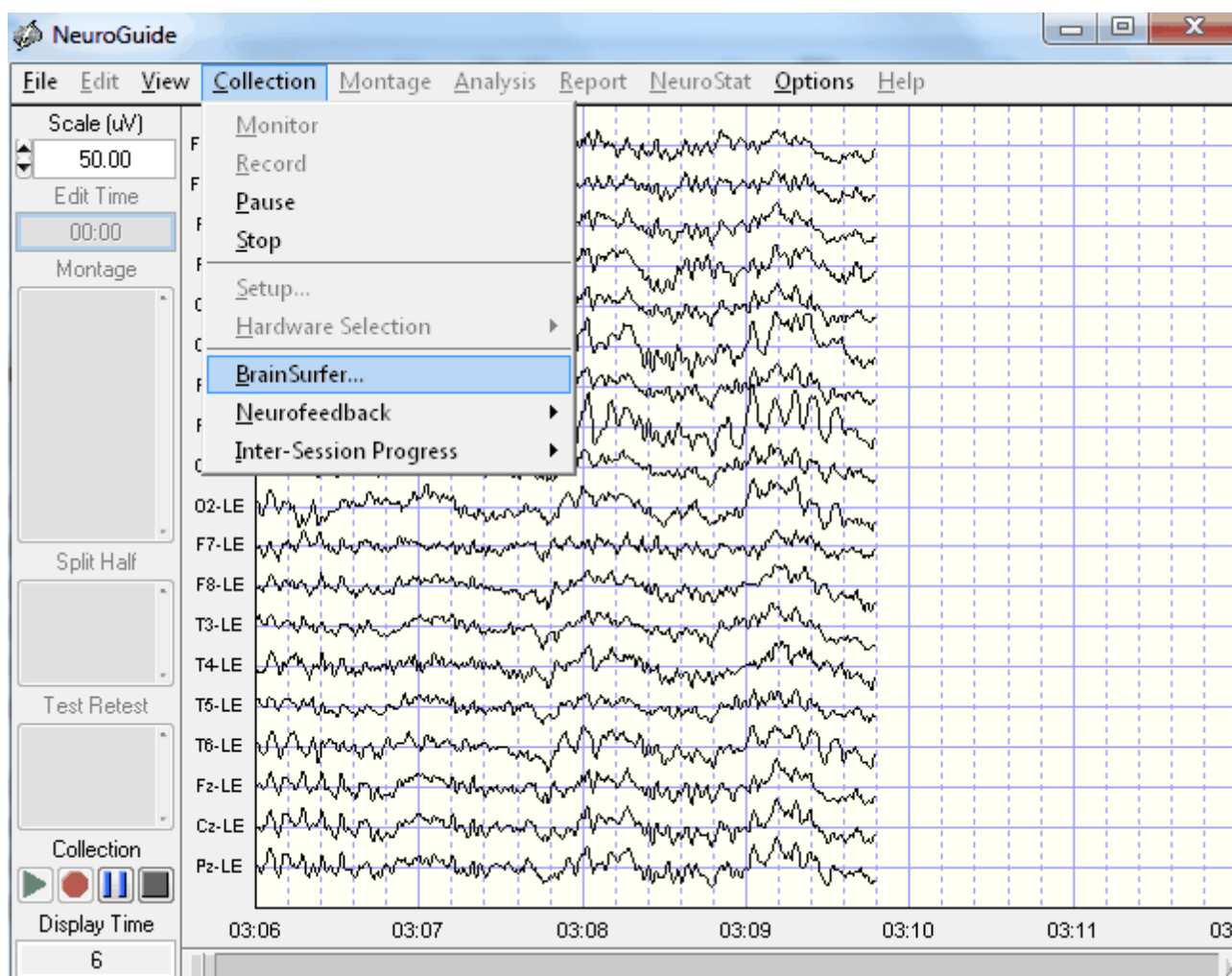
BrainSurfer is a Brain-Computer-Interface (BCI) method to operantly modify the sources of the EEG. The term Brain-Computer Interface (BCI) is a type of EEG biofeedback or neurofeedback (NFB) procedure in which particular EEG activity is detected and then subjects are trained to increase the probability of that EEG activity linked to a device like a computer display or robot or prosthesis. BCI uses the same physiological principals of operant conditioning as with EEG biofeedback to increase the probability of occurrence of a particular EEG event or feature. BCI differs from EEG biofeedback by the use of a continuous control loop between the brain and physical device or prosthesis and focusing primarily on modifications of motor cortical-subcortical networks. For example, in NFB when a given brain event reaches threshold then a feedback signal is delivered (sound or visual display or DVD, etc) to reinforce the brain event at that moment in time. The goal is to modify the synapses involved in producing a given brain event and to achieve increased stability in networks linked to symptoms. BCI also involves modification of a selected brain event but the goal is to control an external device such as a computer screen or robotic arm, etc. using continuous feedback and not turning on or off a feedback signal. Thus, both involve operant conditioning but with a different emphasis on the way that an external device is related to the brain.

BrainSurfer is the patient's own brain rendered by an MRI that provides real-time and continuous feedback about the stability of nodes and connections between nodes in networks of the brain linked to the patient's symptoms. A discrete feedback signal is not used, instead a moment-to-moment continuous closed loop between the patient and the patient's brain is used as the feedback signal and the goal is to modify the brain to reach increased levels of stability and information processing efficiency in particular networks. Brodmann areas are considered as nodes and the cortico-cortical white matter axons are the connections between the nodes. Reinforcement of increased stability in dysregulated nodes and connections between nodes is achieved by real-time LORETA Z Scores. As explained previously, extinction of extreme Z Scores that indicate dysregulation and reinforcement of increased stability and efficiency is likely to result in increased information processing in modules and hubs linked to the patient's symptoms. A clinician can zoom inside of the 3-D rendered brain to a specific node or a specific connection between nodes to increase specificity of instrumental learning in particular Brodmann areas or functional connections between Brodmann areas in real-time. Both conscious strategies and subcortical unconscious processes are involved in BCI and NFB.



**3-Dimensional MRI Volume Dynamics of Real-Time EEG.** sLORETA is used to compute the time series of current density from the center voxel of each 88 Brodmann Areas. The location of the center voxel of each Brodmann Area is assigned a 3-Dimensional Talarach Atlas coordinate in the interior of a MRI Volume. One can view the 3-dimensional current sources inside of the MRI volume by rotating the volume and making the rendered surface transparent. BrainSurfer computes real-time sLORETA from the center voxel Brodmann Area Current Density, including Surface and/or Node views. BrainSurfer also computes real-time functional connectivity Z Scores of Coherence, Phase difference, Phase Lock Duration, Phase Shift duration between Brodmann Areas.

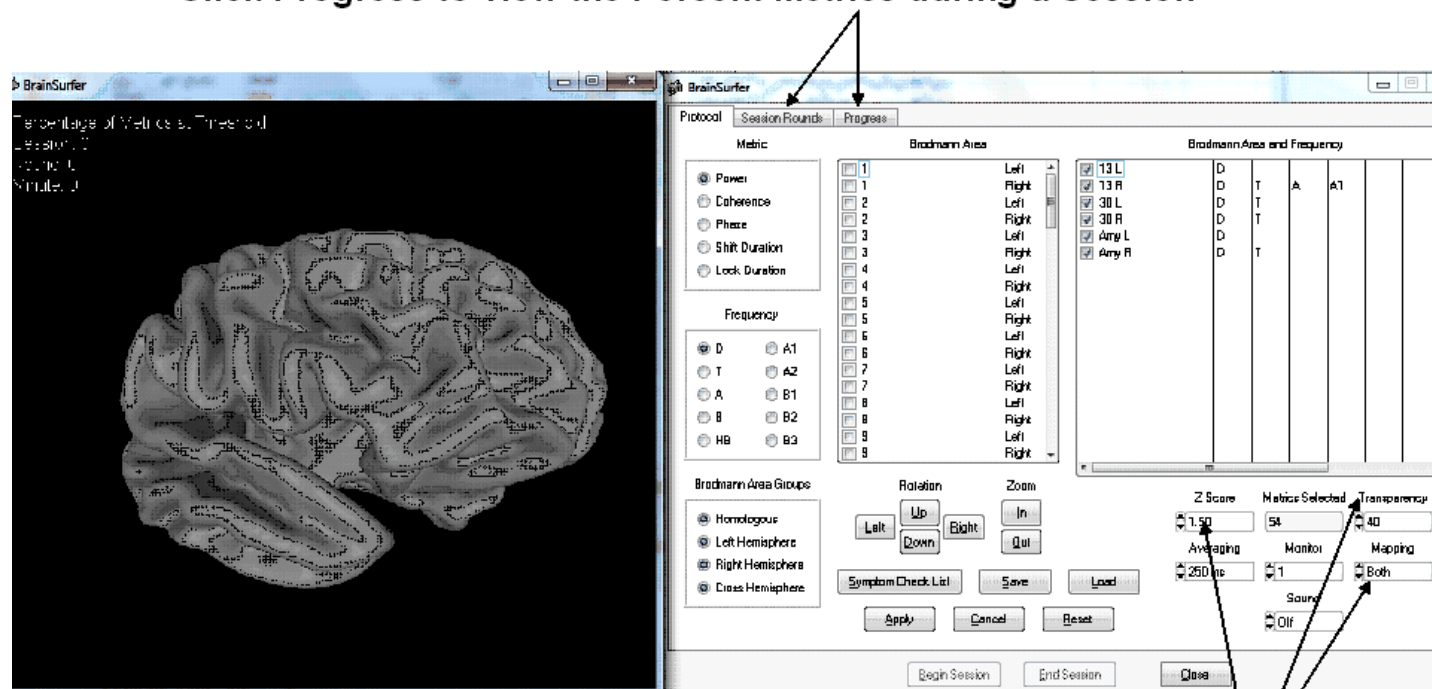
To activate BrainSurfer, click **Collection > Hardware Selection** and then select the amplifier that is used to collect the EEG. Then click **Collection > Setup & Monitor** and OK and observe the EEG traces moving across the screen. Click **Collection > Record** if one wants to save the EEG during the BCI procedure. Click **Collection > BrainSurfer** to activate the BrainSurfer protocol panel.





**BrainSurfer - Opening screen. Move the control panel down and the BrainSurfer image to the left. Expand the BrainSurfer image or re-size the image. Take a test drive and rotate the brain left, right, up and down and click zoom in and then zoom out.**

**Click Session Rounds to Set the Number, Duration and Delays Between Rounds.  
Click Progress to view the Percent Metrics during a Session**



Depress the left mouse and  
Move the Brain

Z threshold, Averaging  
Time, Sound, Mapping,  
Transparency

Click the Session Rounds tab in the protocol panel to activate the session rounds panel. The Total Training Duration = number of rounds x round duration. For example, 8 rounds each at 5 minute duration = 40 minutes. Session duration = total training duration + inter-round delays. For example, 8 rounds each with 30 second delays between rounds = 43 minutes and 30 seconds for the session duration. Round restart method can be automatic or manual and all of the round settings can be changed. When the Apply button is clicked in the settings panel then the Begin Session button will become active. To start the training session click Begin Session in either the session round panel or the protocol panel.



**Click Session  
Rounds**

**Number of Rounds x Round Duration = Training Duration**

**Session Duration = Training Duration + Inter-Round Delays**

The screenshot shows the 'Surface Neurofeedback' window with three tabs: 'Protocol', 'Session Rounds', and 'Progress'. The 'Session Rounds' tab is active, displaying a 'Session Setup' section with the following fields:

- Total Training Duration: 40:00
- Total Session Duration: 43:30
- Number of Rounds: 8
- Round Duration (min): 5
- Inter-Round Delay (sec): 30
- Restart Method: Automatic

Below the setup section is the 'Session Progress' section, which includes:

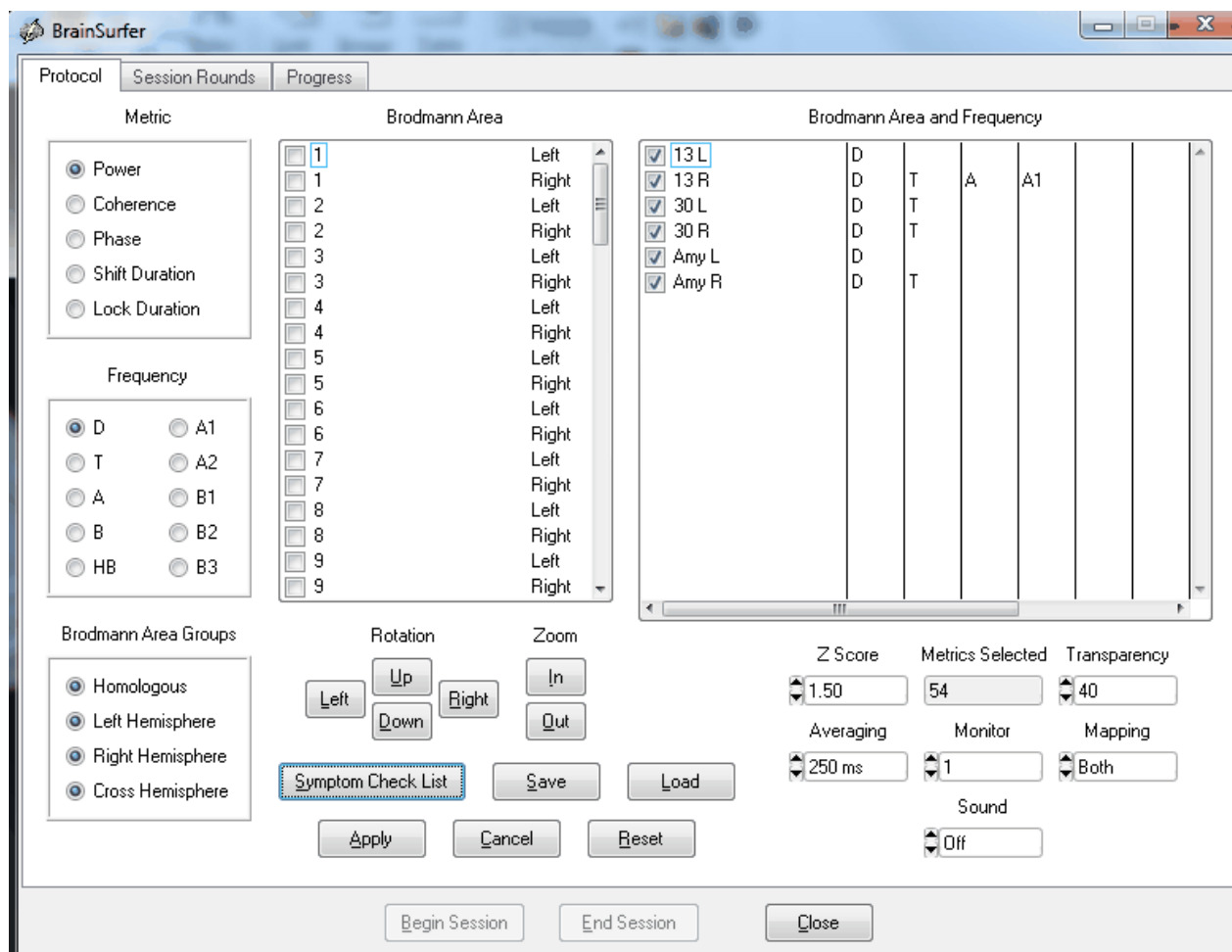
- Current Round Number: 1
- A 'Start Round' button.

At the bottom of the window are three buttons: 'Begin Session', 'End Session', and 'Close'.

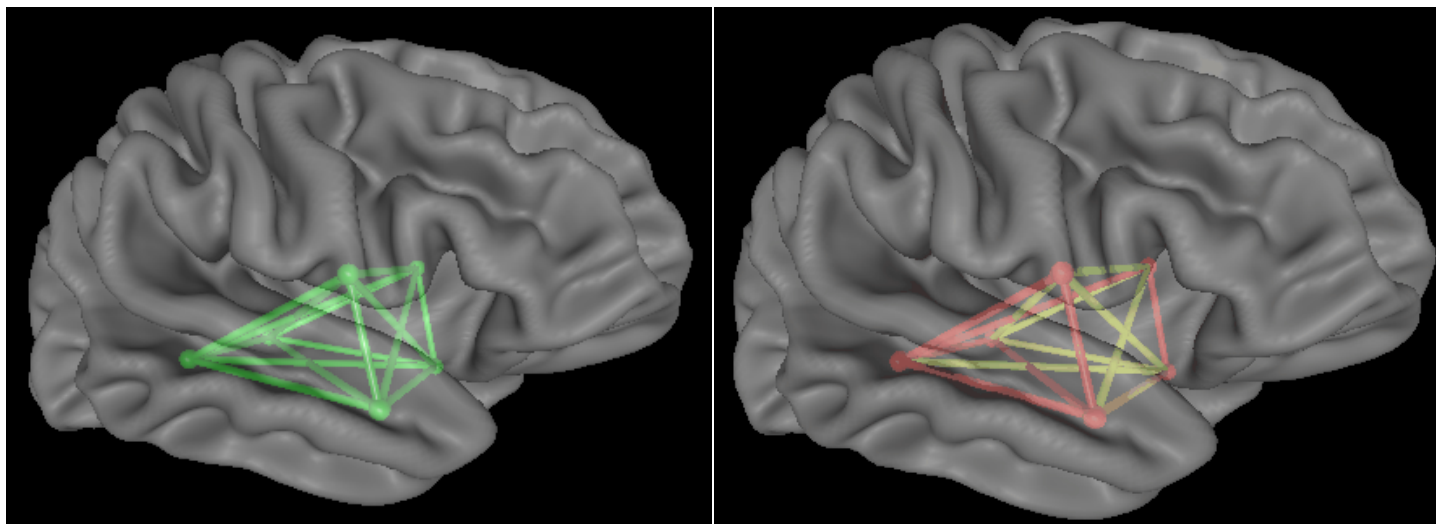
Annotations with arrows point to the following elements:

- Total Training Duration** points to the 'Total Training Duration' field.
- Total Session Duration** points to the 'Total Session Duration' field.
- Number of Rounds** points to the 'Number of Rounds' field.
- Round Duration** points to the 'Round Duration (min)' field.
- Inter-Round Delay** points to the 'Inter-Round Delay (sec)' field.
- Restart Method** points to the 'Restart Method' dropdown.
- Round Counter** points to the 'Current Round Number' field.
- Begin, End & Close Session** points to the 'Begin Session', 'End Session', and 'Close' buttons.

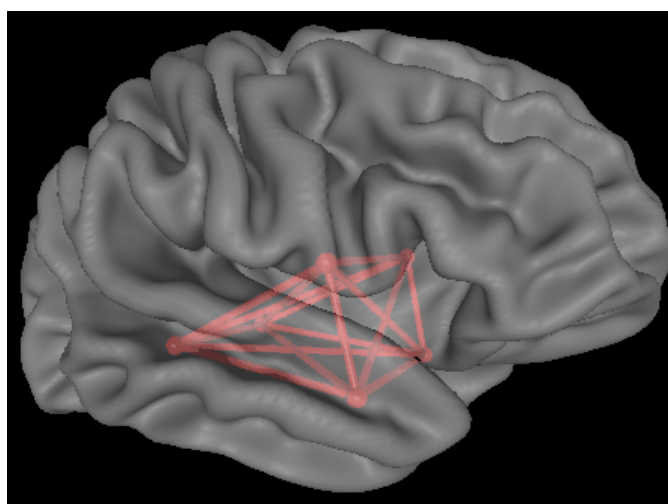
The Protocol Control panel is automatically populated by the symptom check list selection described above. One can manually select Brodmann areas and metrics and frequency, etc., however, it is recommended to use the symptom check list to link symptoms to Brodmann areas and connections between Brodmann areas that are dysregulated. The goal is to reinforce toward  $Z = 0$  which in order to reinforce toward greater stability and efficiency in the relevant nodes and connections of networks.



The Protocol panel shows the metrics and frequencies in the BrainSurfer protocol as well as providing controls over the degree of transparency or zoom in or zoom out or move the rendered brain. Also, there are controls to set the Z Score threshold in which a fixed 1 standard deviation band is operating where a Green color is present when the sLORETA Z Scores are equal to or less than the Z Score threshold, Red is when the Z Scores are 1 standard deviation or greater than the threshold and Yellow appears when the sLORETA Z Scores are between the lower Z Score threshold and 1 standard deviation above threshold.



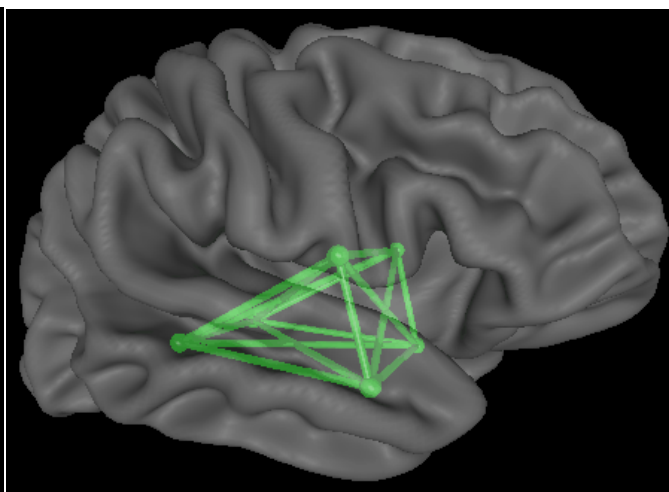
**Green is Equal to or Less than Threshold    Yellow is 1 Standard Deviation above Threshold**



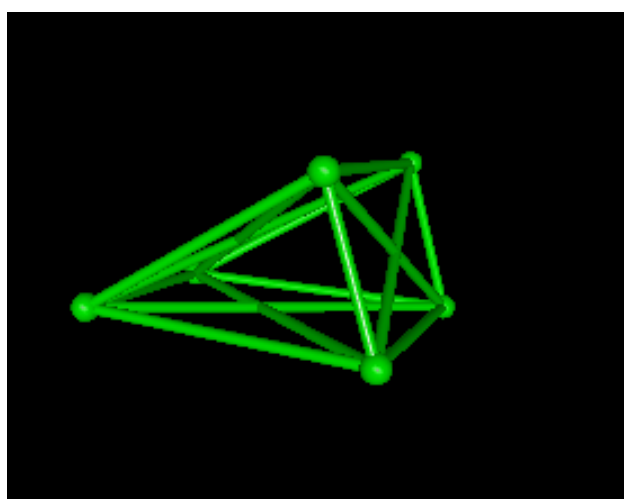
**Red is Greater than 1 Standard Deviation above Threshold**



Transparency = 0

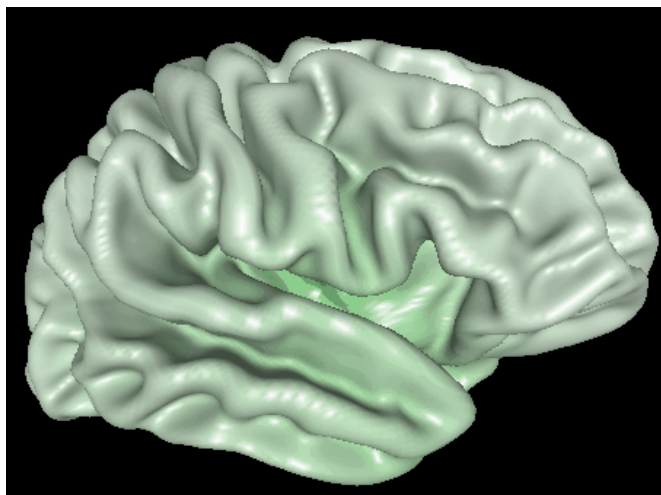


Transparency = 50%

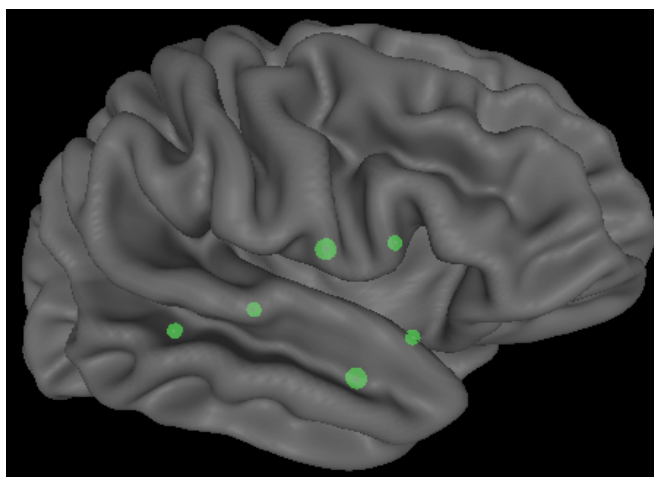


Transparency = 100%

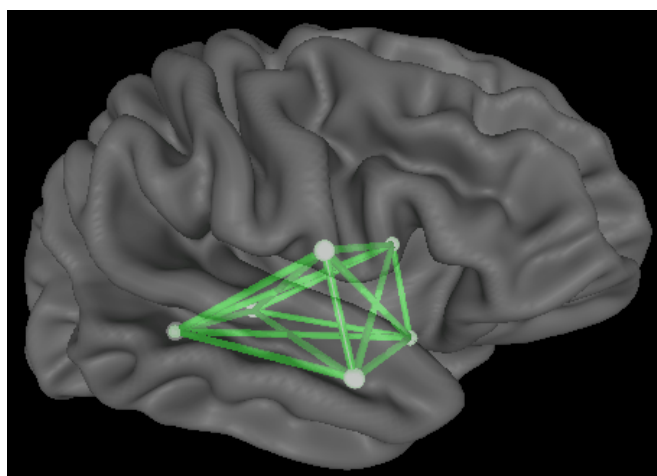




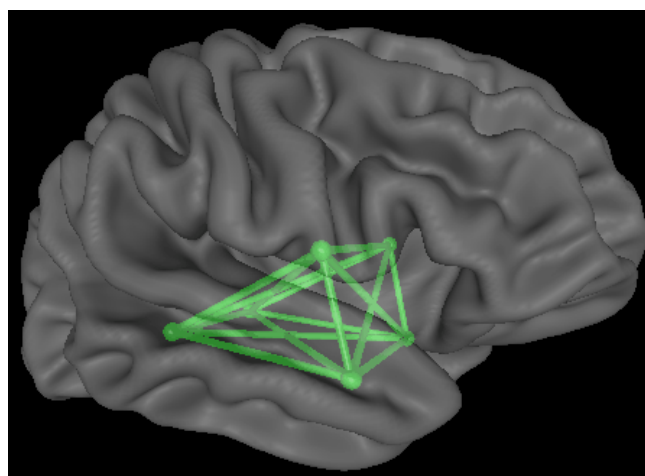
**Surface is Green At or Below Threshold**



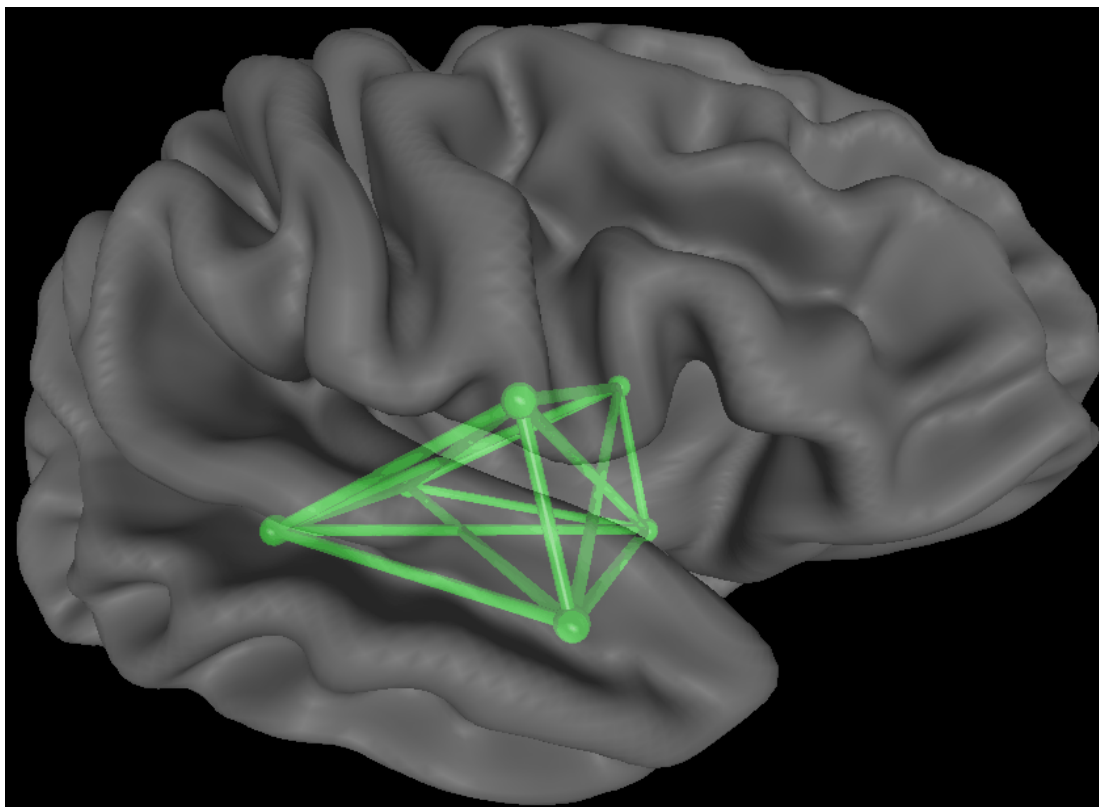
**Select Nodes (Brodmann areas) Only**



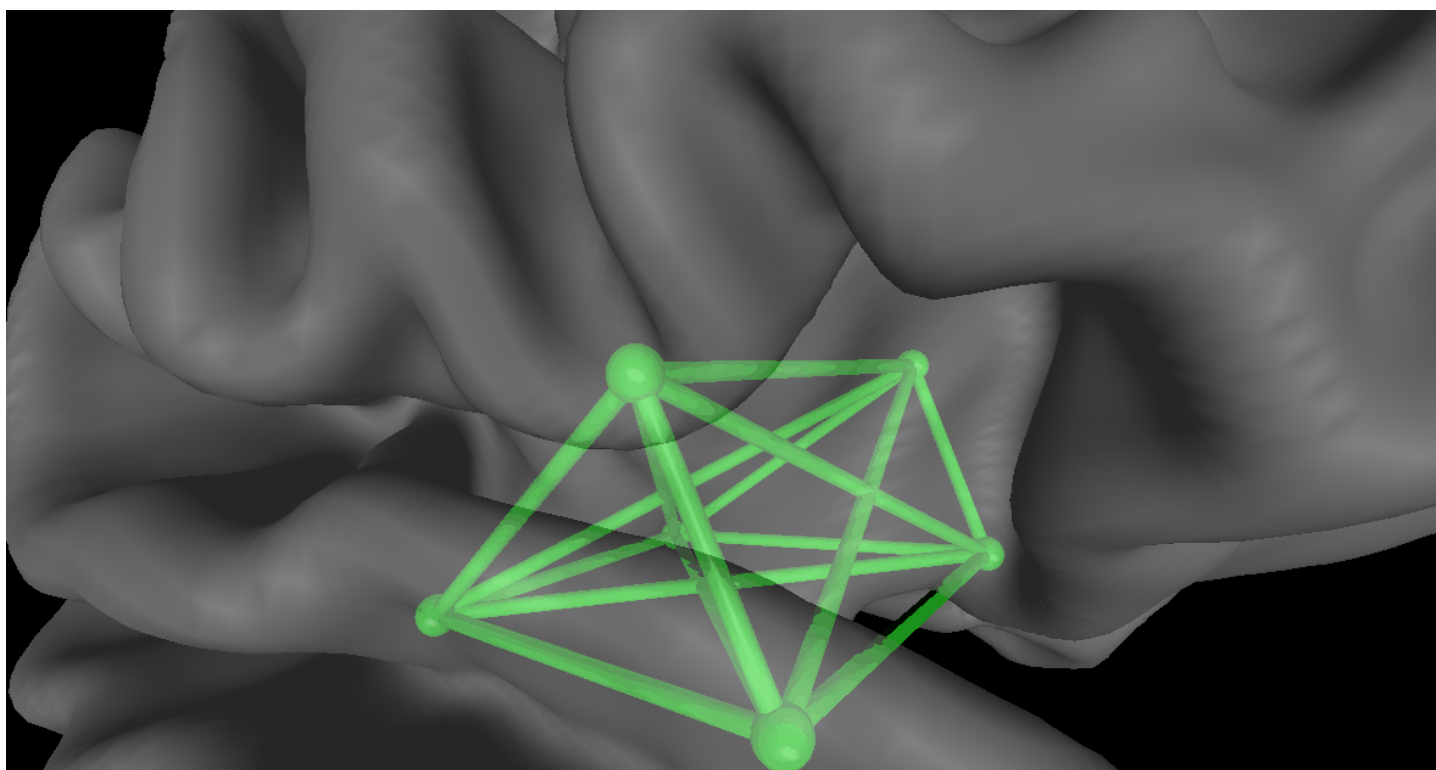
**Select Connections Only**



**Select Both Nodes and Connections**



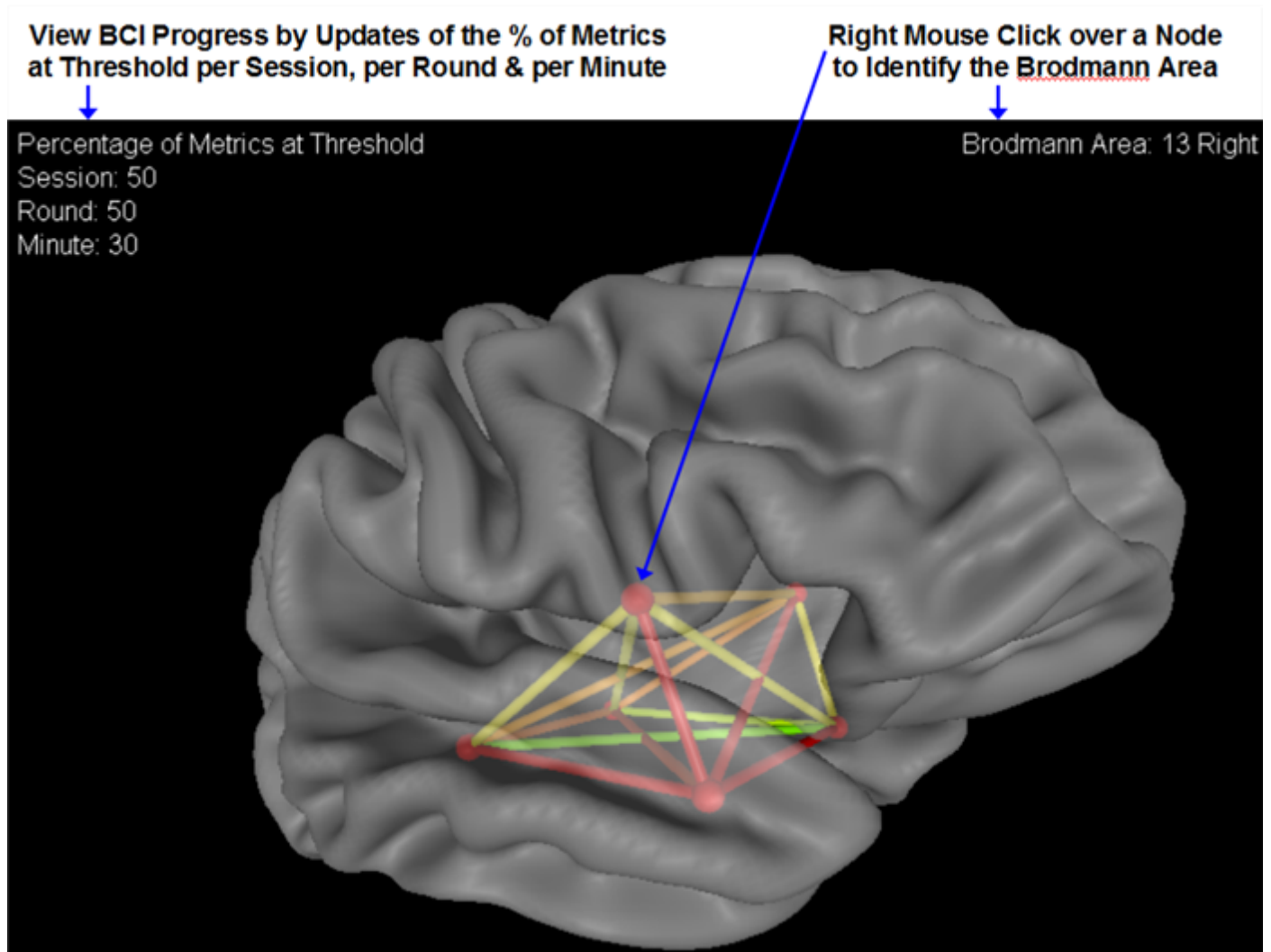
**Zoom in a Little**





**Zoom in Maximum to target a specific node or connection**

**View the progress of treatment in the upper left corner of the BrainSurfer display. Move the mouse over a Node or Brodmann area and Right Mouse Click to Identify the Brodmann area shown in the upper right of the BrainSurfer display**

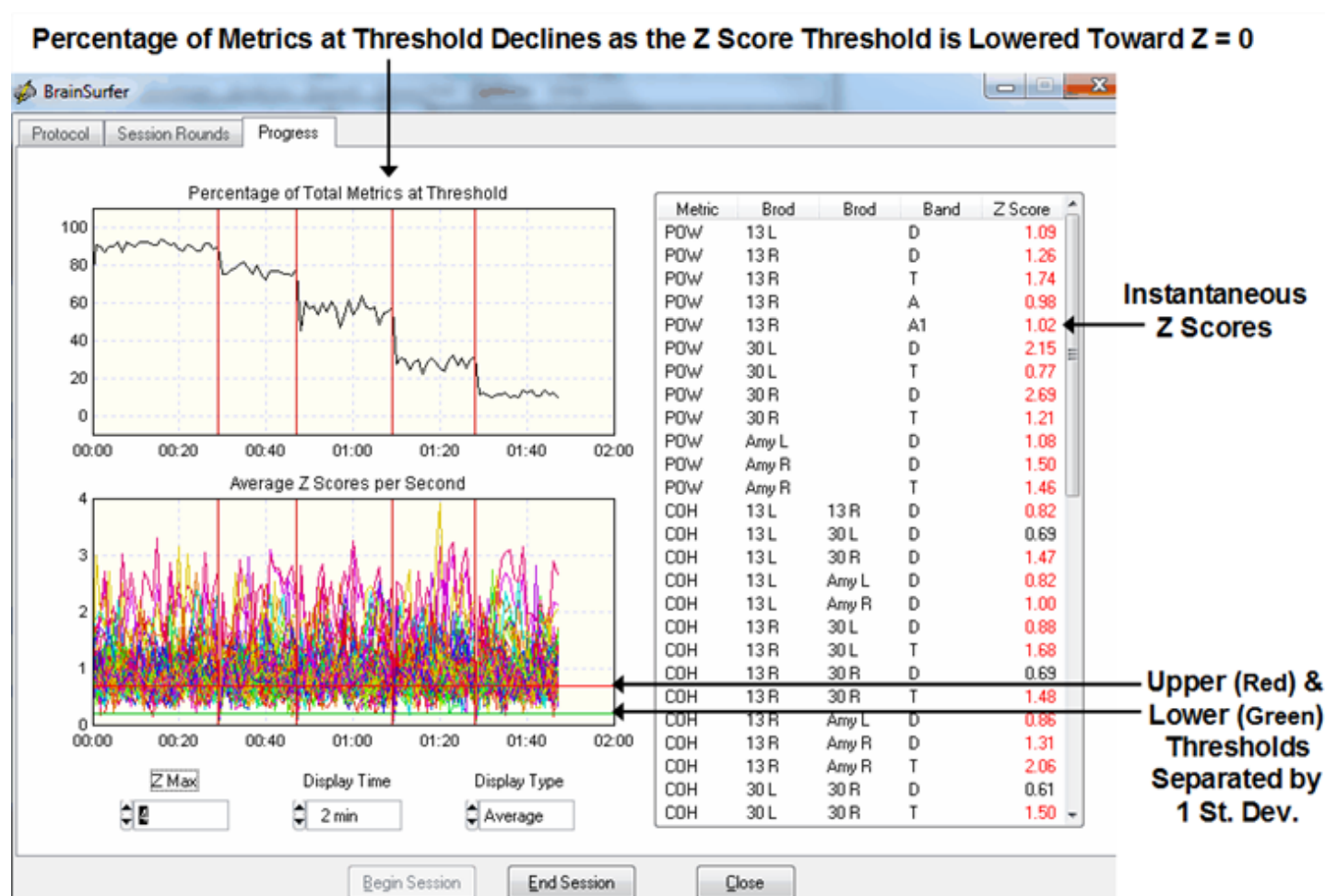


## **BrainSurfer - sLORETA Functional Connectivity as Measured by Instantaneous Coherence, Phase Differences, Phase Shift Duration and Phase Lock Duration**

BrainSurfer functional connectivity is activated by selecting either Coherence, Phase Difference, Phase Lock Duration and/or Phase Shift Duration radial button in the Symptom Check List panel or in the Protocol Panel. The real-time functional connections between Brodmann Areas are then available at different frequencies and for different networks. Rotate or size and zoom into the networks. Change the transparency to 50% to retain the outline of



brain landmarks and view the network coherence or phase Z Scores in real-time. Perform neurofeedback by making the green when the instantaneous Z Scores are equal to or lower than the Z Score threshold. Activate sound feedback and view the counters for the percent of total metrics that reached threshold in a session, round and per minute. Keep adjusting the threshold toward  $Z = 0$  and view that the percentage of metrics at threshold declines and then watch the percentage increase as the subject learns to create the Green color. Repeat by lowering the threshold toward  $Z = 0$  in order to reinforce increased stability in nodes and connections between nodes in networks linked to the patient's symptoms. The successful BCI session will involve a series of sawtooth waves of increasing percentage of metrics that decline and then increase again as the clinician lowers the Z Score threshold and the subject learns to create the Green color again.



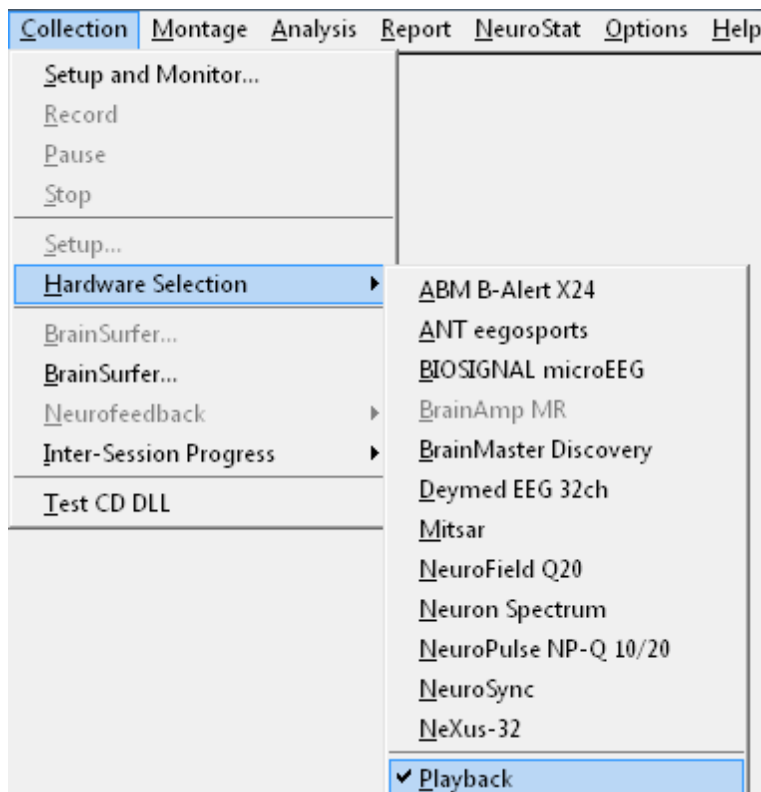
All comments and feedback are welcome.

Contact us at [geeg@appliedneuroscience.com](mailto:geeg@appliedneuroscience.com) and tell us what you think.



## Playback Mode

BrainSurfer can be activated in Playback mode by clicking **Collection > Hardware Selection** and then select **Playback**. Then click **Collection > Setup & Monitor** and OK to activate the demo playback or to navigate to a subject's folder and select a previously recorded EEG and click OK. When the EEG traces start to be played back, then click **Collection > BrainSurfer** to activate the real-time Brodmann area Z Scores.



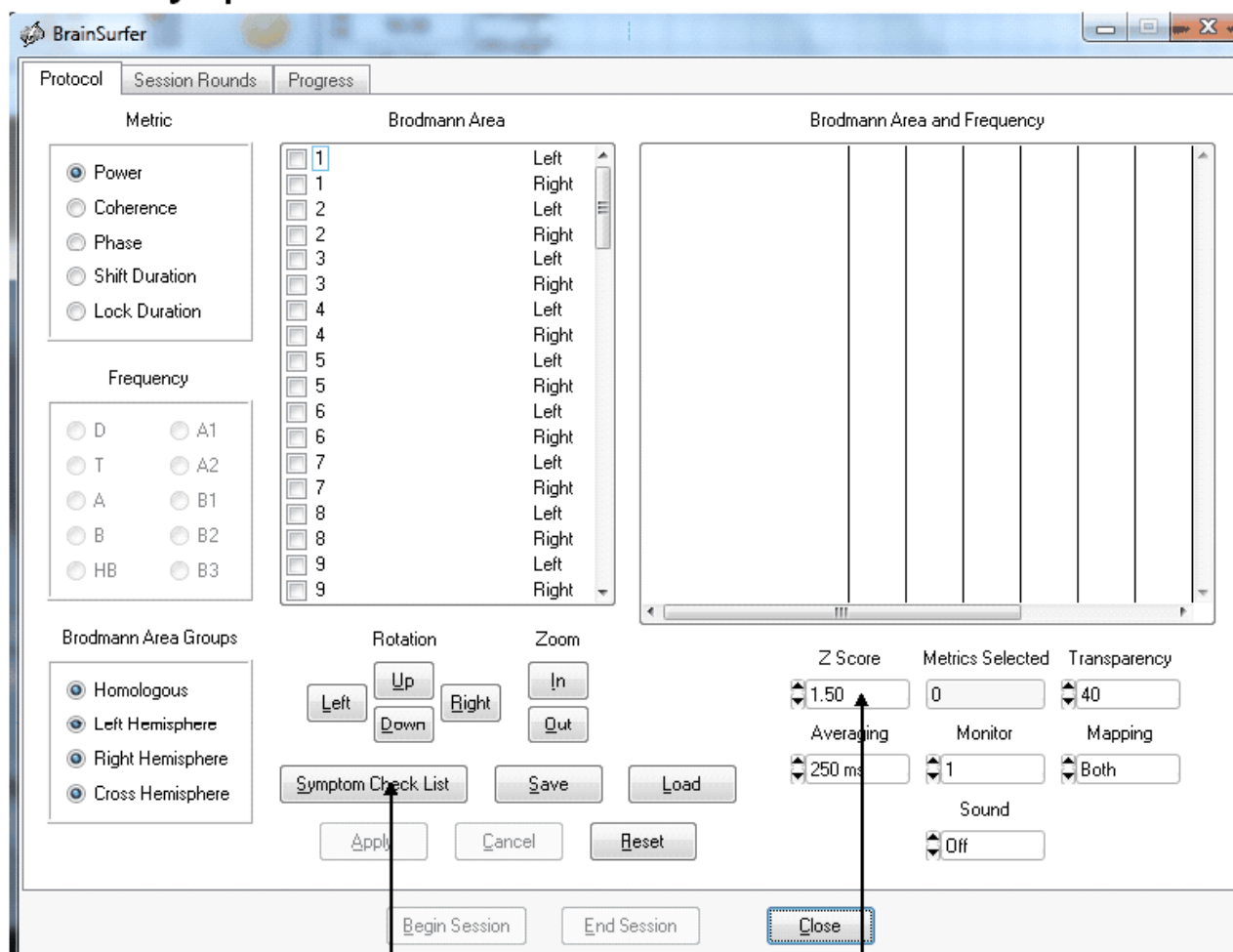
## Symptom Check List BrainSurfer

Create a .scl file in NeuroGuide by selecting at least a minute of artifact free EEG (see [Artifact Free Selections](#)<sup>31</sup>) and then click **Report > Create Symptom Check List Match** (see **Create Symptom Check List Match**)

Click **Symptom Check List** in the BrainSurfer Protocol panel and then navigate to where the .scl file was saved (see **Create Symptom Check List Match**). The protocol panel is a control panel by which one can manually select Brodmann areas, frequencies and metrics as well as the rendered brain transparency, zoom and rotation. Also, the Z Score threshold and sound controls are in this panel.



## BrainSurfer Protocol Panel – Use Manual Selections of Brodmann Areas or Use the Symptom Check List for Automatic Protocol Generation



Click Symptom Check List

Select Z Threshold

After clicking the Symptom Check List button, then navigate to the subject's folder where the .scl file was saved and load the file. The symptoms check list panel will appear and then select a single symptom that is most troubling and relevant to the patient and double click the severity cell and assign a number from 1 to 10. The Hypothesis panel is based on the fMRI, PET and neurological scientific literature of studies linking symptoms to Brodmann areas and network nodes (see [www.anipublishing.com](http://www.anipublishing.com))





Select a Symptom or ICN  
or Network, etc.

Adjust the Z Score  
for Entry to the Protocol

Select Metrics

**Symptom Check List**

Symptoms | ICN | Networks | Neuropsychological | DoD/VA

Symptom / Complaint	Severity
Anosognosia - Denial of a Problem	0
Anxiety	10
Attention Deficits - Easily Distractable	10
Auditory Sequencing Problems	0
Balance Problems	0
Blurred Vision	0
Chronic Pain	0
Compulsive Behaviors and/or Thoughts	0
Concentration Problems	0
Decreased Tactile or Skin Sensitivity	0

**Hypothesis**

Brodman	Hem
13	Left
13	Right
26	Left
26	Right
30	Left
30	Right
Amygdala	Left
Amygdala	Right

**Match**

Brodman	Hem
13	Left
13	Right
30	Left
30	Right
Amygdala	Left
Amygdala	Right

**Mismatch**

Brodman	Hem
1	Right
2	Right
3	Right
4	Left
4	Right
5	Left
5	Right
6	Left
6	Right
7	Left

OK Cancel

**Z Score**

2.00

☒ Power  
☒ Coherence  
☐ Phase  
☐ Phase Shift  
☐ Phase Lock

Hypothesized Brodmann areas linked to Symptoms that Match the Patient's QEEG

Increase the Z Score to select only the most deviant and dysregulated Brodmann areas and connections between Brodmann areas (coherence, phase differences, phase shift & phase lock). The match column are those Brodmann areas that match the hypothesized Brodmann areas. Adjust the Z Score selection to only include the most deviant Z Scores inside of the .scl file. Then click OK to create a protocol of metrics and frequencies in locations linked to the patient's symptoms.

## Session Rounds

Click Session Rounds tab in the protocol panel to activate the session rounds panel. The total training duration = number of rounds x round duration. For example, 8 rounds each at 5 minute duration = 40 minutes. Session duration = total training duration + inter-round delays. For example, 8 rounds each with 30 second delays between rounds = 43 minutes and 30 seconds for the session duration. Round restart method can be automatic or manual and all of the round settings can be changed. When the Apply button is clicked in the settings panel then



the Begin Session button will become active. To start the training session click Begin Session in either the session round panel or the protocol panel.

**Click Session Rounds**

**Number of Rounds x Round Duration = Training Duration**

**Session Duration = Training Duration + Inter-Round Delays**

The screenshot shows the 'Surface Neurofeedback' window with three tabs: 'Protocol', 'Session Rounds', and 'Progress'. The 'Session Rounds' tab is active, displaying 'Session Setup' and 'Session Progress' sections.

**Session Setup:**

- Total Training Duration: 40:00
- Total Session Duration: 43:30
- Number of Rounds: 8
- Round Duration (min): 5
- Inter-Round Delay (sec): 30
- Restart Method: Automatic

**Session Progress:**

- Current Round Number: 1
- Start Round button

**Bottom Panel:**

- Begin Session button
- End Session button
- Close button

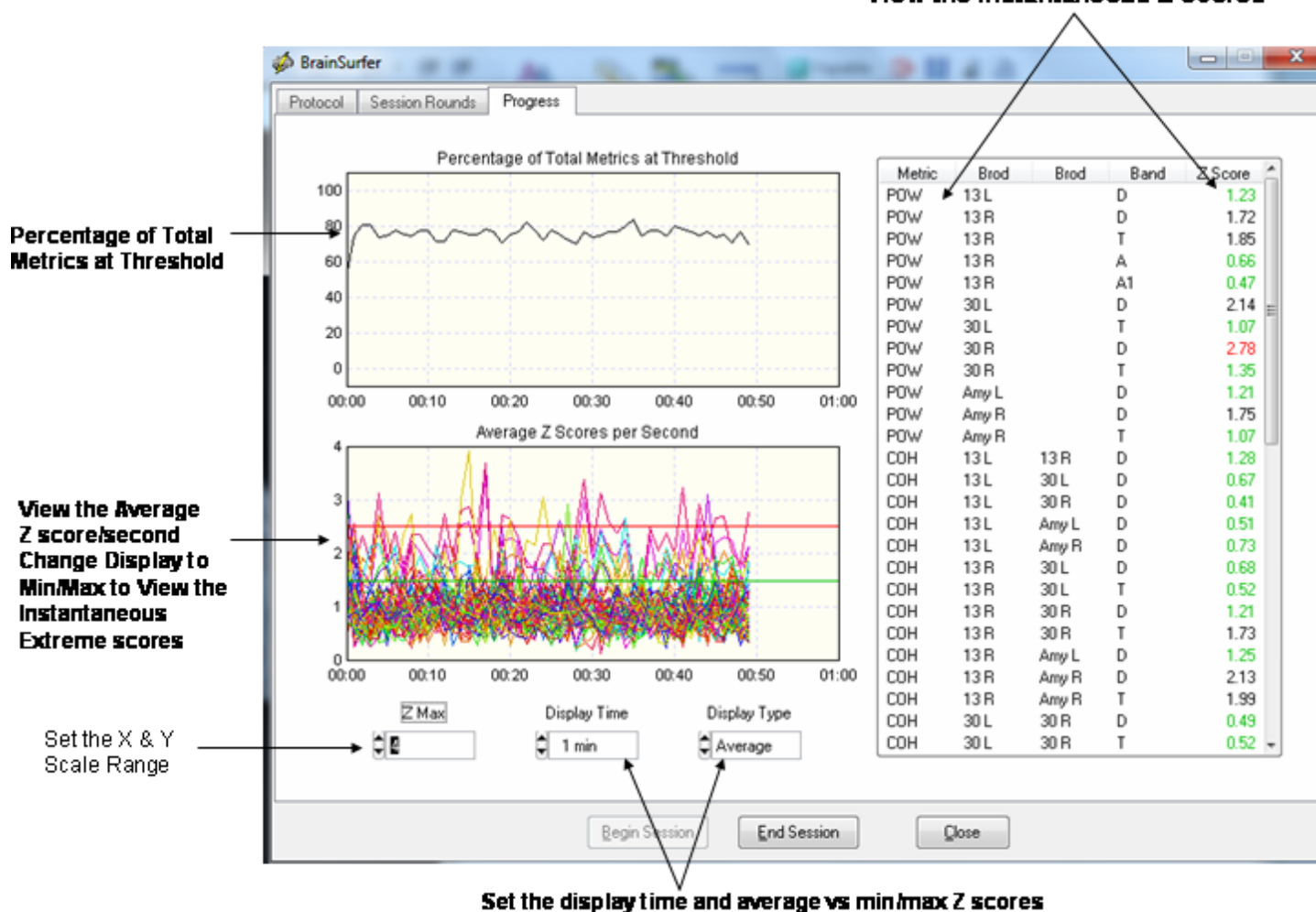
Labels and arrows pointing to UI elements:

- Total Training Duration** points to 'Total Training Duration: 40:00'.
- Total Session Duration** points to 'Total Session Duration: 43:30'.
- Number of Rounds** points to the 'Number of Rounds' input field (value 8).
- Round Duration** points to the 'Round Duration (min)' input field (value 5).
- Inter-Round Delay** points to the 'Inter-Round Delay (sec)' input field (value 30).
- Restart Method** points to the 'Restart Method' dropdown menu (value Automatic).
- Round Counter** points to 'Current Round Number: 1'.
- Begin, End & Close Session** points to the 'Begin Session', 'End Session', and 'Close' buttons.

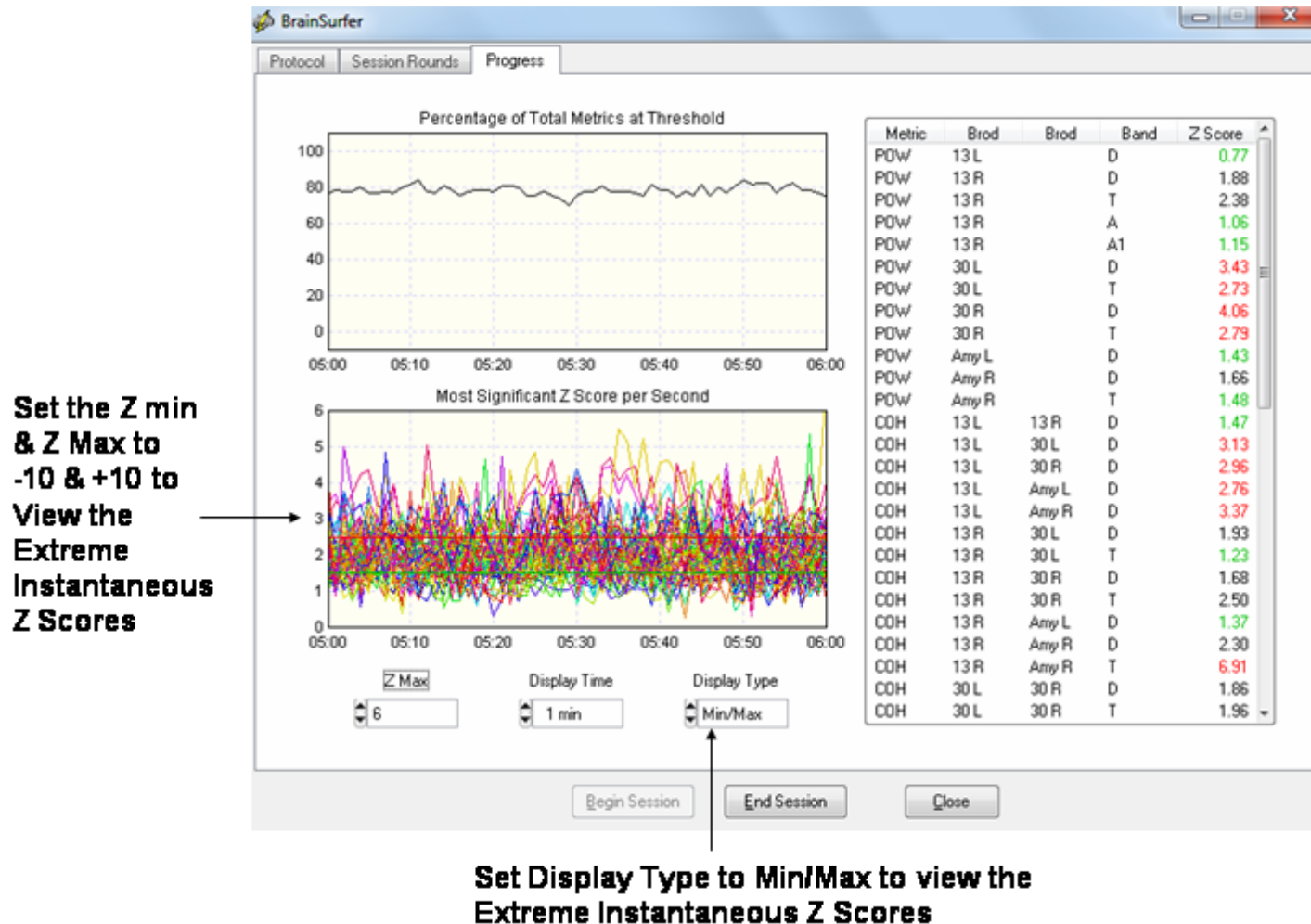
## Intra-Session Progress Chart

After starting the session, then click the Progress tab to view the Intra-Session progress charts.



**View the Instantaneous Z Scores**

Set the display time to Min/Max to view the extreme instantaneous Z Scores rather than the average of 32 Z Scores in a second which can result in small Z Scores.



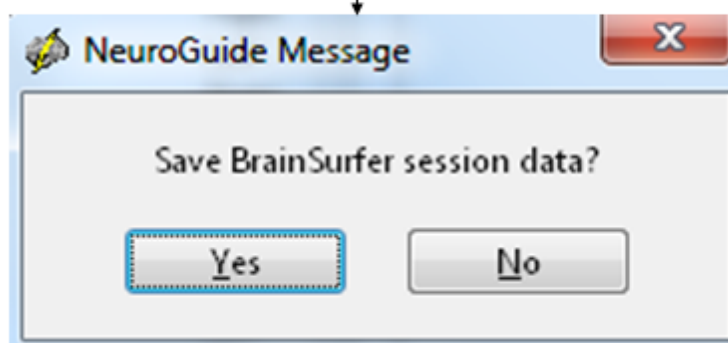
## Inter-Session Progress Chart

After each BrainSurfer session close the session and then save the session in the client's folder. The session files end in the extension \*.bsf and will be automatically selected and used to generate an Inter-Session Progress chart based on the chronological order of the sessions.

It is important that subject's sessions not be mixed with different clients and to save each session in the same subject's folder.



**To Create an Inter-Session Progress Chart, click End Session and then Click OK to the Brainsurfer Message. Save the .bsf files in the patient's Folder.**





BrainSurfer Inter-Session Progress

Plot Selections | Plotted Data

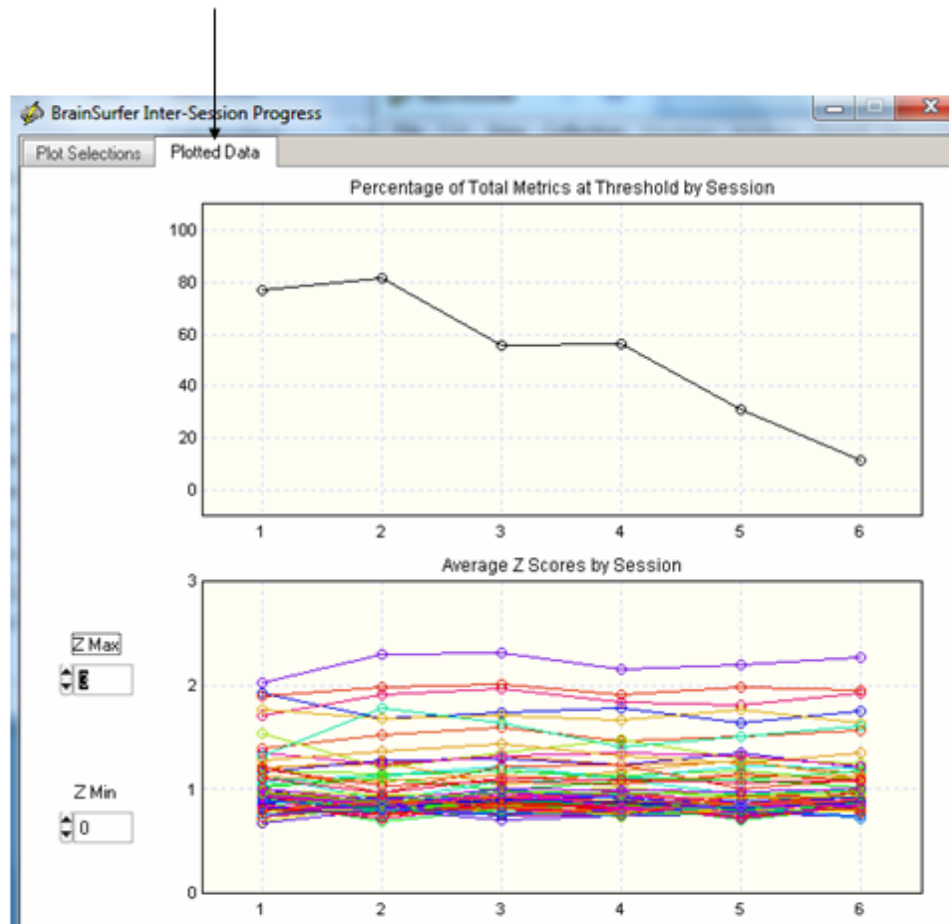
		T	A	B	HB	A1	A2	B1	B2	B3	Ave
AP	13 L	Yes									Yes
AP	13 R	Yes	Yes	Yes		Yes					Yes
AP	30 L	Yes	Yes								Yes
AP	30 R	Yes	Yes								Yes
AP	Amy L	Yes									Yes
AP	Amy R	Yes	Yes								Yes
CO	13 L - 13 R	Yes									Yes
CO	13 L - 30 L	Yes									Yes
CO	13 L - 30 R	Yes									Yes
CO	13 L - Amy L	Yes									Yes
CO	13 L - Amy R	Yes									Yes
CO	13 R - 30 L	Yes	Yes								Yes
CO	13 R - 30 R	Yes	Yes								Yes
CO	13 R - Amy L	Yes									Yes
CO	13 R - Amy R	Yes	Yes								Yes
CO	30 L - 30 R	Yes	Yes								Yes
CO	30 L - Amy L	Yes									Yes
CO	30 L - Amy R	Yes	Yes								Yes
CO	30 R - Amy L	Yes									Yes
CO	30 R - Amy R	Yes	Yes								Yes
CO	Amy L - Amy R	Yes									Yes

Clear All | Select All

**Select or Deselect the Frequencies and Brodmann Areas to Be Included in the Inter-Session Progress Plots**



**After Plot Selections then Click Plotted Data to View the Inter-Session Progress Chart**

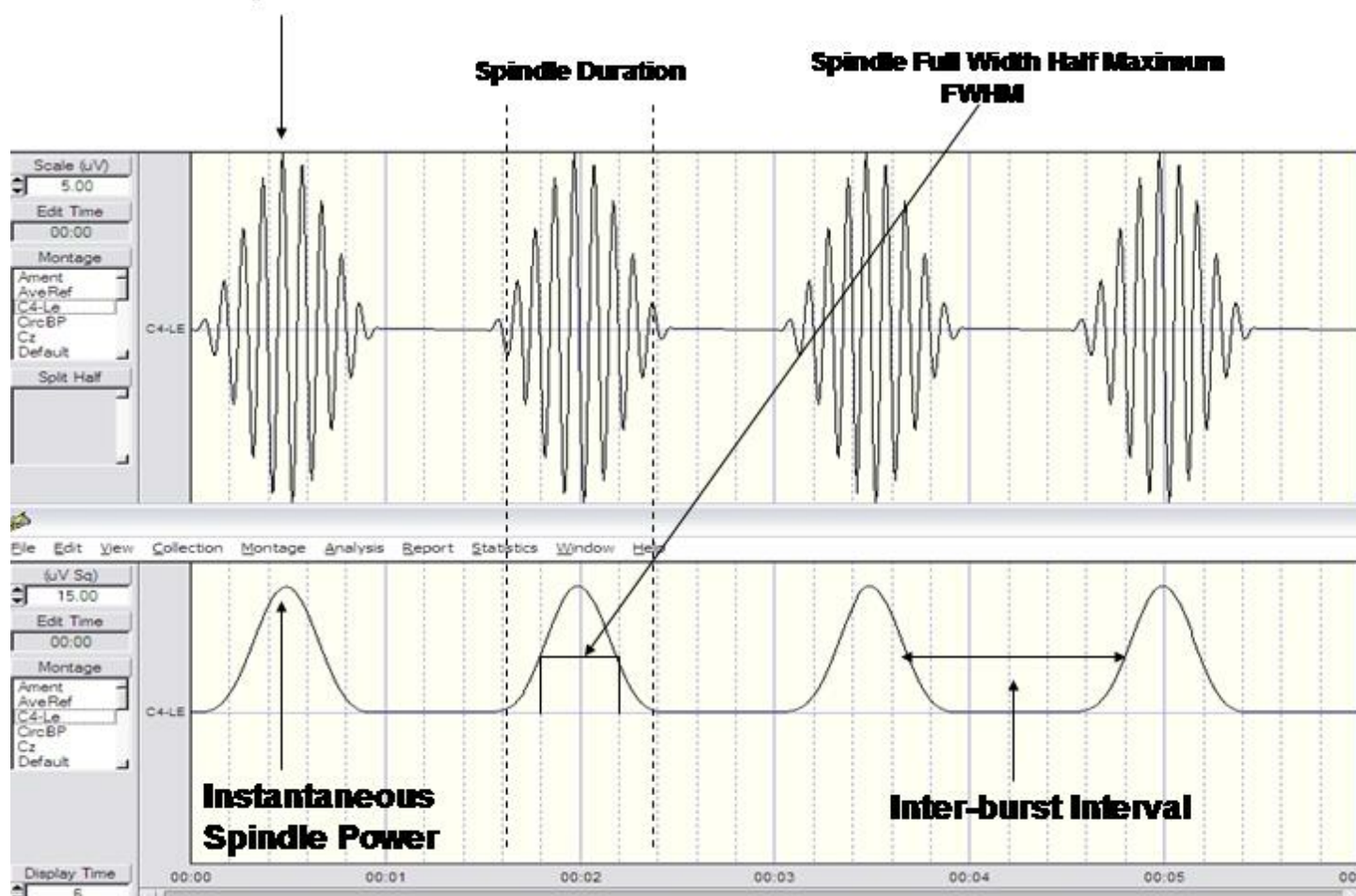


## Burst Metrics

Click Report > Report Selections and then select Burst Metrics options to activate the Spindle analyses and Burst Metrics which include the number of bursts/sec, average duration of bursts (sec), average amplitude of bursts (uV) and average inter-burst interval (sec) for each frequency band. Technical details of EEG burst metrics are at <http://www.appliedneuroscience.com/Articles.htm> and then download Article "EEG and Brain Connectivity: A Tutorial"



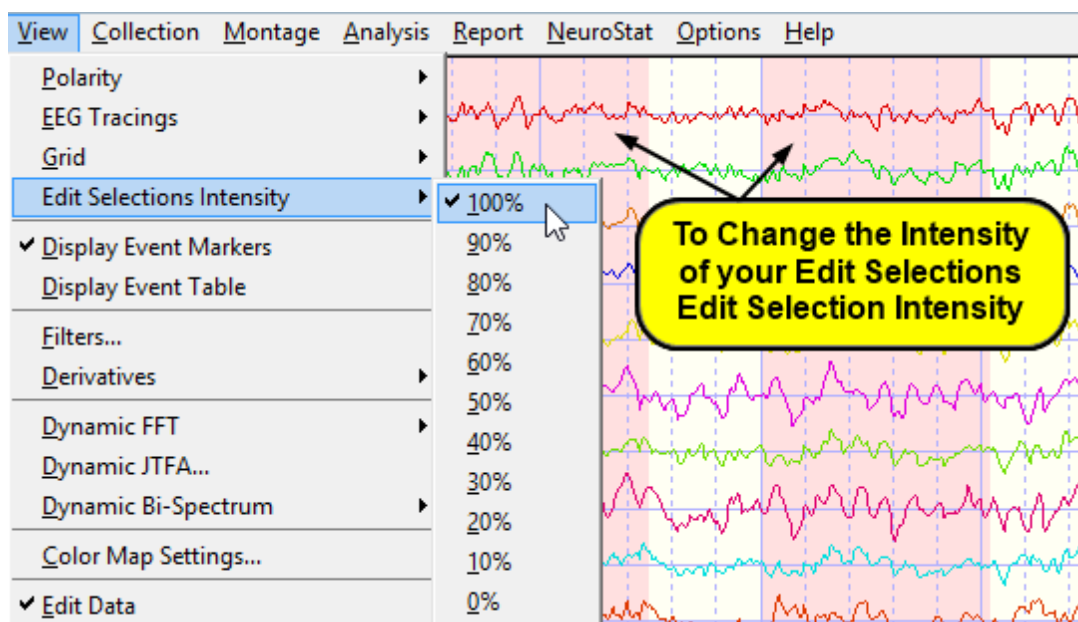
## Simulated Spindles



A burst is defined as a significant departure from the baseline level of the instantaneous power of the EEG in a particular frequency band (e.g.,  $> 2$  sd) with a significant rise time and fall time as measured by the 1st derivative. If this criteria is met then there is a "burst". The second derivative is used to determine the intra-burst interval or the duration of the burst as well as the full-width-half-maximum (FWHM). That is, the 2nd derivative measures the inflexion points of the burst onset and burst offset. The inter-burst interval is the time between the falling phase of one burst and the rising phase of the subsequent burst. Bursts per second are computed by adding up the total number of bursts and then dividing by the total amount of time in the selected record. The amplitude of a burst is the absolute amplitude at the peak of a burst as defined by the 1st derivative = 0 or the amplitude at the maximum peak value of the burst.

## Color Intensity of Edit Selections

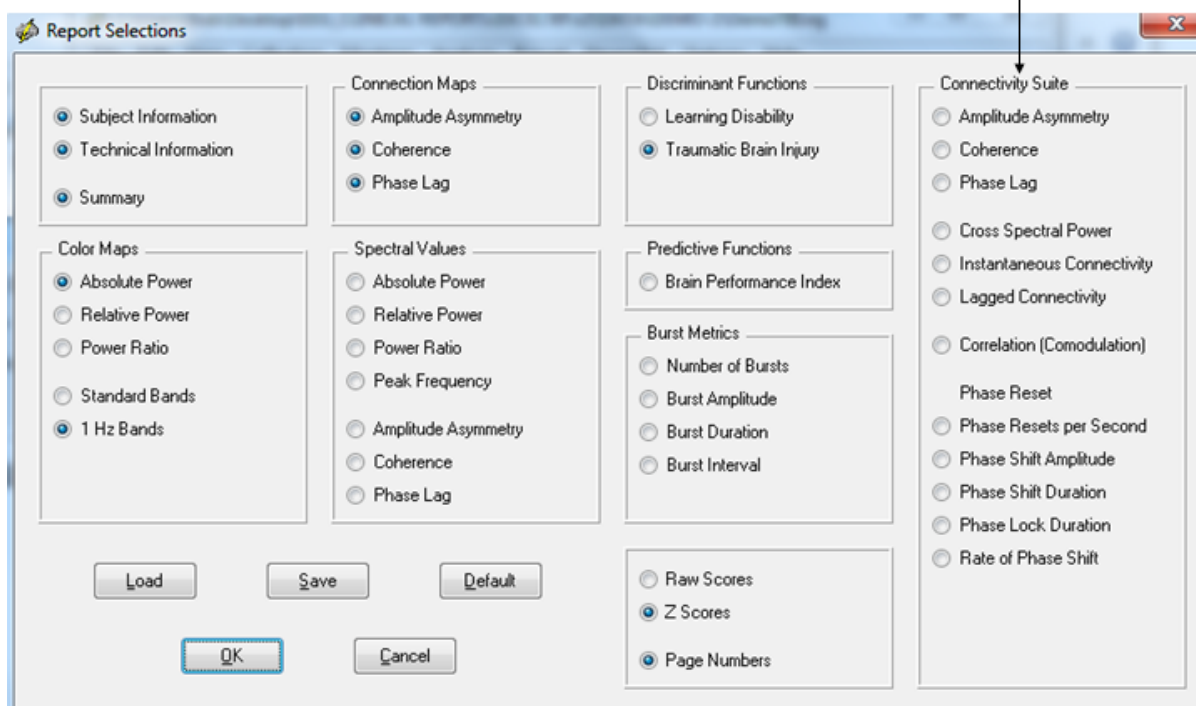
Change the color intensity of the Edit Selections by clicking View > Edit Selection Intensity



## Connectivity Suite

Click Report > Report Selections in the Menu. Then select the Connectivity Suite to produce the Full 171 combination maps of amplitude asymmetry, coherence, correlation ("co-modulation"), cross-spectral power, cospectral power, quadspectral power, phase and phase reset. The Connectivity Suite is an add on product to NeuroGuide. Technical details of the Connectivity Suite are explained at [www.appliedneuroscience.com/Articles.htm](http://www.appliedneuroscience.com/Articles.htm) and then download Article "How to compute EEG coherence with a hand calculator".

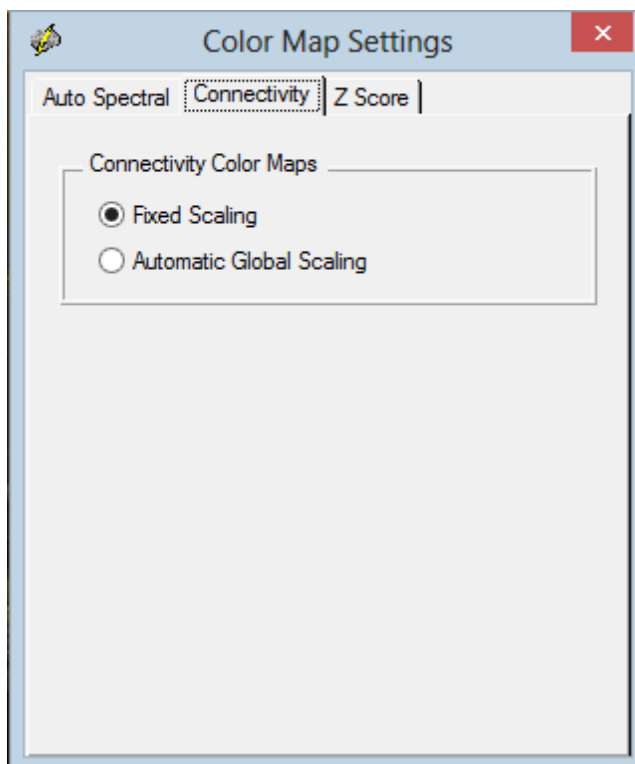


**Click Report > Report Selections and Connectivity Suite Options**

Select the color scales for the Connectivity Suite under Report > Color Map Settings.

- **Fixed Scaling** uses the Min and Max of fixed values to adjust the color scales for each map (e.g., Amplitude Asymmetry is fixed from -200 to +200).
- **Automatic Global Scaling** uses the Min and Max of each measure to adjust the color scales for each map (e.g., Amplitude Asymmetry is fixed from -50 to +150).

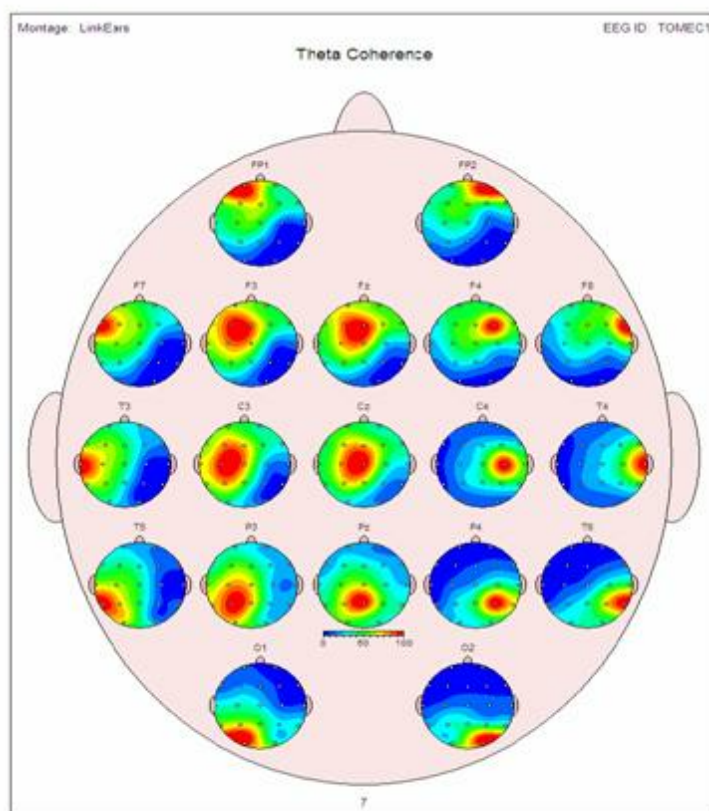




Below is an example of the full 171 combination maps that are available in the Connectivity Suite

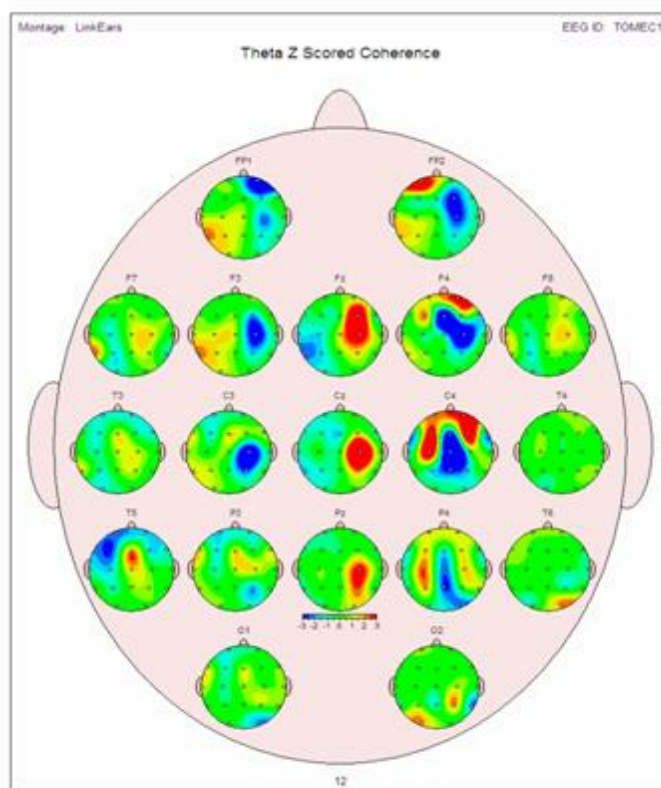


**Full raw score Coherence in the Connectivity Suite. There are 19 small topographic maps corresponding to the 10/20 system location inside of a single head display. This map provides the full picture of all 171 electrode combinations.**





**Full Z Score Coherence in the Connectivity Suite.** There are 19 small topographic maps corresponding to the 10/20 system location inside of a single head display. This map provides the full picture of all 171 electrode combinations and the full range of Z scores are available



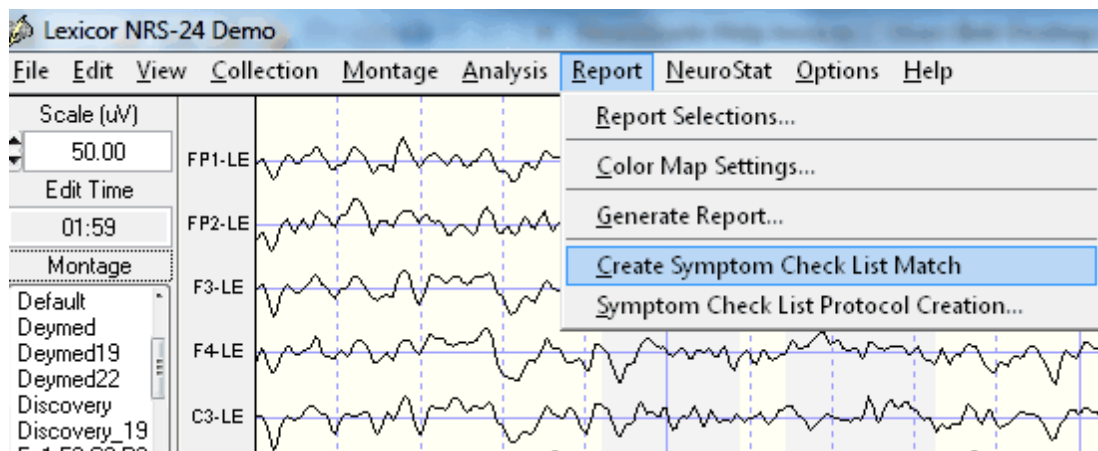
The cross-spectrum is the sum of the in-phase potentials (i.e., cospectrum) and out-of-phase potentials (i.e., quadspectrum). The in-phase component (Instantaneous Coherence) contains volume conduction and the synchronous activation of local neural generators. The out-of-phase component (Lagged Coherence) contains the network or connectivity contributions from locations distant to a given source. In other words, the cospectrum = volume conduction and the quadspectrum = non-volume conduction which can be separated and analyzed by independently evaluating the cospectrum and quadspectrum.

## Create Symptom Check List Match

Create a .scl file by selecting at least a minute of artifact free EEG (see [Artifact Free Selections](#) <sup>31</sup>) and then click Report > Create Symptom Check List Match. The Symptom Check List Match file (\*.scl) contains about 5,000 Z Scores for absolute power, relative power, power ratios, amplitude asymmetry, coherence, phase differences and LORETA current density Z



**Scores.** The file is in binary format and designed to be imported into the Protocol panel for [Surface Neurofeedback](#)<sup>165</sup>, [LORETA Neurofeedback](#)<sup>182</sup> and [BrainSurfer](#)<sup>54</sup> Brain-Computer-Interface modules.

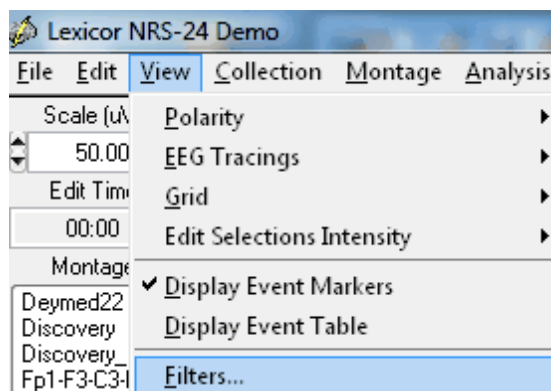


Save the Symptom Check List File (\*.scl) in the patient's folder.

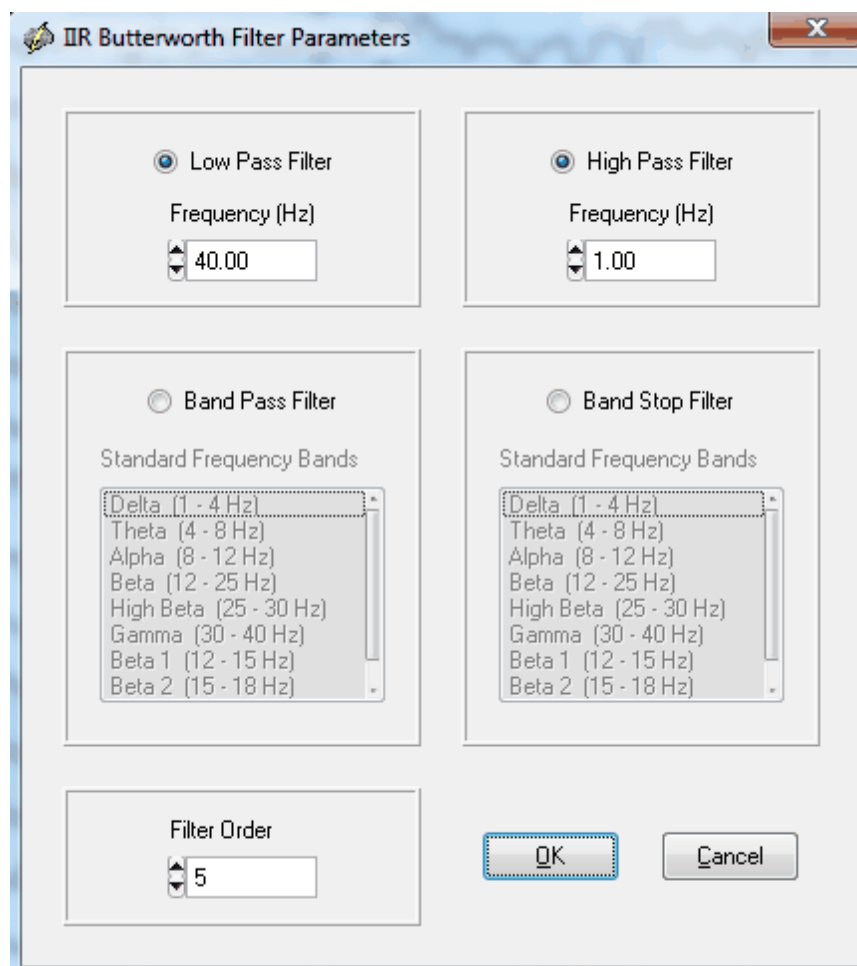
## Digital Filters

Digital Filter Viewer is a IIR Butterworth Filter that only changes the appearance of the EEG tracings and does not have any impact on the FFT or Normative Database comparisons. This is a valuable visual tool to examine the time and frequency details of the EEG tracings themselves.

Click View > Filters to open the Filter Parameter panel:



Type the low and high pass filter settings that one is interested in. Or select Band Pass Filter and one of the chosen common frequency bands. To eliminate a particular frequency select the Band Stop Filter and then one of the common frequency bands. Change the order of the Butterworth Filter



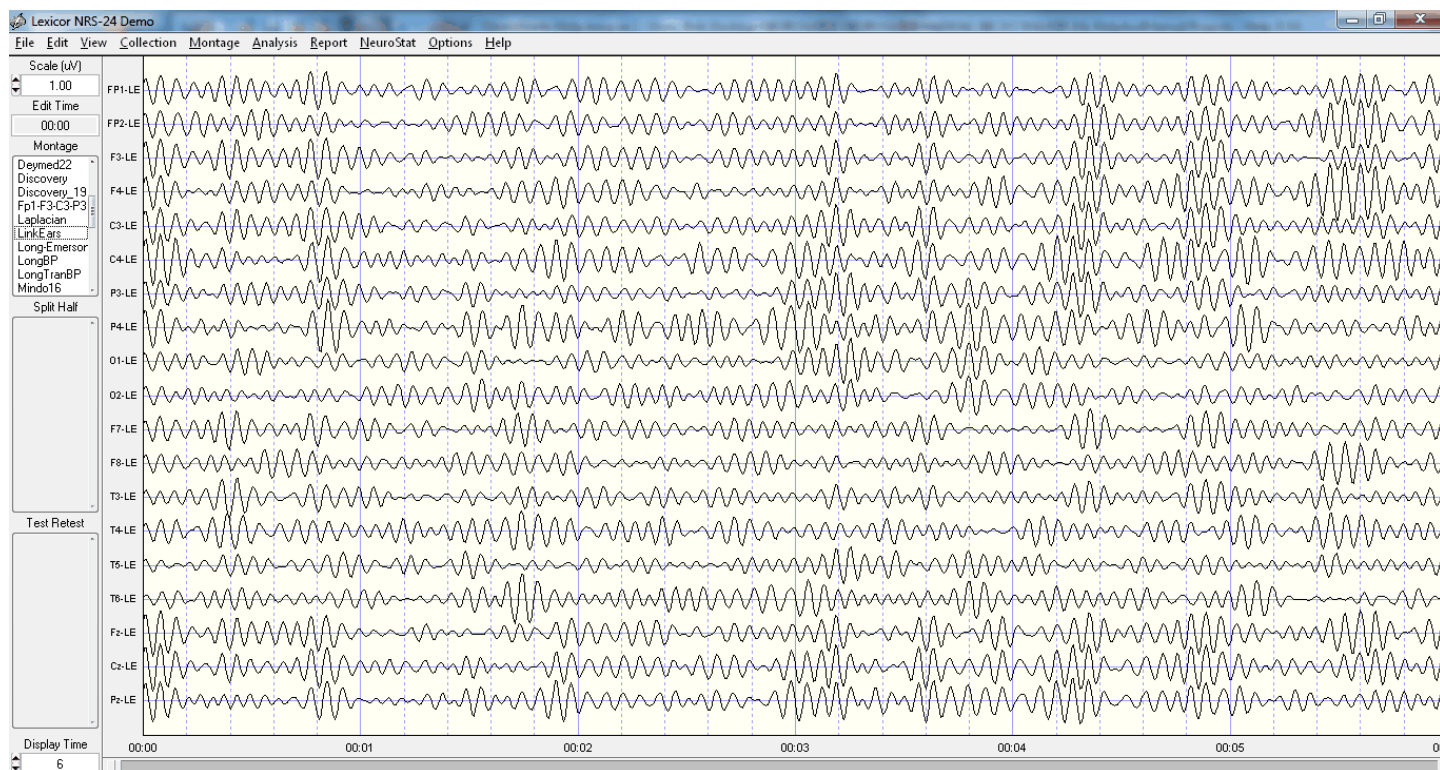
The dialog box is titled "IIR Butterworth Filter Parameters" and contains four filter type options, each with a radio button and a frequency input field. The "Low Pass Filter" option is selected, with a frequency of 40.00 Hz. The "High Pass Filter" option is also visible, with a frequency of 1.00 Hz. The "Band Pass Filter" and "Band Stop Filter" options are unselected and each have a list of standard frequency bands. The "Filter Order" is set to 5. "OK" and "Cancel" buttons are at the bottom right.

Filter Type	Frequency (Hz)	Standard Frequency Bands
<input checked="" type="radio"/> Low Pass Filter	40.00	
<input checked="" type="radio"/> High Pass Filter	1.00	
<input type="radio"/> Band Pass Filter		Delta (1 - 4 Hz) Theta (4 - 8 Hz) Alpha (8 - 12 Hz) Beta (12 - 25 Hz) High Beta (25 - 30 Hz) Gamma (30 - 40 Hz) Beta 1 (12 - 15 Hz) Beta 2 (15 - 18 Hz)
<input type="radio"/> Band Stop Filter		Delta (1 - 4 Hz) Theta (4 - 8 Hz) Alpha (8 - 12 Hz) Beta (12 - 25 Hz) High Beta (25 - 30 Hz) Gamma (30 - 40 Hz) Beta 1 (12 - 15 Hz) Beta 2 (15 - 18 Hz)

Filter Order: 5

Buttons: OK, Cancel

Here is an example of the SMR or Mu frequency range of 13 Hz to 15 Hz

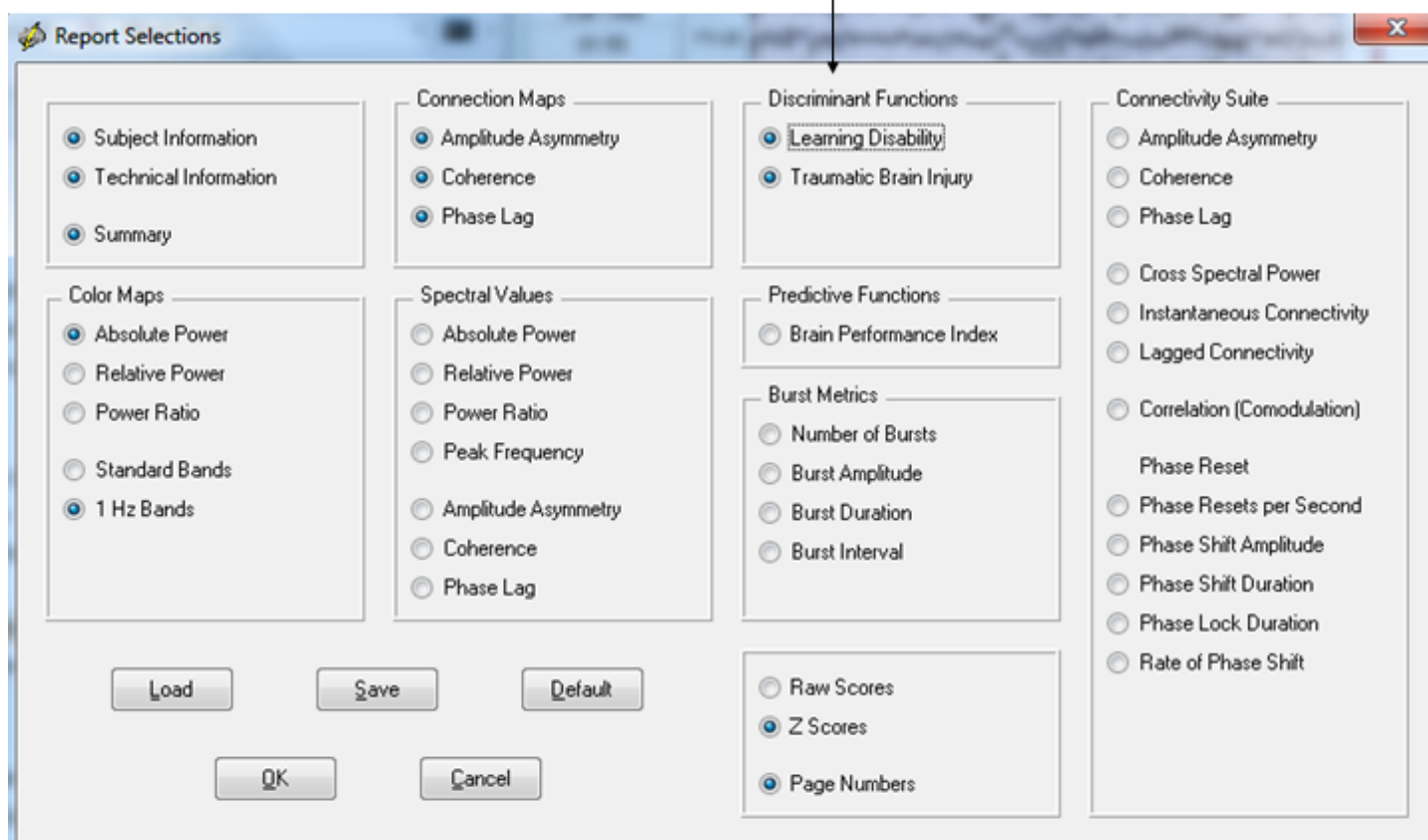


## Discriminant Functions

Access Discriminant Functions by clicking Report > Report Selections and then select the Learning Disability and/or Traumatic Brain Injury radial buttons (an add on product). Uncheck and check the Discriminant Functions that you want in your Report. Then click OK and then click Report > Generate Report.



**Click Report > Report Selection to Open Panel and then Select Discriminant Function(s)**



The discriminant functions are not designed to be used to render a clinical diagnosis. Instead the discriminant functions are to be used for assessment of patients/clients that have already been diagnosed with academic problems and/or mild traumatic brain injury. The discriminant functions are pattern recognition routines designed to probe more deeply into the link between symptoms and dysregulation in networks known to be dysregulated and linked to a history of academic problems and/or a history of mild traumatic brain injury. The learning disability discriminant function is to be used only if the patient/client has a history of academic problems and over the age range of 5 years to 18 years. Also, the mild traumatic brain injury discriminant function is to be used only if the patient/client has a history of mild traumatic brain injury. The mild TBI discriminant functions was based only on patients with a history of mild TBI and not patients with moderate or severe TBI.

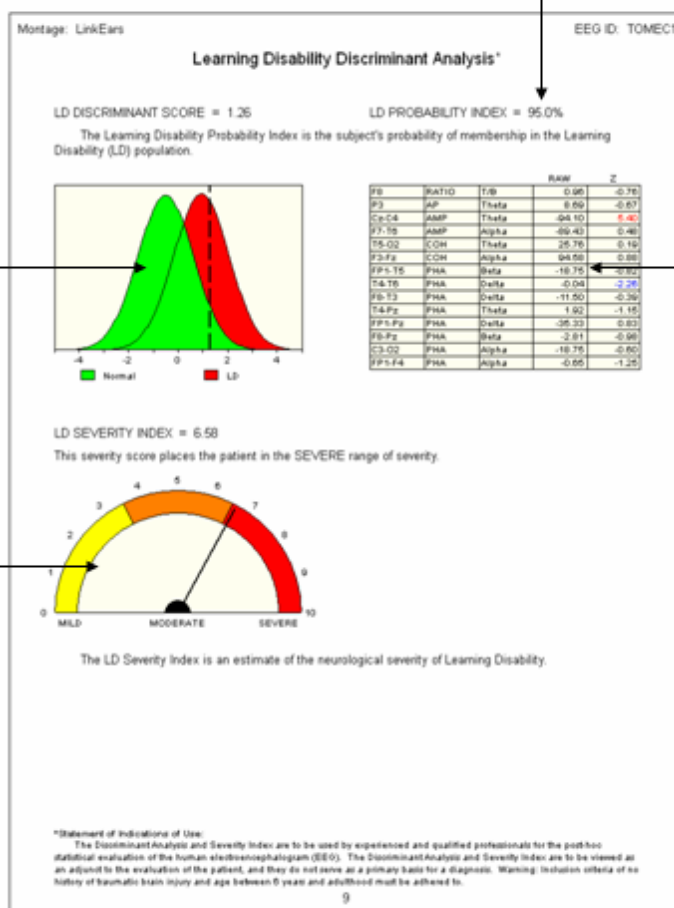
Here is an example of the Learning Disability discriminant analysis output.



Probability of >50% is statistically significant

Relative location  
Of client/patient  
EEG pattern with  
respect to a  
Normal control  
group

Metrics & Frequency  
Band of EEG measures  
Representing a pattern  
In the EEG commonly  
Present in individuals  
With a history of  
Academic problems



Here is an example of the Mild Traumatic Brain Injury discriminant analysis output.

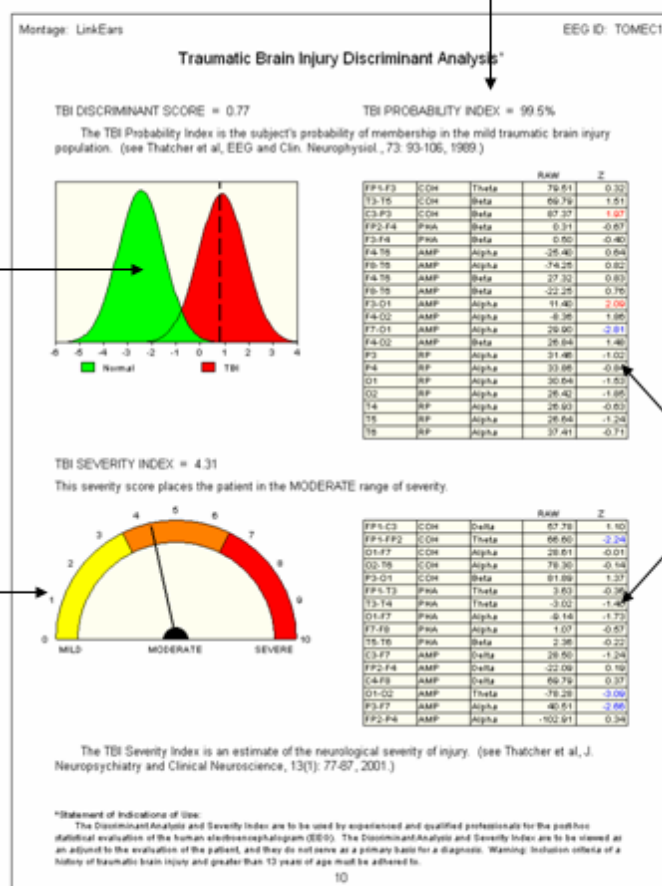




Probability of >50% is statistically significant

Relative location  
Of client/patient  
EEG pattern with  
Respect to a  
Normal control  
group

Severity Index  
from normal,  
mild to severe  
Based on an  
Estimated Glass  
Gow-Goma Score  
(GCS) at the time of  
Injury



Metrics & Frequency  
Band of EEG measures  
Representing a pattern  
In the EEG commonly  
Present in individuals  
With a history of  
Mild traumatic Brain  
Injury

## Dynamic Normative FFT Databases

Activate the Dynamic Normative FFT Databases and examine the raw EEG and normalized power spectrum to identify Z Scores  $\geq 2.0$  and to compare the  $> 2$  SD deviant Z frequencies and EEG channels using the Average Reference and Laplacian norms and Linked Ears and Bipolar montage norms.

Click Options > Subject Information and specify the recording condition as Eyes Open or Eyes Closed. In addition, Age must also be specified in order to activate the Normative Databases.

Then Click View > Dynamic FFT > Absolute Power Spectrum to activate the absolute power normative database Z Scores or Relative Power Spectrum to activate the relative power normative database Z Scores. This will display the FFT Absolute Power or Amplitude or the Relative Power values in the Upper Right quadrant and the Z Scores in the Lower Right





**Subject Information**

Name: Demo2-Mr. John Doe

Subject ID:

Date of Birth: 05/02/1949

Age: 54.61

Gender: Male

Handedness: Ambidextrous

EEG ID: TOME1

Date of Test: 12/12/2003

Time of Test:

Technician: Mr. Competent

Clinician: Dr. Qualified

Medication: Dilantin, Zolof,

Comments: Patient was struck on the right side of head by a bat in August 2001. No loss of consciousness, however, patient became weak and nauseous and sleepy. The following day patient was found prone on the floor and delirious with difficulty responding to verbal commands. Patient was taken to the emergency room and a CT scan revealed a right hemisphere epidural hematoma with a pocket of blood in the right occipital region. In surgery, small holes were drilled in the skull over the right central and right occipital regions and blood was drained from the space between the dura and skull.

☐ Eyes Closed

☒ Eyes Open

OK Cancel

Now click View > Dynamic FFT > Absolute Power Eyes Open, then view Eyes Closed, then do the same for Relative Power Eyes Closed, then view Eyes Open, etc. Click & move the left mouse button over the Z Score of Relative Power and read the frequency and Z Scores on the left of the EEG display. Note Frequency of 6.59 Hz & the Red Z Scores at P3, O1, Pz & T3.

## EEG Collection

To acquire and/or collect EEG using NeuroGuide one must purchase the correct NeuroGuide Collection module. To below is a list of the many amplifiers available for EEG collection



[ABM B-Alert X24](#)  
[ANT eegosports](#)  
[BIOSIGNAL microEEG](#)  
[BrainAmp MR](#)  
[BrainMaster Discovery](#)  
[Deymed EEG 32ch](#)  
[Mitsar](#)  
[NeuroField Q20](#)  
[Neuron Spectrum](#)  
[NeuroPulse NP-Q 10/20](#)  
[NeuroSync](#)  
[NeXus-32](#)

There are two classes of amplifier control:

- 1 - Software control of the start and stop of the amplifier and streaming of digital EEG data to memory in microseconds of time; and
- 2 - Launch the EEG amplifiers acquisition software simultaneously with NeuroGuide and then stream digital EEG data to memory using UDP communication with the PC.

There are 8 amplifiers that are direct and do not require simultaneous acquisition software:

1. ABM;
2. ANT;
3. BrainMaster;
4. Mitsar;
5. NeuroField;
6. Neuron Spectrum;
7. NeuroPulse/Mindset;
8. Nexus

There are 2 amplifiers that require launching the EEG amplifier company's software simultaneously with NeuroGuide:

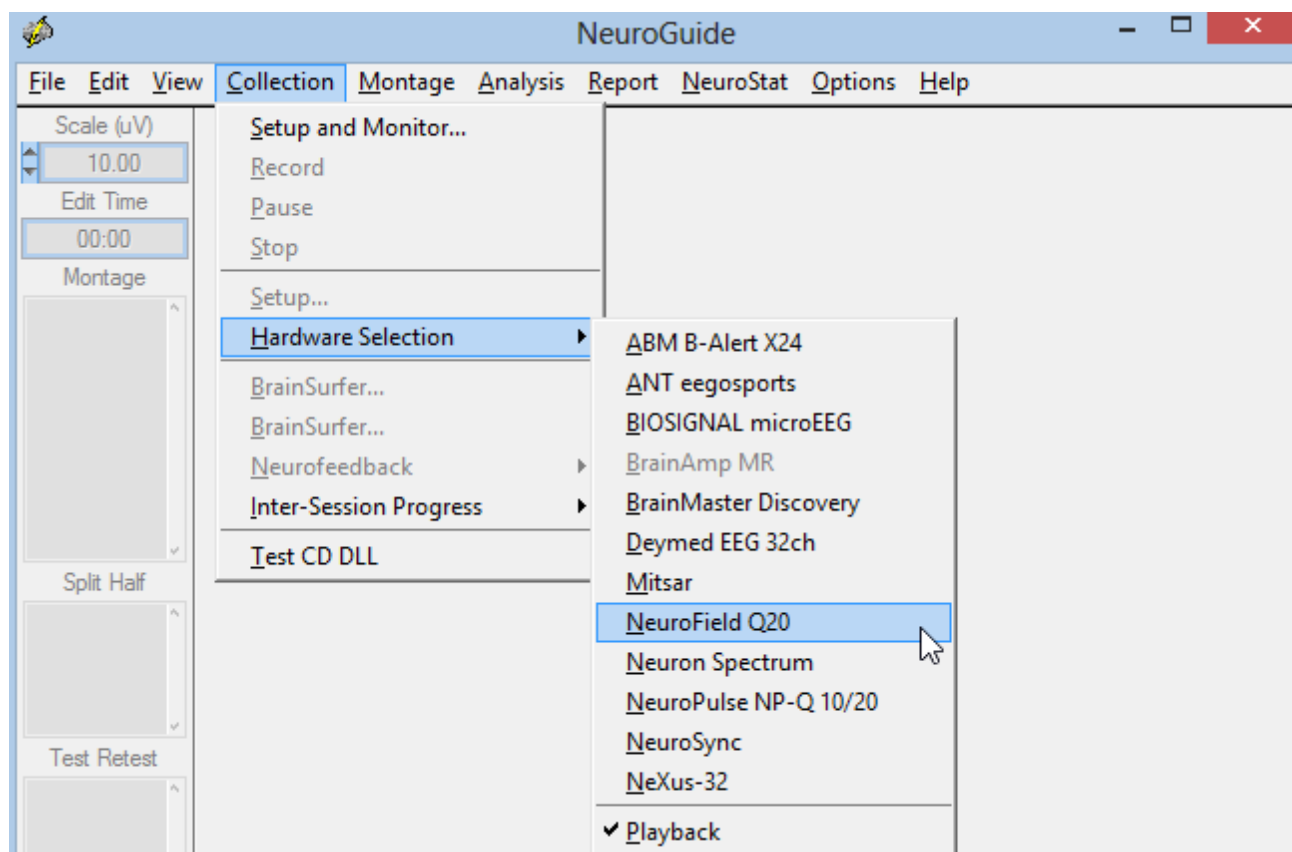
1. BIOSIGNAL - MicroEEG



## 2. Deymed

Start EEG collection by first selecting the correct hardware, click **Collection > Hardware Selection** and then select the amplifier. Then click **Collection Setup & Monitor** to open the hardware setup panel. Create your own montages by Clicking **Montage > Create Montage** if one wants a different arrangement or selection of recording channels.

Click **Collection > Hardware Selection > NeuroField Q20**. This selection will determine which Setup is to be used for collection. Then click **Collection > Setup and Monitor**



ANT, Mitsar, NeuroField, NeuroPulse, Neuron Spectrum, Nexus-32 involve simply clicking **Collection > Setup and Monitor**. The BrainMaster Discovery-24 and the Nexus-32 Amplifiers require clicking **Collection > Setup and Monitor** and then contacting the amplifier company to obtain a key code.

### BrainMaster Discovery-24 Amplifier

To determine what port the USB Discovery connection is on click **Start > Control Panel >**



Device Manager > Ports. The Discovery device driver must be installed before a USB port connection can be established. The Discovery Serial Number is on the back of the Discovery amplifiers. Obtain the Discovery passkey and the Discovery device drivers from BrainMaster ([www.brainmaster.com](http://www.brainmaster.com)). After all information is entered then click OK.

**Click Collection > Setup & Monitor to activate the amplifier setup window**

The screenshot shows the 'Amplifier Setup' window with the following fields and annotations:

- Port Number:** 14. Annotation: "Click > Control Panel > System > Device Manager To determine the USB port".
- Serial Number:** 60021. Annotation: "Discovery Serial No., & BrainMaster Pass Key".
- Pass Key:** 1SAJ-29DL-1G7D. Annotation: "Discovery Serial No., & BrainMaster Pass Key".
- Sampling Rate:** 256.
- Display Time:** 6. Annotation: "EEG display time".
- Collection Montage:** Discovery. Annotation: "Collection channels & order is fixed for acquisition".
- Display Montage:** Discovery 19. Annotation: "Select the number % Order of channels".
- Collection Order:** FP1-A1, F3-A1, C3-A1, P3-A1, O1-A1, F7-A1, T3-A1, T5-A1, Fz-A1, FP2-A1, F4-A1, C4-A1.
- Display Order:** FP1-A1, FP2-A1, F3-A1, F4-A1, C3-A1, C4-A1, P3-A1, P4-A1, O1-A1, O2-A1, F7-A1, F8-A1.
- Buttons:** OK, Cancel.

**Nexus-32 Amplifiers - Contact Mind Media for a Key Code**

### NeuroPulse/Mindset Amplifier Systems

Before turning on the computer, turn the NeuroPulse/Mindset amplifiers on and make sure the NeuroPulse/Mindset-24 amplifiers are connected to the computer. Then turn on the computer and launch NeuroGuide. To begin EEG acquisition click Collection > Hardware > NeuroPulse NP-Q10/20. Then click Collection > Setup and Monitor. The NeuroPulse/Mindset amplifiers use linked ears as a reference, thus if one makes new montages by clicking Montage > Create Montage make sure that one uses LE as the reference. Check that the display montage is what



is desired and then click OK to begin EEG collection. Once collection is stopped, then save the EEG in .ng format or EDF or Lexicor or Text (ASCII) format by clicking File > Save As. Simple and unified collection and analysis can be achieved with a few mouse clicks and no file import is necessary.

## **Deymed Amplifier Systems - Contact Deymed for Configuration Code**

NeuroGuide waits for a short period of time to receive UDP data from the TruScan software. If it does not receive this data, it displays the error message "error code 0 Could not receive data from TruScan Acquisition application". Any thing that blocks the transmission of data will result in this error message. Please make sure that the following items are working:

1. Make sure that the TruScan software is authorized to send UDP data to NeuroGuide, and make sure that this feature is turned on. This may require a security key from Deymed.
2. Make sure that the TruScan software is running; make sure it is actively displaying EEG data in real time, and make sure that it is not in the "Pause" or "Stop" state.
3. **MAKE SURE THAT YOUR SECURITY SOFTWARE** is not blocking the transmission of UDP data from TruScan to NeuroGuide. Security software also blocks Nexus-32 acquisition. This is a common problem. Each new version of NeuroGuide may need to have permission to receive UDP data depending on what security software you have and what settings have been selected; each computer is unique in this respect.

If you still have problems, please determine the TruScan version number and then contact Applied Neuroscience, Inc. at [geeg@appliedneuroscience.com](mailto:geeg@appliedneuroscience.com)

Start EEG collection by first selecting the correct hardware, click Collection > Hardware Selection and then select the amplifier. Create your own montages by Clicking Montage > Create Montage if one wants a different arrangement or selection of recording channels.

**Note:** If acquired EEG data is saved in Text (ASCII) format then it is necessary to open the tab delimited text file and remove the patient information at the top of the file if users want to import the text formatted file into NeuroGuide.



**After setup & monitor enter subject information and click OK**

The screenshot shows the NeuroGuide software window with a menu bar (File, Edit, View, Collection, Montage, Analysis, Report, NeuroStat, Window, Help) and a left sidebar with controls for Scale (uV), Edit Time, Montage, Split Half, Test, and Retest. The main area displays the 'Subject Information' dialog box. The dialog box has the following fields and controls:

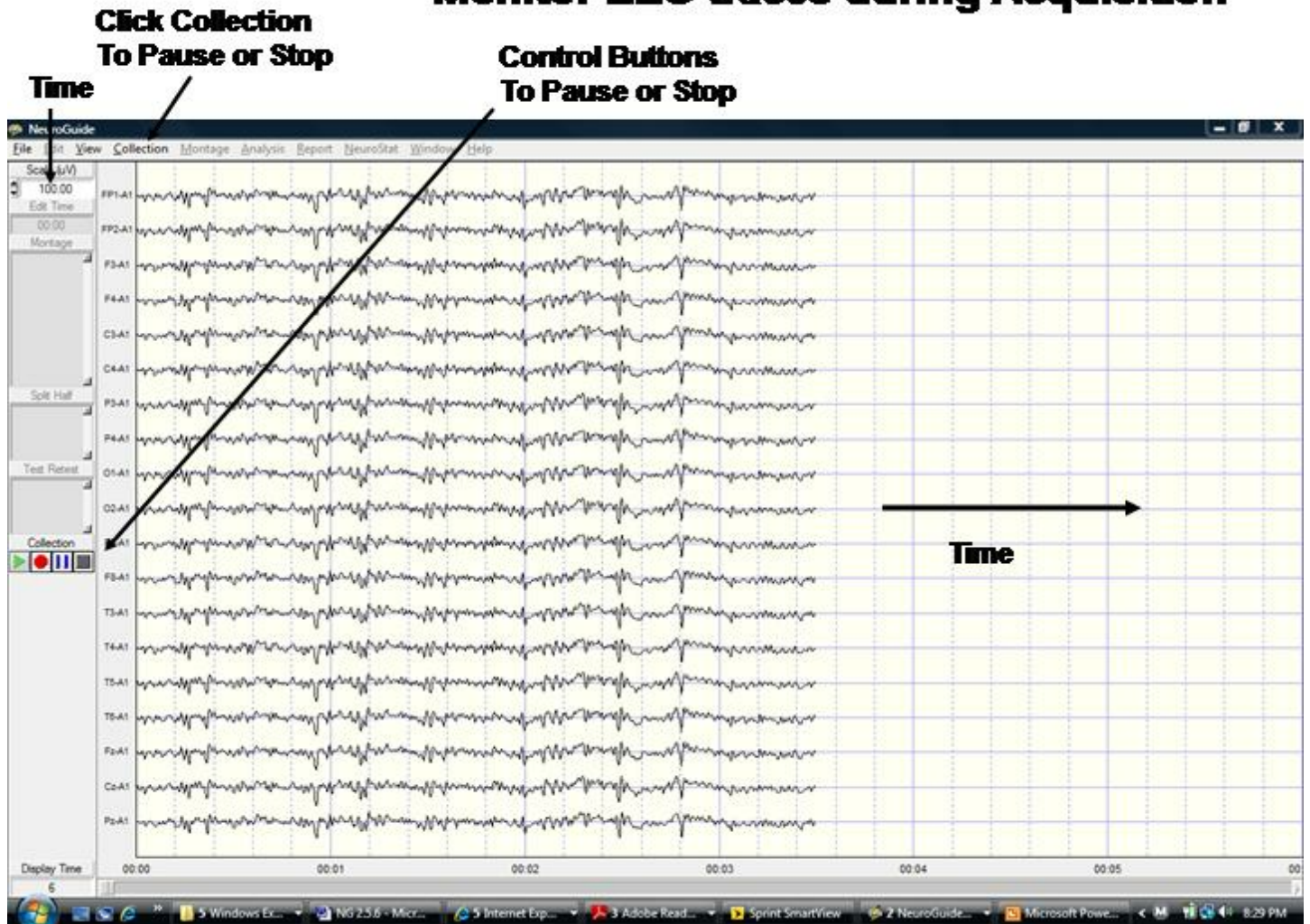
- Name:
- Subject ID:
- Date of Birth:
- Age:
- Gender:
- Handedness:
- EEG ID:
- Date of Test:
- Time of Test:
- Technician:
- Doctor:
- Medication:
- Comments:
- Buttons: OK, Cancel
- Radio buttons: Eyes Closed, Eyes Open

**Monitor the EEG during acquisition. Stop or pause collection by clicking one of the control tools to the left of the screen or by clicking Collection > Pause or Stop.**



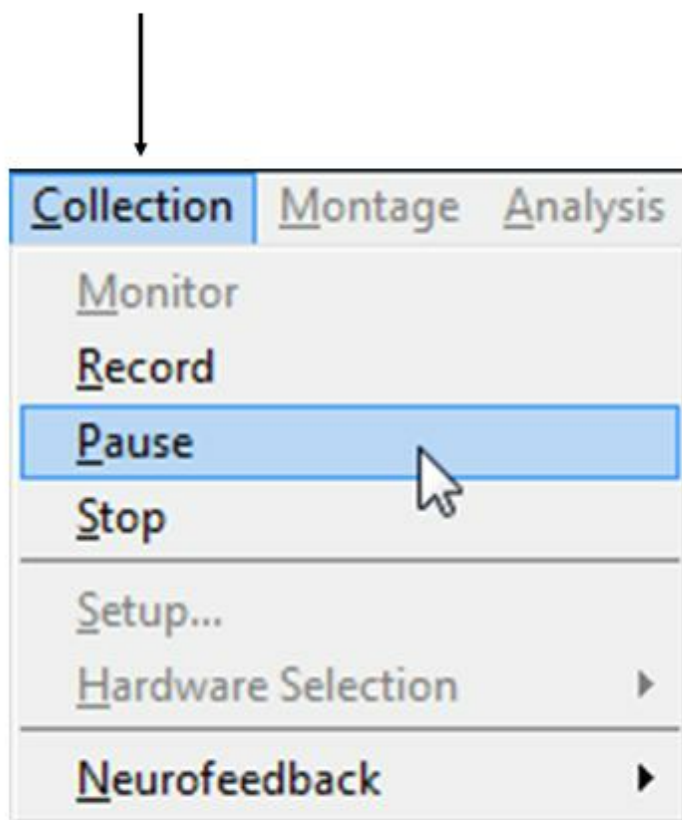


## Monitor EEG traces during Acquisition



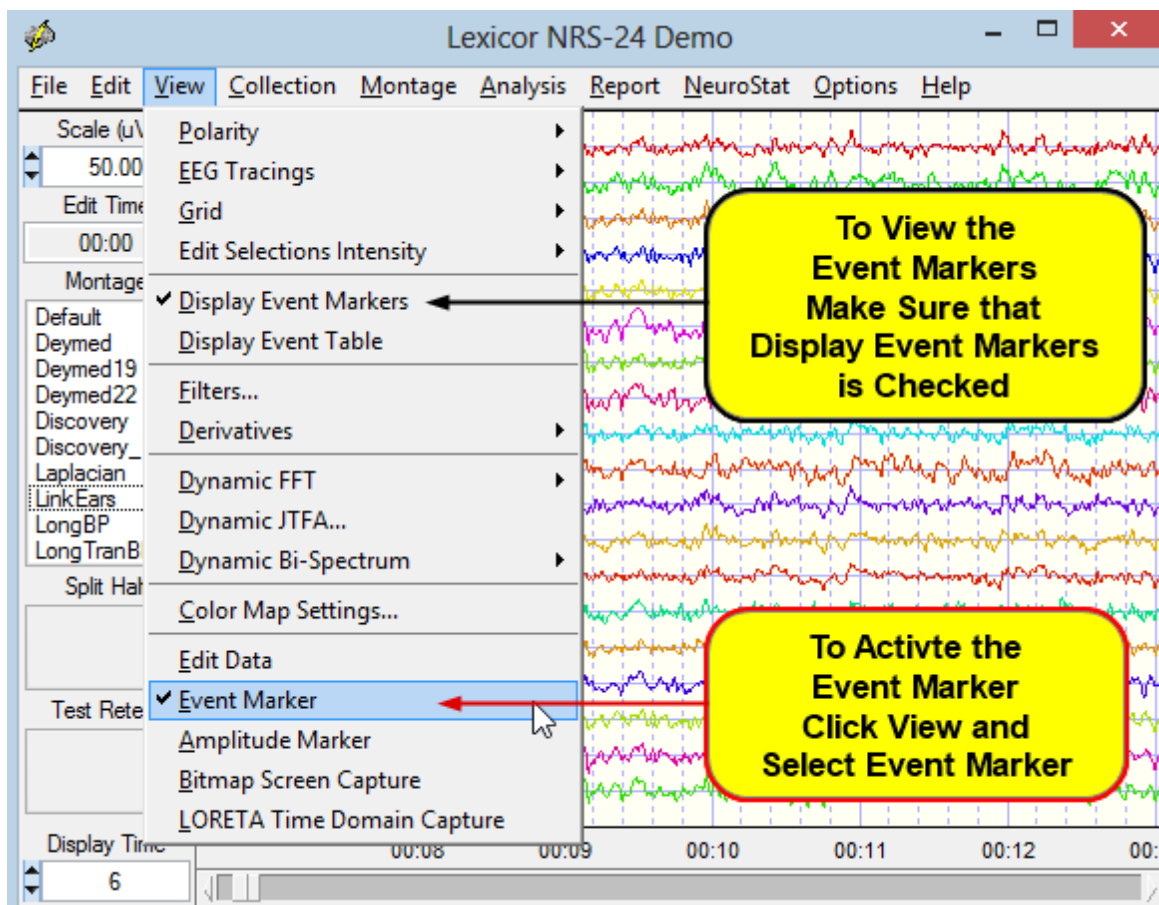


## Click Collection > Record or Pause or Stop or to Start Neurofeedback



## Event Marker

Event Markers to mark events in the EEG traces and then later sort the events by time or type. To active the Event Marker Click View > Event Marker. To view the Event Markers make sure that Display Event Markers is checked.



Move the mouse to the event to be marked and left click to open the event list. Select an event from the list to mark the event in the EEG record.

To Mark Events move the mouse to the event and Left Mouse Click to open the Event Marker List, then Select an Event Type. Now continue scanning the EEG and Marking various Events.



Lexicor NRS-24 Demo

File Edit View Collection Montage Analysis Report NeuroStat Options Help

Scale (uV) 50.00

Edit Time 00:00

Montage

Default  
Deymed  
Deymed19  
Deymed22  
Discovery  
Discovery\_19  
Laplacian  
LinkEars  
LongBP  
LongTranBP

Split Half

Test Retest

Display Time 6

FP1-LE  
FP2-LE  
F3-LE  
F4-LE  
C3-LE  
C4-LE  
P3-LE  
P4-LE  
O1-LE  
O2-LE  
F7-LE  
F8-LE  
T3-LE  
T4-LE  
T5-LE  
T6-LE  
Fz-LE  
Cz-LE  
Pz-LE

Theta Burst  
Theta Burst  
Eye Movement  
Unspecified Artifact

00:18 00:19 00:20

Eyes Closed  
Eyes Open  
Active Task Onset  
Active Task Offset  
Mu Rhythm  
Delta Wave  
Theta Burst  
Alpha Burst  
Beta Spindle  
Spike and Wave  
Sharp Waves  
Phase Reversal  
Disorganized  
Desynchronization  
Hemispheric Asymmetry  
Drowsiness  
Sleep  
K Complex  
Eye Blink  
Eye Movement  
EMG  
Unspecified Artifact  
Pause  
Onset  
Offset  
Unspecified

**Event List**

To View or Review the Events you have previously Marked, then Click View > Display Event Table, now you can view all the Events Sorted by Time. To view the Events - Sorted by Type Click the Event Table Label to change the Sort and then change it back to Sorted by Time. Next Double Click on one of the Events listed in the Table to move the EEG Edit Screen to where the selected event occurred.



**Click the Label to Sort Events by Time and/or Type**

**Double Click an Event to move the EEG Edit Screen to the Time of that Event**

Events - Sorted by Time	
00:00:01.01	EMG
00:00:01.44	EMG
00:00:02.36	Eye Movement
00:00:07.34	Eye Movement
00:00:09.99	Eye Movement
00:00:12.48	EMG
00:00:17.74	Theta Burst
00:00:17.92	Theta Burst
00:00:18.89	Eye Movement
00:00:20.03	Unspecified Artifact

## Frequency Domain Export

The results of power spectral analysis on the selected data samples can be saved in a tab delimited for export to other programs. The FFT frequency resolution is 0.5 Hz and the columns are channels and the rows are frequency. One can save raw relative or absolute power values or Z Scores of absolute and relative power.

### Click Analysis > FFT Power Spectra

**Click Analysis > FFT Power Spectra**

**FFT Power Spectra**

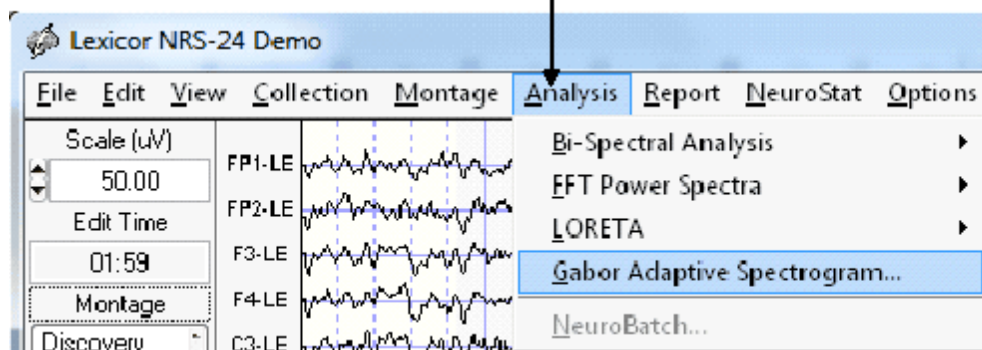
- Absolute Power...
- Relative Power...
- Z Transformed Absolute Power...
- Z Transformed Relative Power...



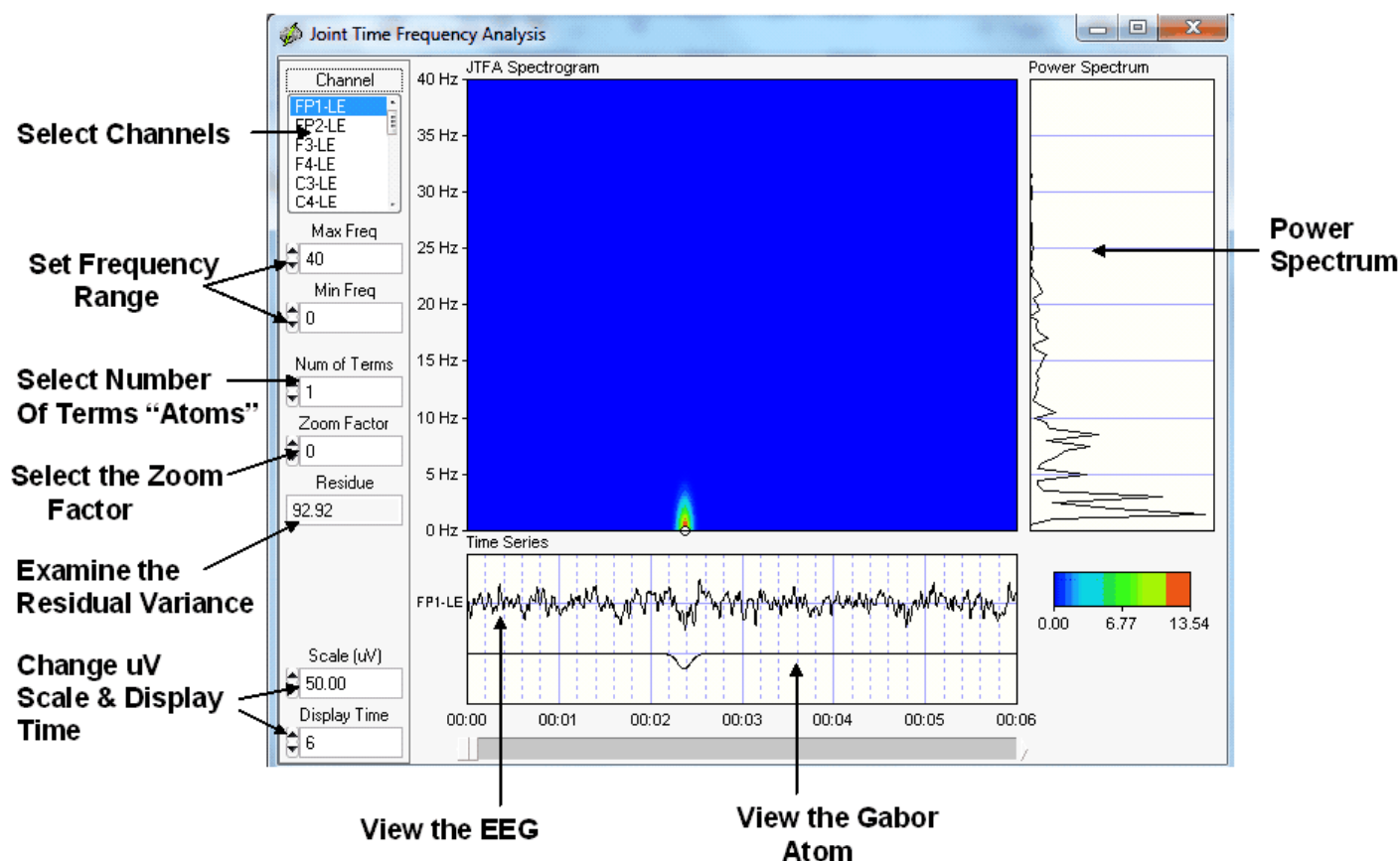


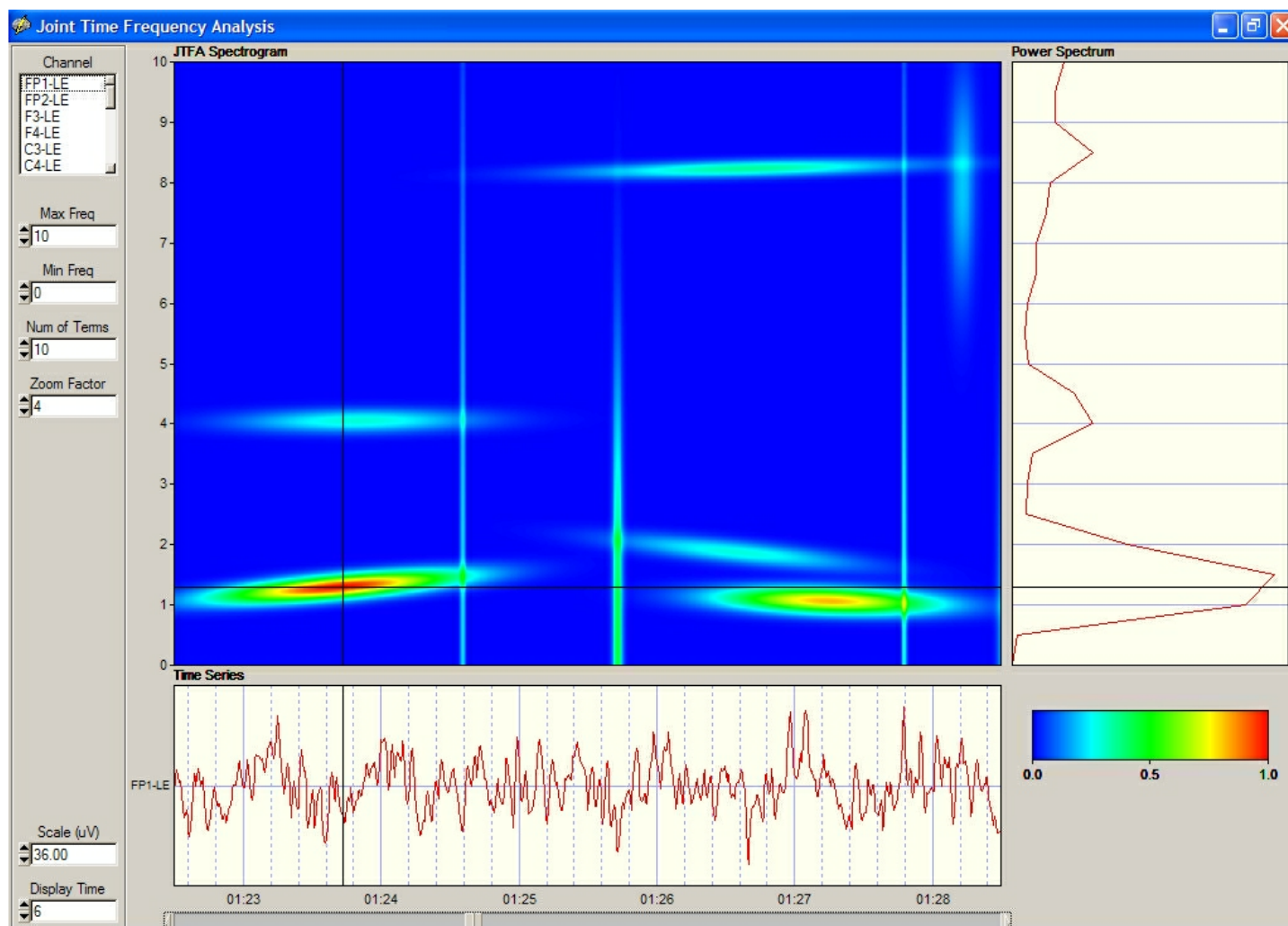
## Gabor Adaptive Spectrogram

Click Analysis > Gabor Adaptive Spectrogram



## Gabor Adaptive Spectrogram



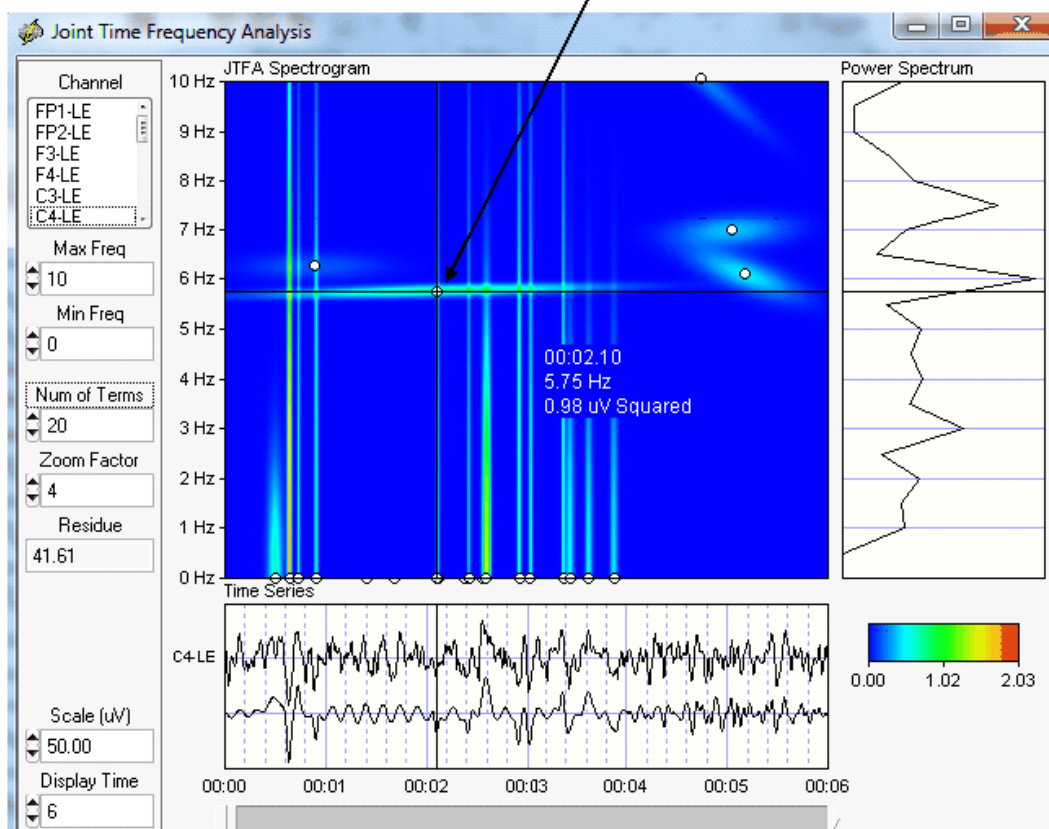


Change the parameters of JTFA such as Maximum and Minimum Frequency, Zoom and Select C4. Then click the left mouse button and move it over the JTFA viewer to identify the frequency and power at a moment in time.

The default is 1 term. View the value of the residue and increase the number of terms until the residue is approximately 10%. The residue is the ratio of the energy of the residual signal to the energy of the original signal expressed as a percentage. Increase the number of terms and observe the reconstruction of the original signal and the step by step decrease in the residue. To add or remove terms from the reconstruction place the mouse over the white marker in the JTFA display and right click. Position the mouse over a white 'dot' on the JTFA screen and right click on the white dot to de-select a Gabor term. Right click on the red 'dot' to select a Gabor term. Examine the accuracy of the reproductions of the time series by increasing the number of terms and minimizing the residue. 5% residue is a reasonable level of reproduction accuracy. Once the residue has been minimized, then de-select and re-select different Gabor terms in order to evaluate the time series in detail.



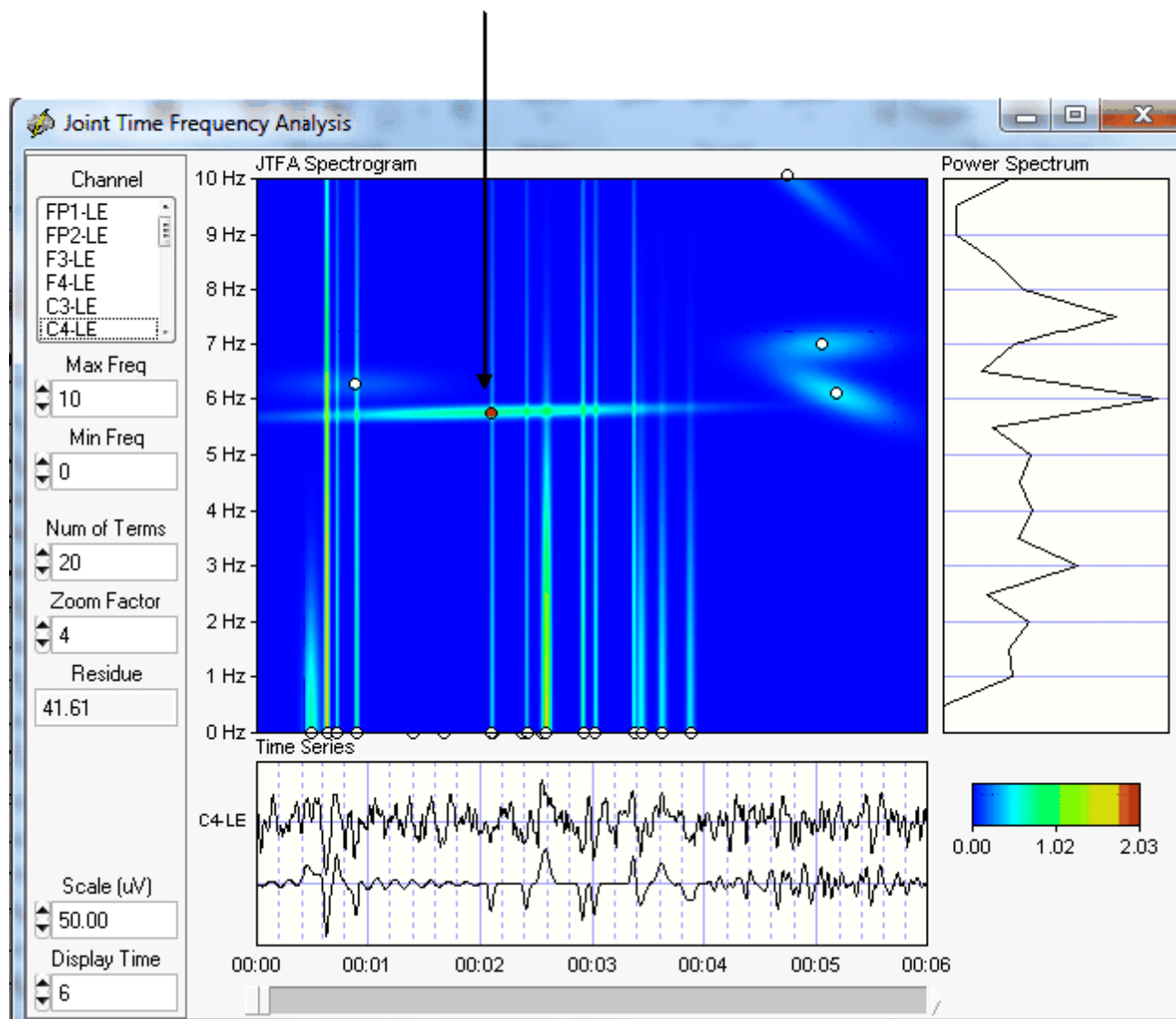
**Depress the Left Mouse Button over the White Circle to Read the Frequency & Power for an Atom**







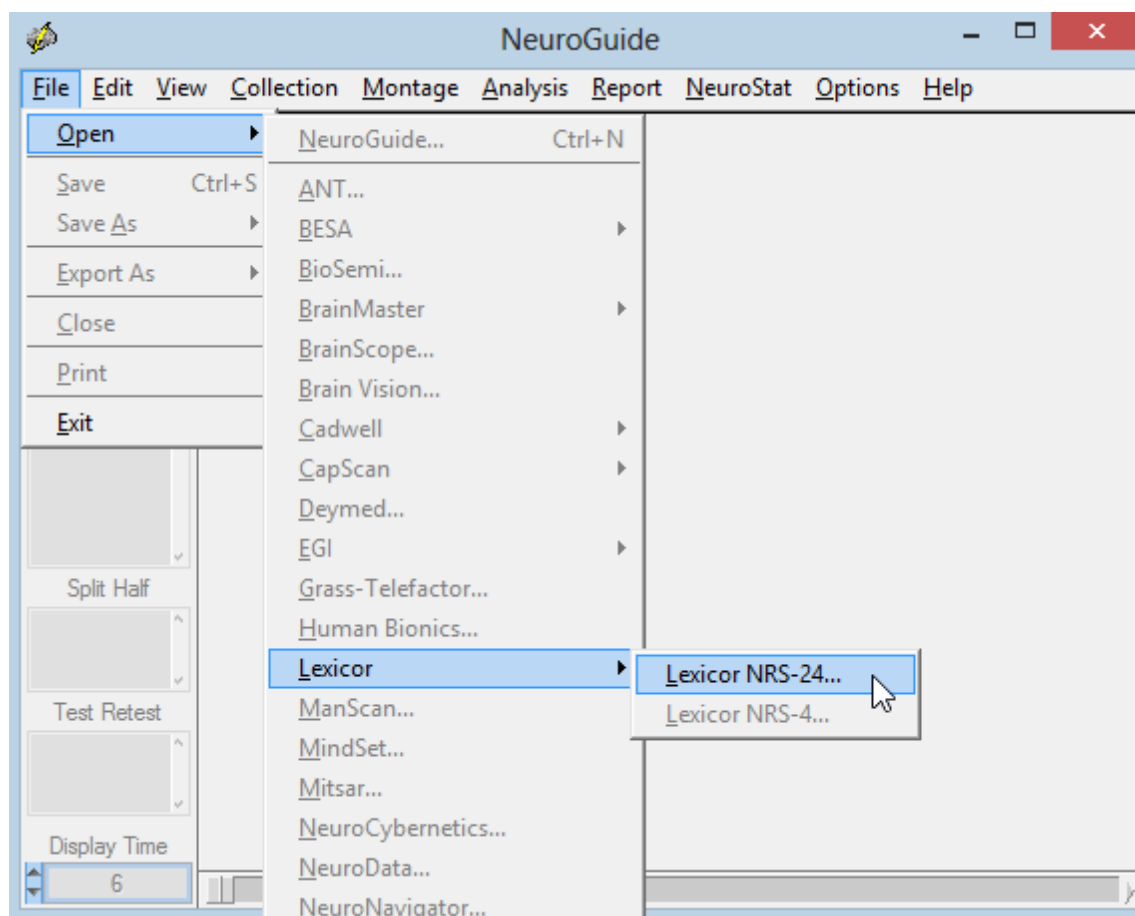
**Right Mouse Click in an open circle to toggle an Atom (or Factor) on or off**



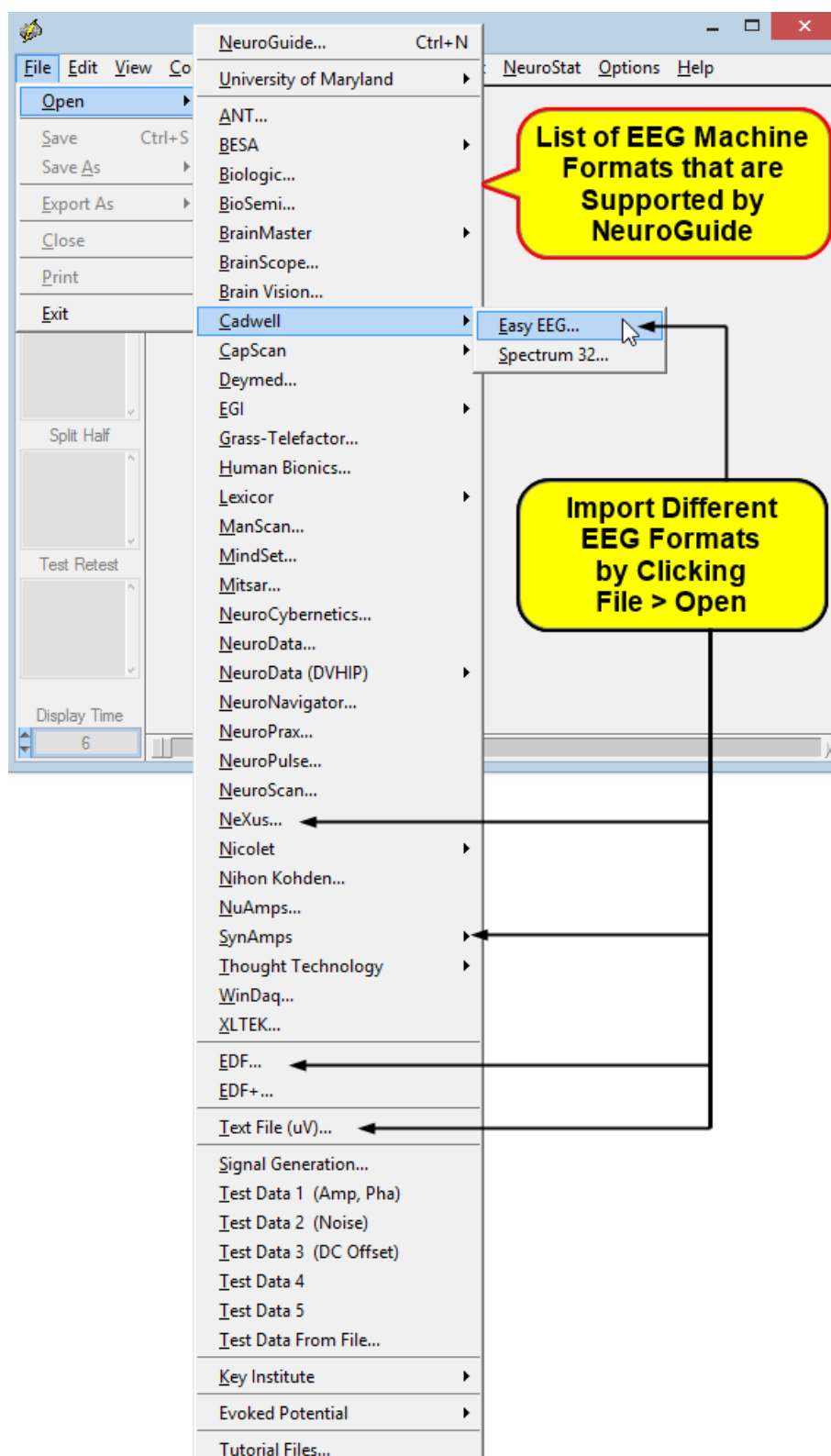
## Import EEG File and Enter Age

The EEG Demo file was obtained from a unidentified 54.6 year old patient with trauma to the right parietal lobe resulting in a epidural hematoma. This EEG sample is only an example tutorial selected to help users step through NeuroGuide's basic software features and there is no diagnosis or clinical interpretation. NeuroGuide is only an adjunct to other clinical information (competent clinical experience is required to use the electrophysiology of the brain for clinical purposes). If you are a NeuroGuide user and want to explore different add ons then the Demo mode is perfect for that. Click Help > Enter Demo Mode

From the Menu bar Left Click on File > Open > Lexicor > Lexicor NRS24 and then release the mouse button to open the Demo example.



Universal file formats such as ASCII and EDF, plus many EEG Machine formats (Native Formats) are available in the non-Demo mode.



**Access to NeuroGuide Age Dependent Norms Requires Specifying an Age.**



This can be done by simply typing an age in the Age row or by typing in the Date of Birth and the Date of EEG Test. Also, type in all of the subject information including Comments and click Eyes Closed or Eyes Open depending on the recording condition. If you close the subject information window, then to re-activate the subject information panel click Window > Subject Information.

**Subject Information**

Name: Joe TBi

Subject ID: Demo\_01

Date of Birth: 05/02/1949

Age: 54.61

Gender: Male

Handedness: Paralyzed on Left

EEG ID: DEMO

Date of Test: 12/12/2003

Time of Test: 10:33:25

Technician: Mr./Ms. Competent

Clinician: Dr. I M Qualified

Medication: None

Comments: TBI resulting in right hemisphere epidural hematoma.

☒ Eyes Closed  
☐ Eyes Open

OK Cancel

Age is Calculated by Entering the Date of Birth and Date of EEG Test

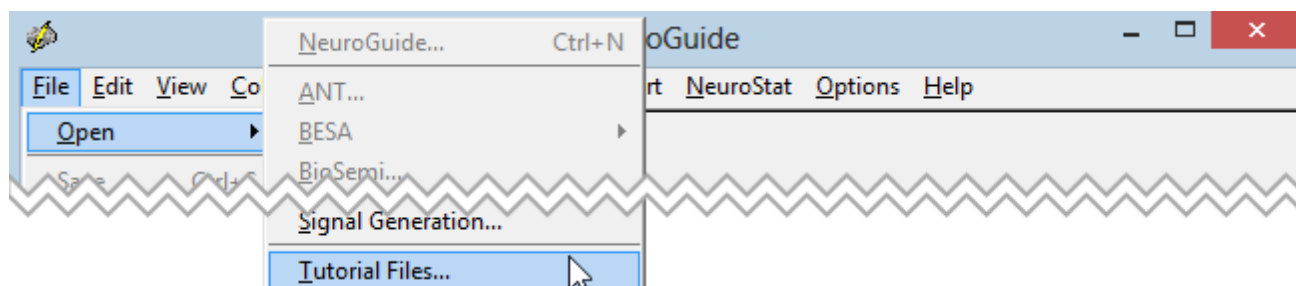
For demonstration purposes one can just type in a given Age, e.g., 55 years, select Eyes Closed and click on OK .



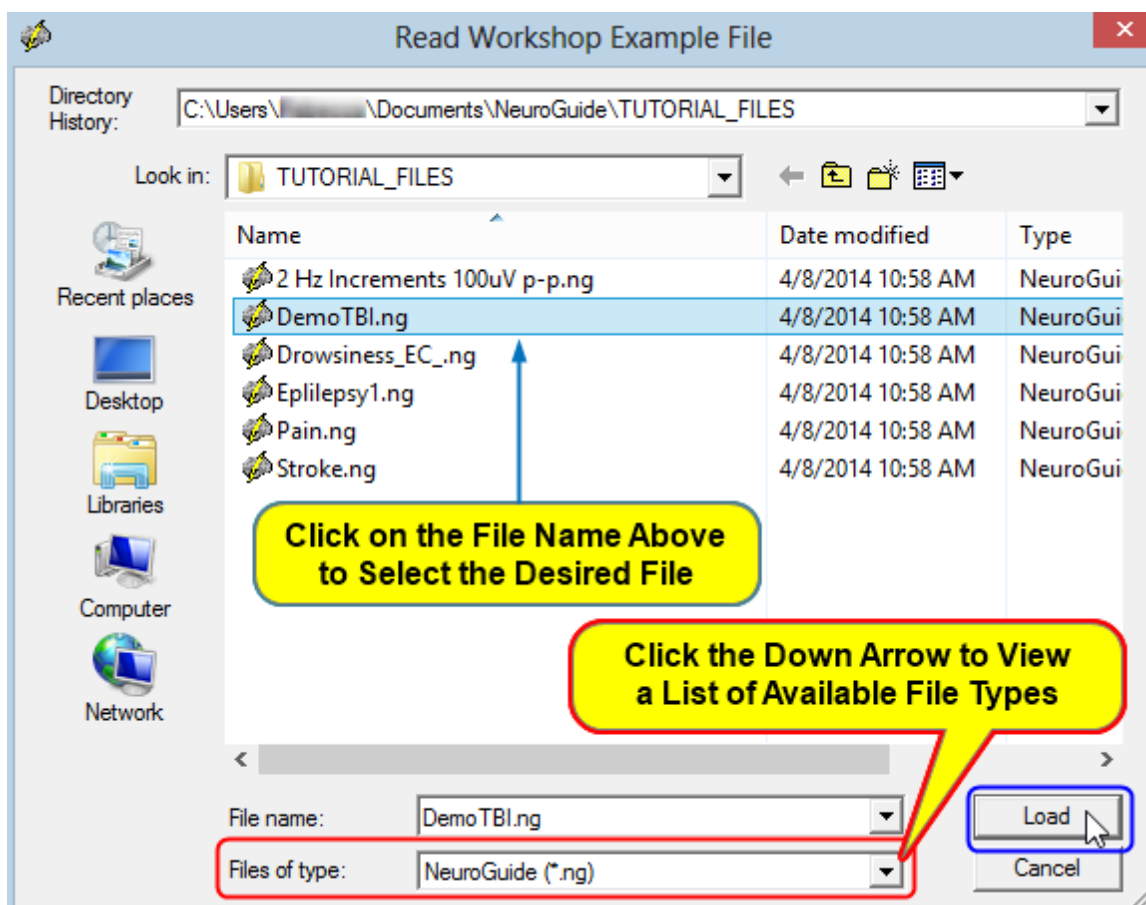
The 'Subject Information' dialog box contains the following fields and options:

- Name: [Text Field]
- Subject ID: [Text Field]
- Date of Birth: [Text Field]
- Age: [Text Field] (Value: 55.00)
- Gender: [Text Field]
- Handedness: [Text Field]
- EEG ID: [Text Field]
- Date of Test: [Text Field]
- Time of Test: [Text Field]
- Eyes Closed: ☒ (Selected)
- Eyes Open: ☐
- Buttons: OK, Cancel

To Open and Use the Tutorial Files that you previously downloaded and installed using the [Installation](#) <sup>12</sup> Section of the Getting Started Manual and Tutorial. Click File > Open and then Select Tutorial Files.

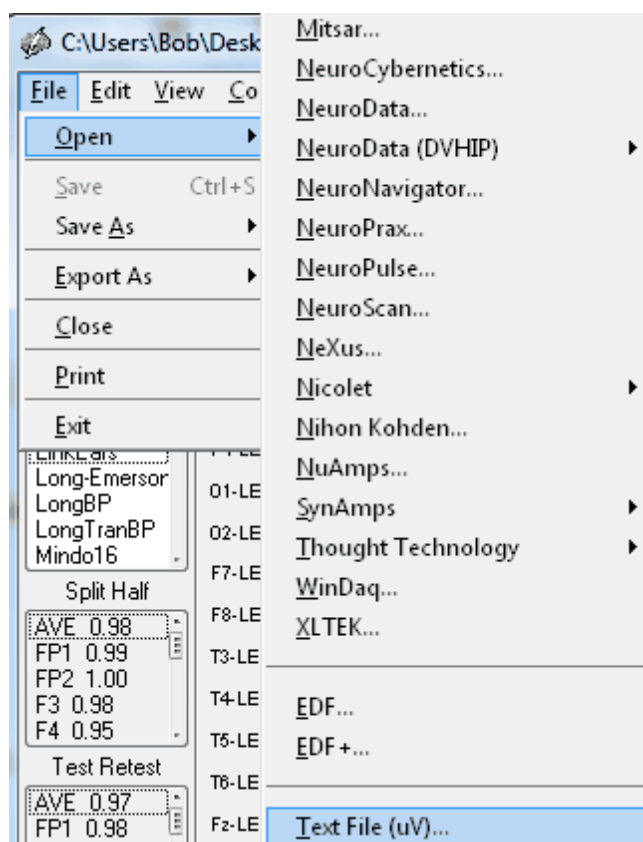


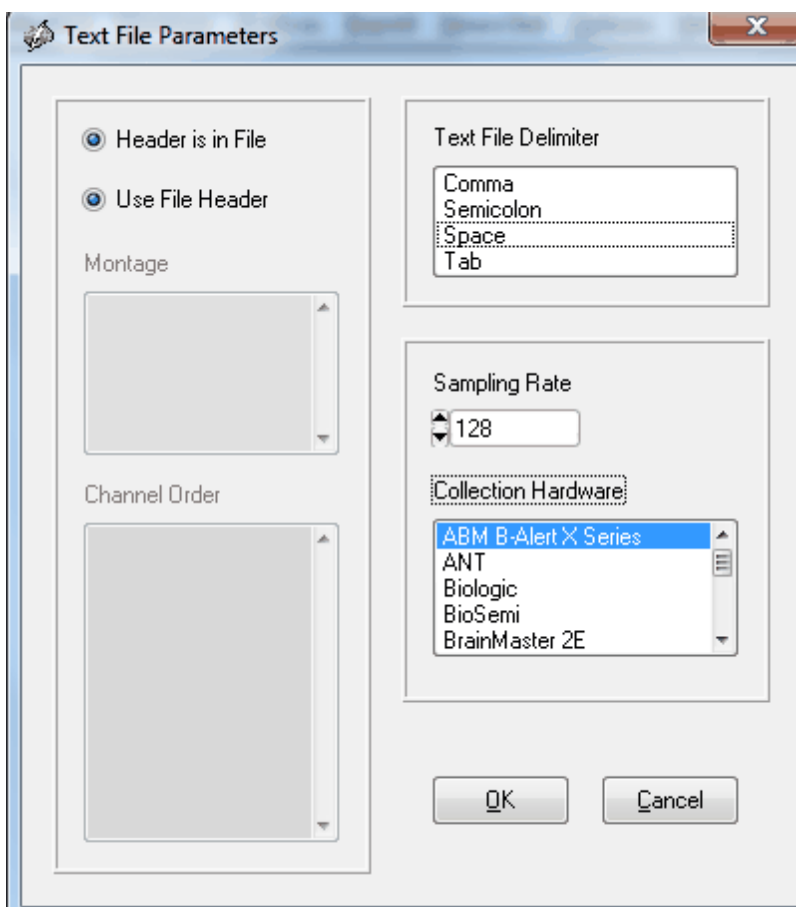
From the Read Workshop Example File window, Click on the down arrow at the end of the File Type area and Select the NeuroGuide (\*.ng) from the list of available file types, then Select the Demo TBI.ng file from the list of available .ng Tutorial files. After Demo TBI.ng appears in the File Name area, then click Load.



## Import ASCII or Text Files

Click **File > Open > Text file** in order to select an ASCII formatted EEG file.



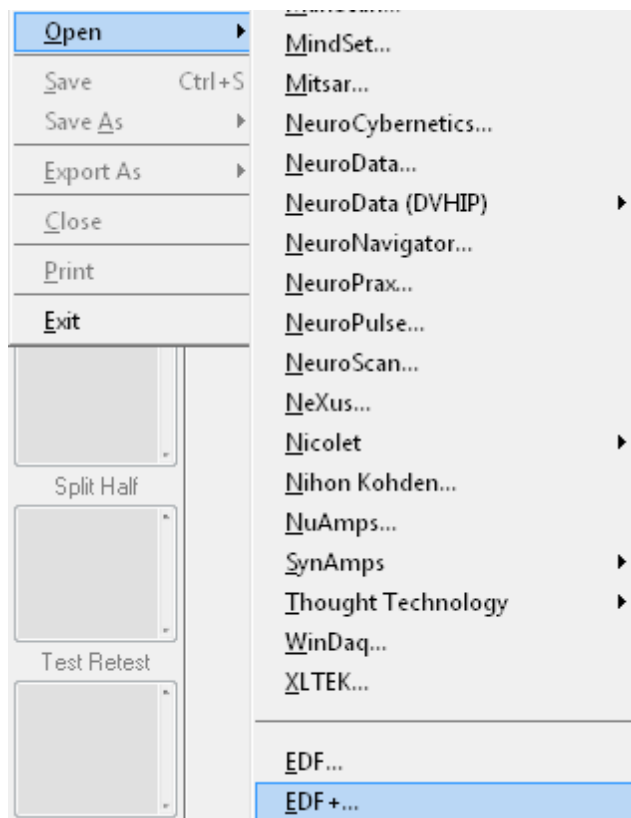


Navigate to the ASCII file and open the file. The ASCII import window below appears. Open the ASCII file in Word or Excel and examine the file and determine the channel order and delimiters and whether or not there is a header in the file. One must know the Amplifier that recorded the EEG, Montage or order of the channels, the sample rate and the delimiters. NeuroGuide will search the file and help determine the delimiters or headers. If none is found then the default window below is opened. If a different channel order is used, then select Montage and Create New Montage. After creating a Montage to match the channel order, name the montage, save and close. Re-open the ASCII import window and select this new montage.

## Import EDF and EDF+ Formats

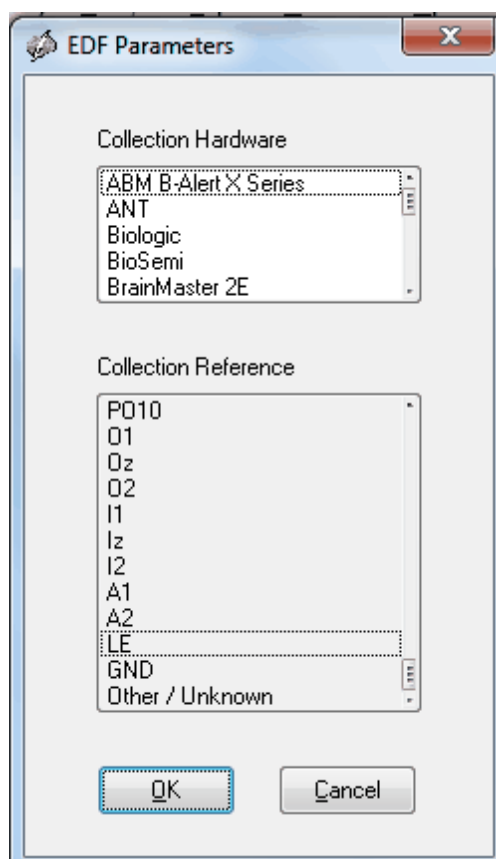
To Import EDF+ and EDF formatted files Click File > Open EDF+ or EDF. NeuroGuide assumes that all channels were digitized at the same rate.





## EDF+ & EDF Collection Hardware and Collection Reference

Users must know the Amplifier that recorded the EEG (Collection Hardware) and Collection Reference of the EDF+ and EDF file that you are importing.



## Compute Joint-Time-Frequency-Analysis

NeuroGuide uses two JTFA analysis methods to compute the Joint-Time-Frequency-Analysis as follows:

- ❖ The Adaptive Gabor Transform also called "Matching Pursuit"

The adaptive spectrogram automatically achieves the best joint time-frequency resolution possible.

The method involves the adaptive oriented orthogonal projective decomposition algorithm from Qian, S. and D. Chen. "Signal Representation Using Adaptive Normalized Gaussian Functions." *IEEE Trans. Signal Processing*, vol. 36(10): 1 - 11, 1994 and Mallat, S., and Z. Zhang, "Matching Pursuits with Time-Frequency Dictionaries", *IEEE Trans. Signal Process*, vol. 41(12): 3397-3415, 1993.

Click Analysis > JTFA to activate the Gabor Adaptive spectrogram.

- ❖ The Complex Demodulation

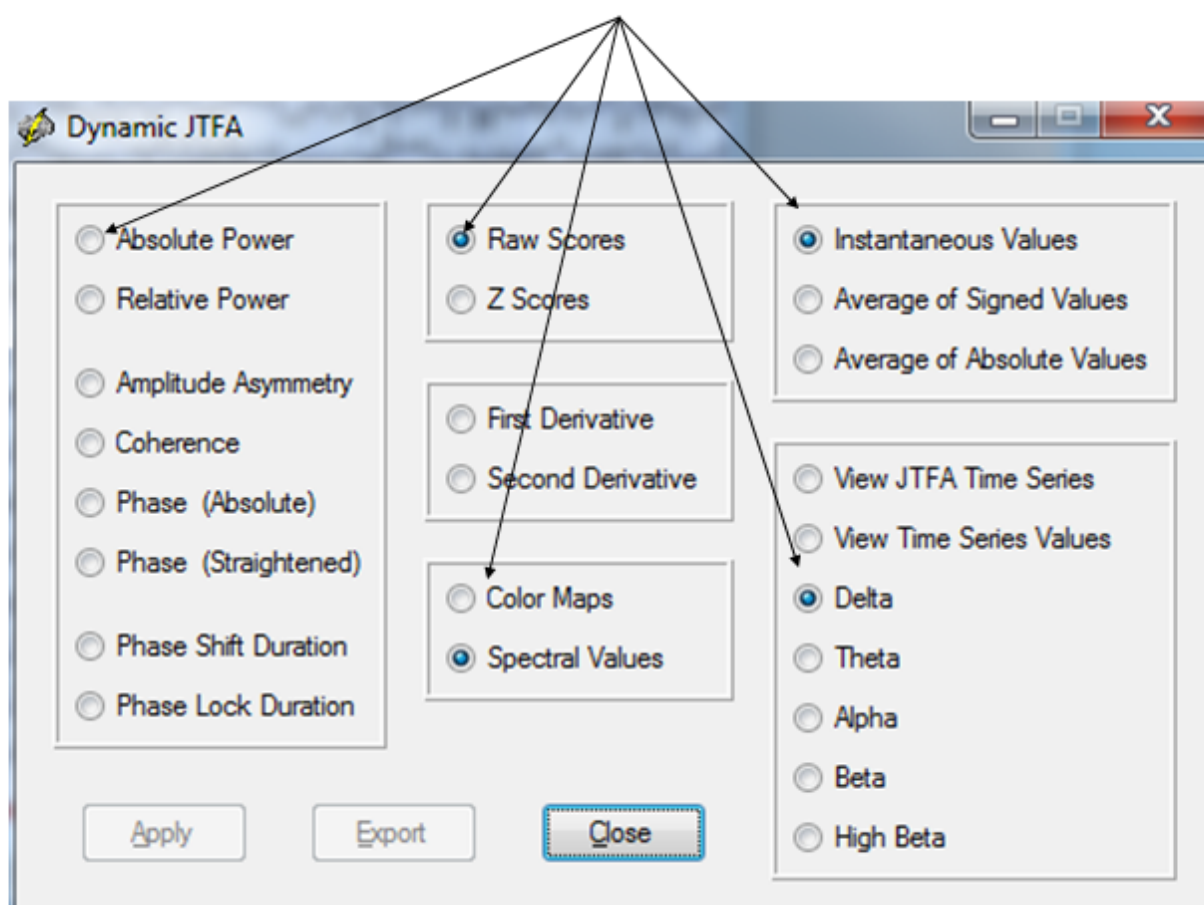


Dynamic JTFA uses complex demodulation to compute Instantaneous Power and Phase.

Click View > Dynamic JTFA to activate this tool.

Click View > Dynamic JTFA to open the Dynamic JTFA Panel.

**Click View > Dynamic JTFA and then Select the Metric, Z or Raw Scores Color Maps or Spectral Values, Frequencies and Display Options. Then Click Apply and View the Dynamic JTFA. Change your selections click Apply**

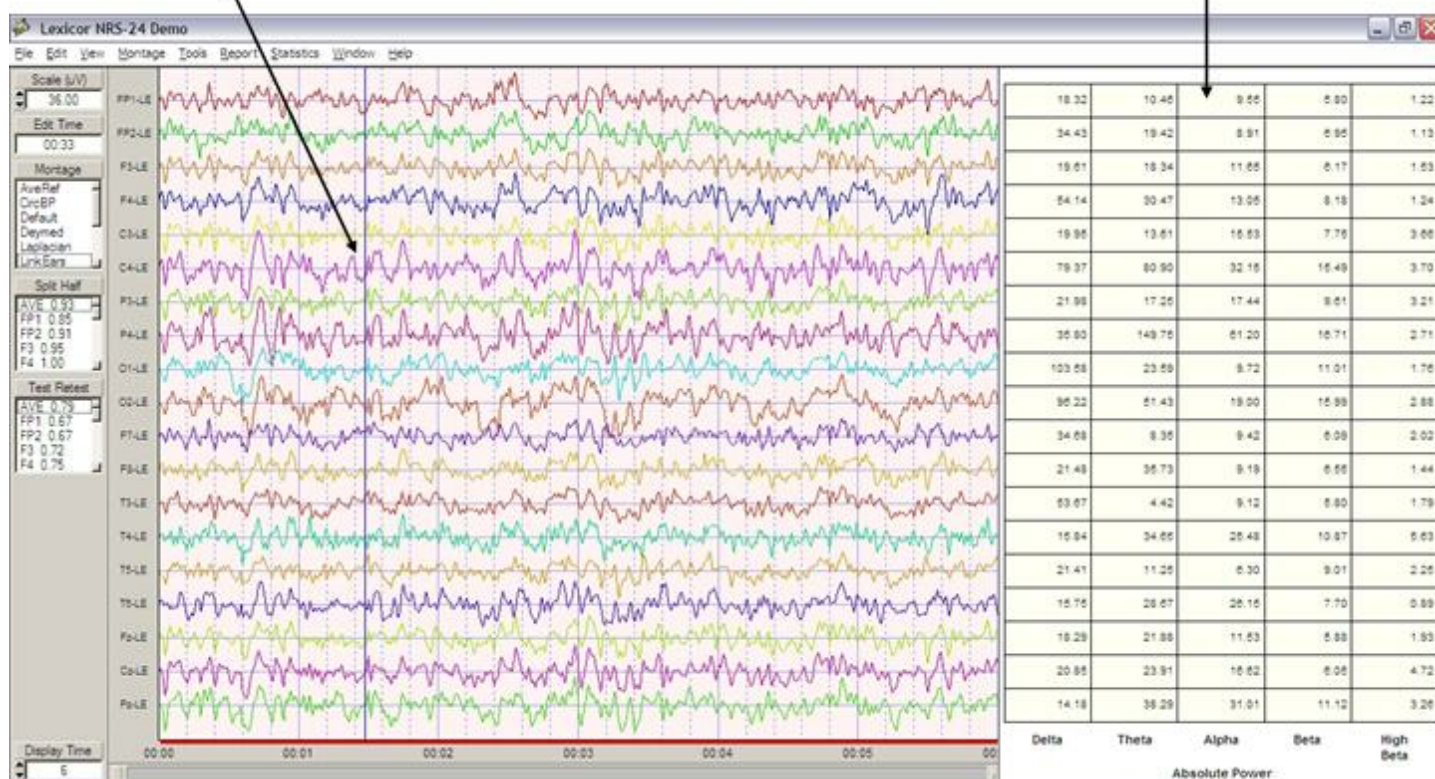


Select Absolute Power and Z Scores and click Apply. Then depress the left mouse button and drag the mouse over the EEG tracings to dynamically produce absolute power. Change to relative power or coherence or raw scores in the time domain, etc.



**Depress the left mouse button and  
drag over the EEG tracings**

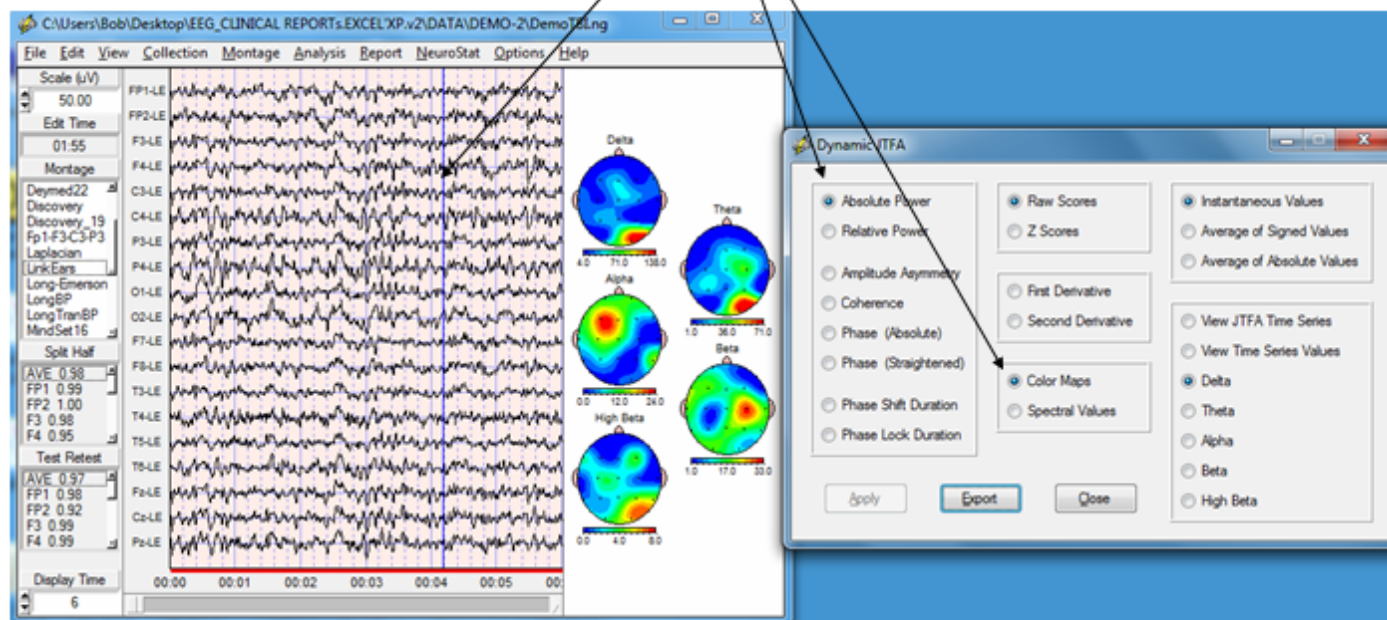
**Read the Instantaneous  
absolute power or relative  
Power or Magnitude or  
Z scores as the mouse moves**



**Dynamic JTFA Color Topographic Maps. To view Instantaneous EEG Power Values click View > Dynamic JTFA and select Color Maps. Then drag the mouse over the EEG tracings to obtain millisecond time resolution.**



**To View Dynamic Color Maps, select Absolute Power and Color Maps and click Apply and then depress the left mouse button and drag over the Traces.**

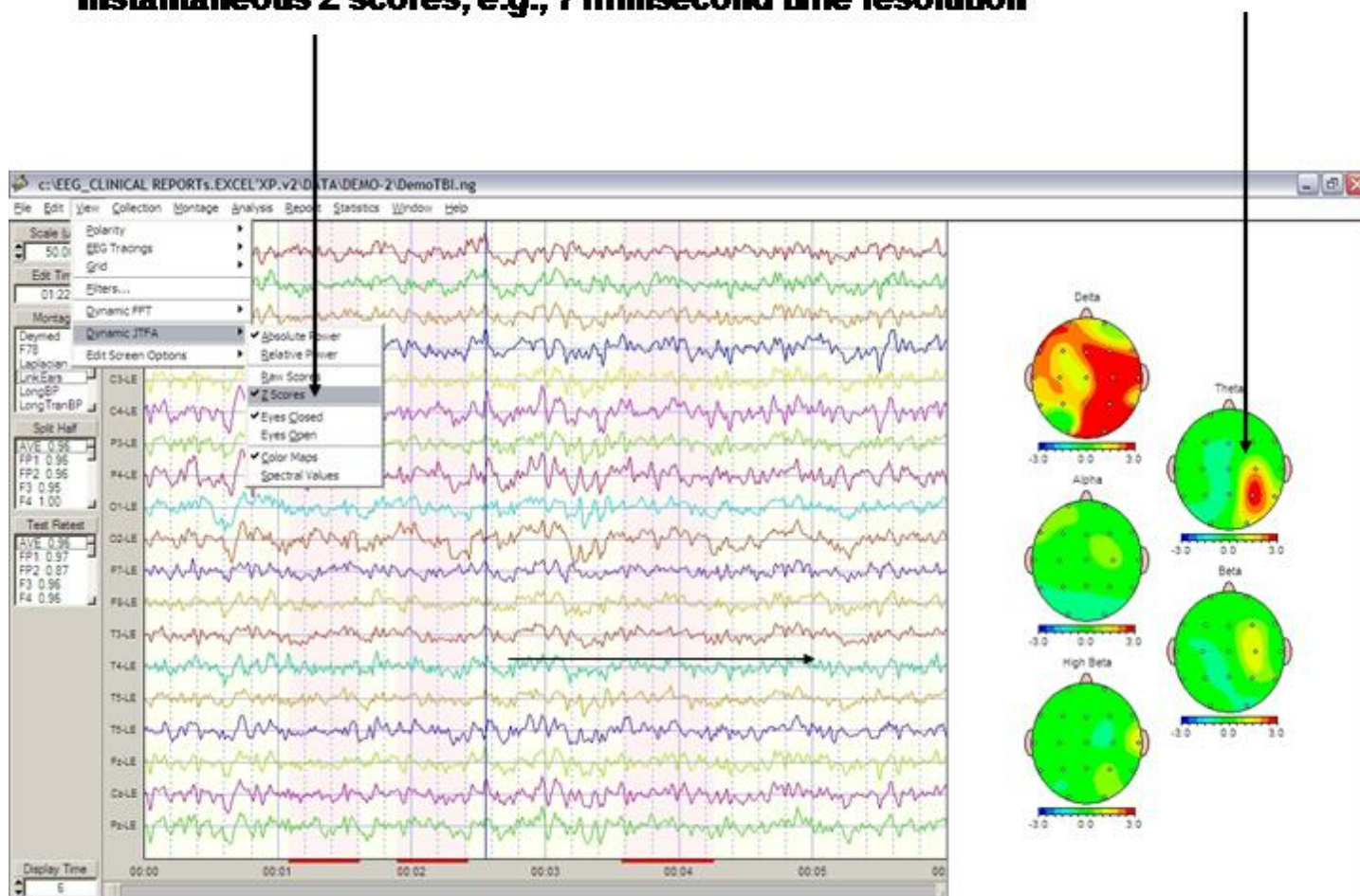


**To view Instantaneous EEG Z Score Values click View > Dynamic JTFA > Color Maps and select Z Scores. Then drag the mouse over the EEG tracings to obtain 7 millisecond Z Score time resolution.**





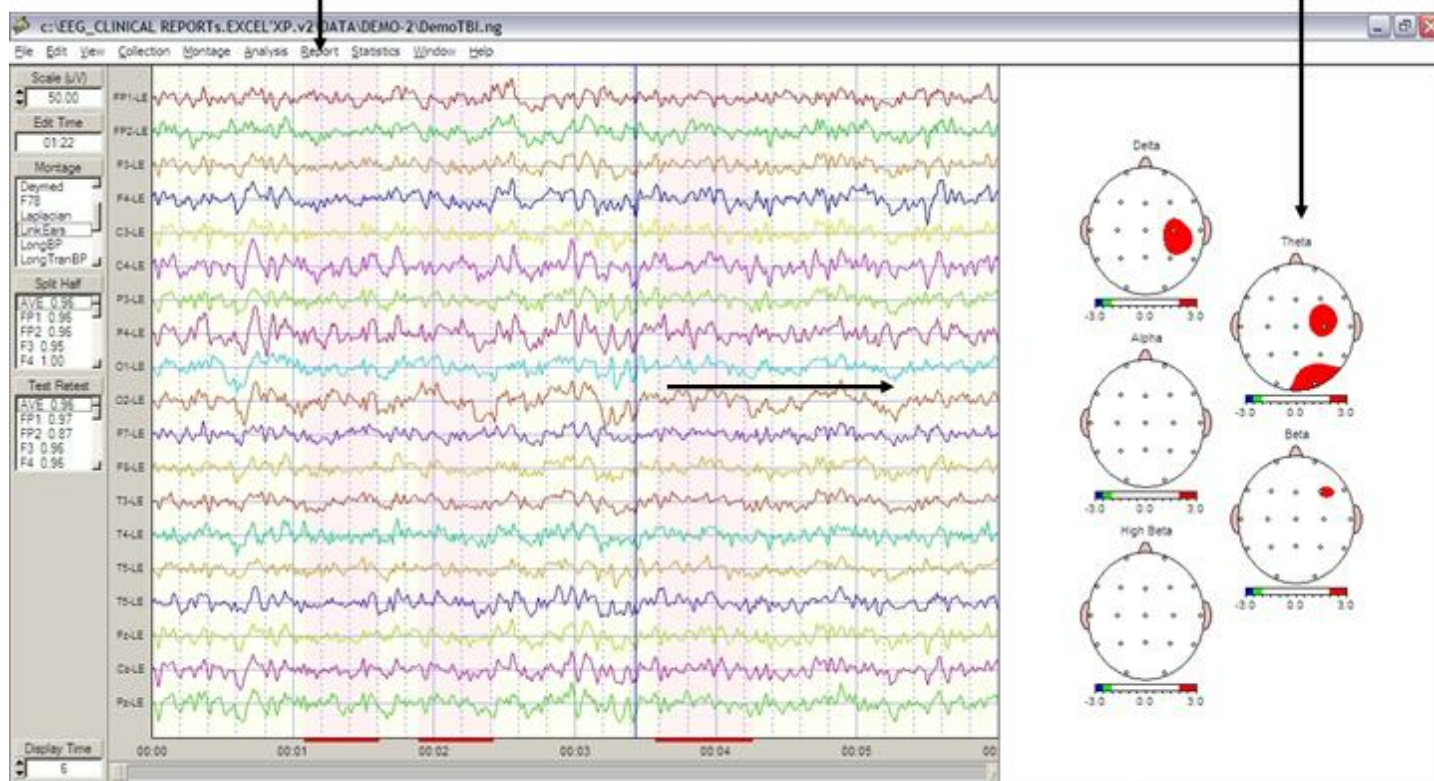
**Click View > Dynamic JTFA > Absolute Power and Color Maps and then Click and Click Z Scores. Drag the mouse over the EEG tracings to view Instantaneous Z scores, e.g., 7 millisecond time resolution**



After launching the dynamic JTFA Z Scores then click Report > Report Options > Z Scores and set Normal color = white and Normal Z Score range = 2.0 (see section 10f). To view Instantaneous EEG Power Values click View > Dynamic JTFA > Color Maps.



**Click View > Dynamic JTFA > Absolute Power and Color Maps and then Click and Click Z Scores. Change the Z score settings by clicking Report > Report Options > Z Score and then select normal color white and normal Range = 2.0. Then Drag the mouse over the EEG tracings to view Instantaneous Z scores at 7 millisecond time resolution**

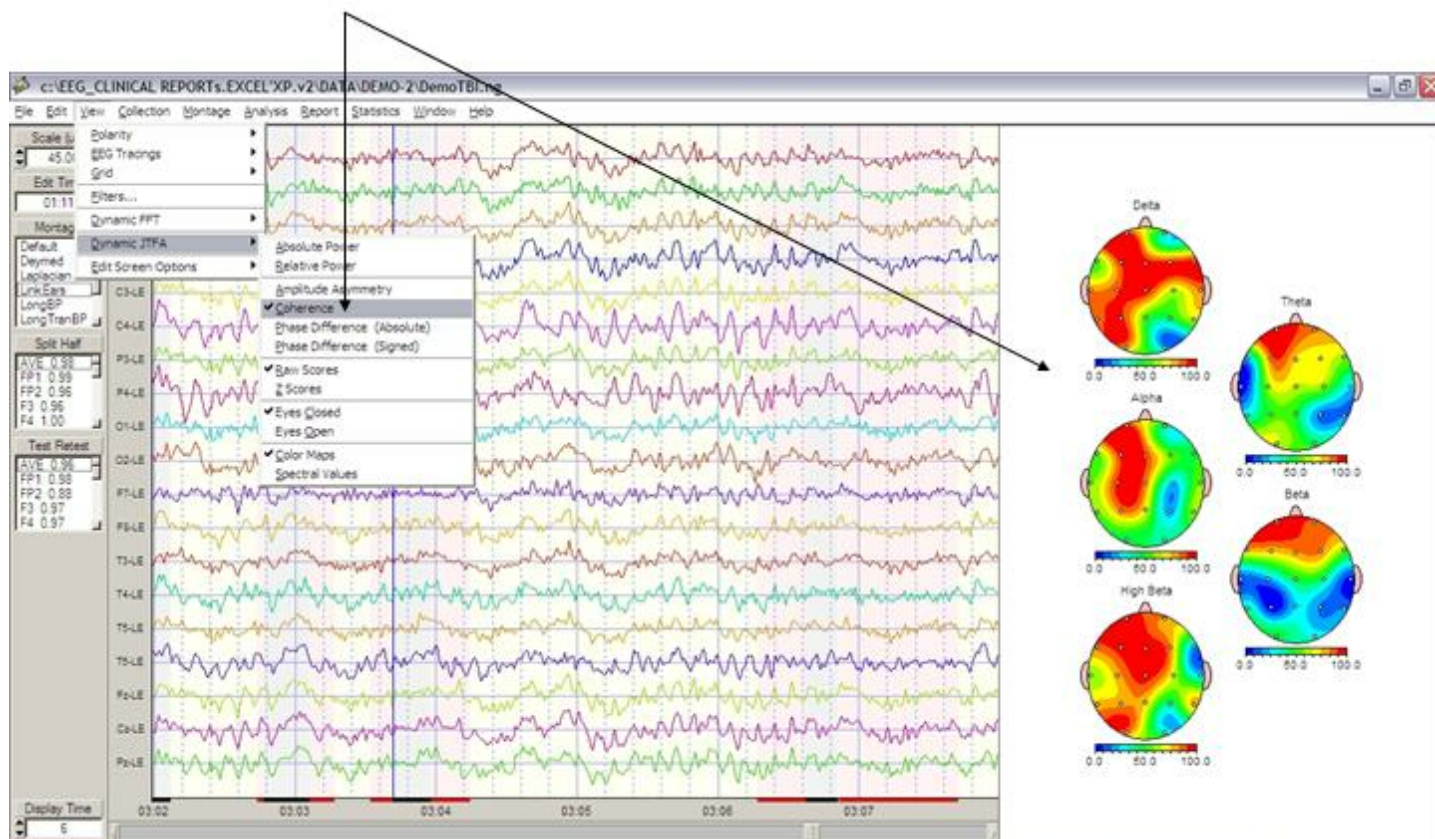


**Activate the instantaneous coherence JTFA by clicking View > Dynamic JTFA > Coherence. The default reference channel is Fp1, double click the label of a different channel to change the reference. Depress the left mouse and drag over the EEG tracings to view the instantaneous changes in coherence.**





**Click View > Dynamic JTFA > Coherence to activate instantaneous Coherence. The Fp1 is the default channel as one of the pair of channels. Double click a different channel label to select a different channel as the channel that is the used in the coherence computations. Drag the mouse over the EEG tracings and view the dynamic updates of the color topographic maps.**

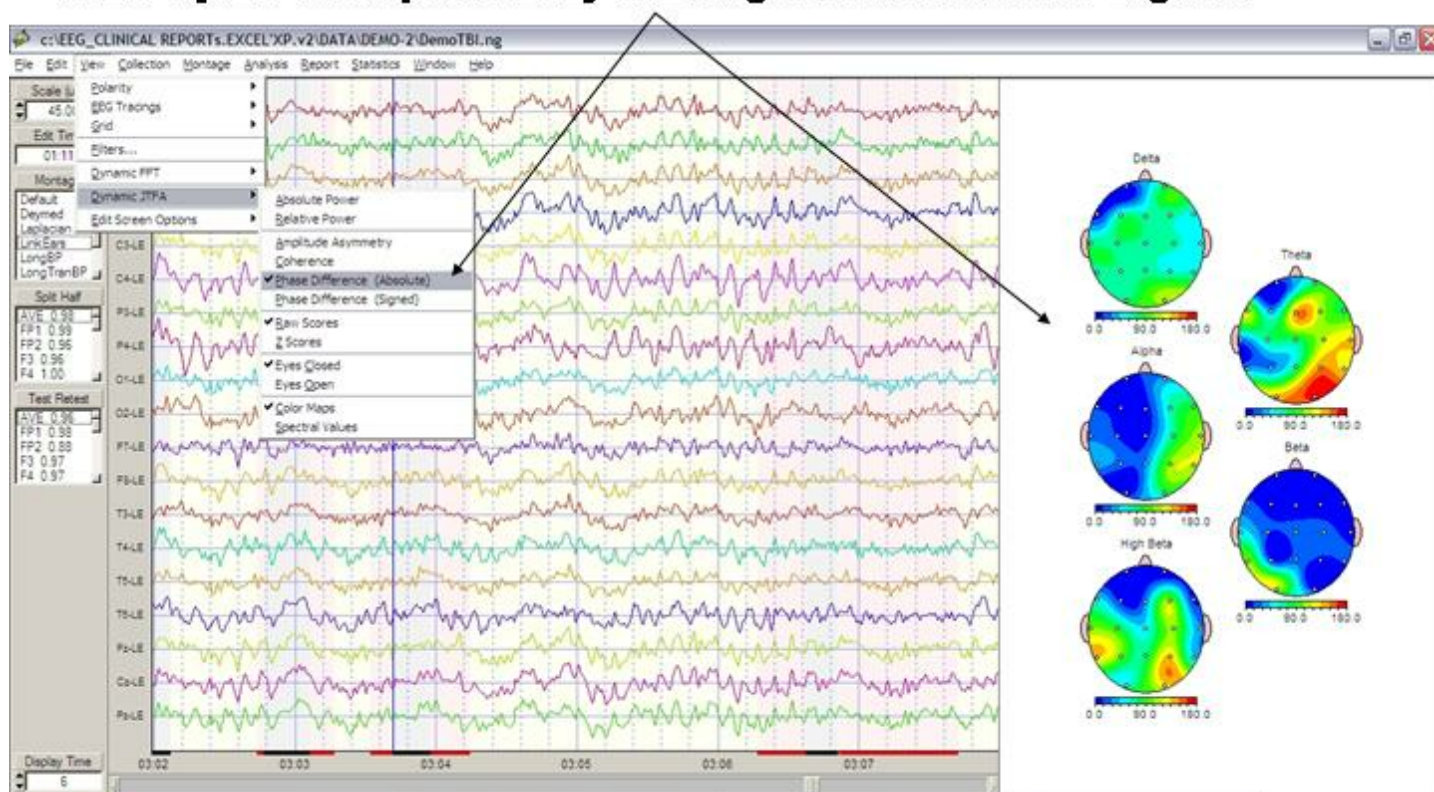


Activate the instantaneous phase JTFA by clicking View > Dynamic JTFA > Absolute Phase or Signed Phase. The default reference channel is Fp1, double click the label of a different channel to change the reference. Depress the left mouse and drag over the EEG tracings to view the instantaneous changes in phase delay. Absolute phase varies from 0 to 180 degrees and signed phase varies from 0 to 360 degrees and contains the singularity when 0 = 360.





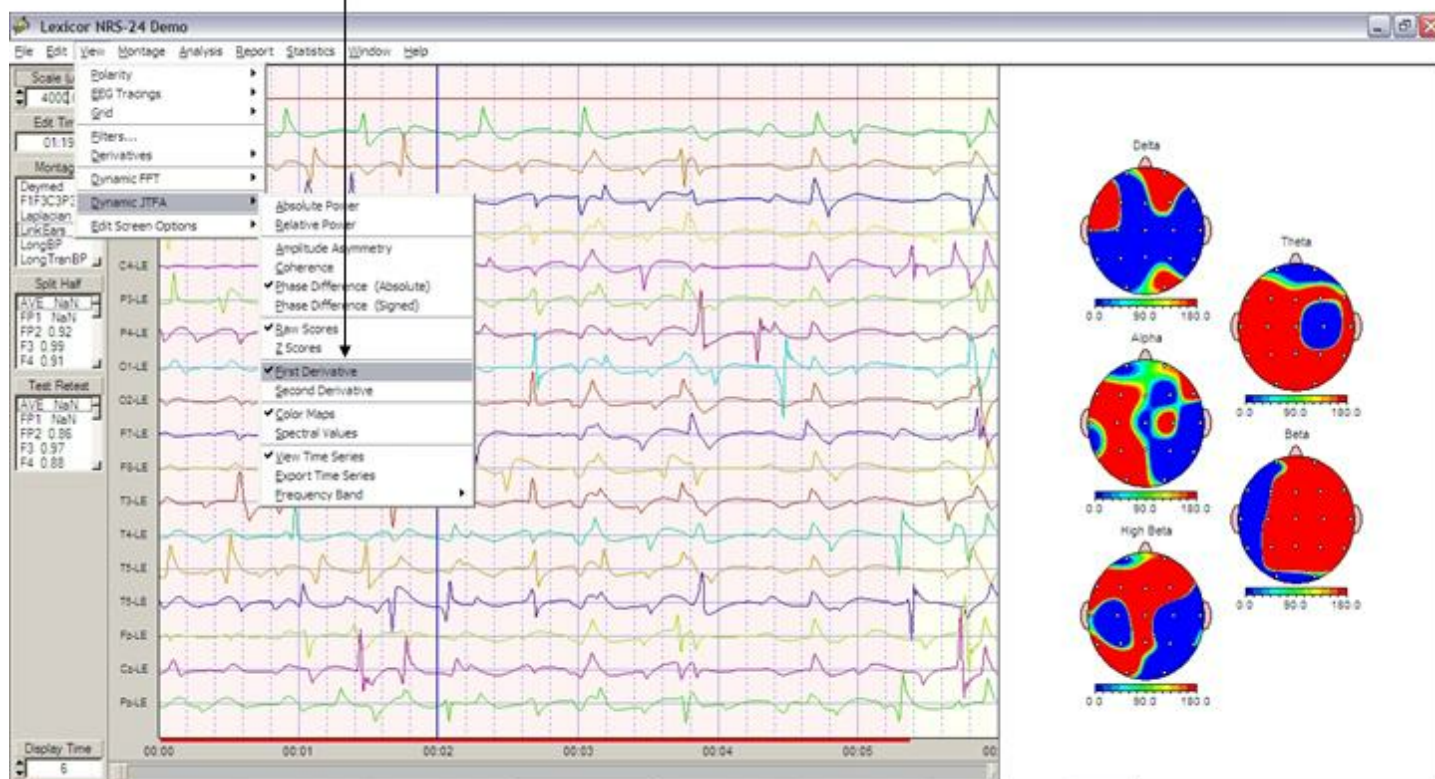
**Click View > Dynamic JTFA > Phase to activate instantaneous Phase delays. The Fp1 is the default channel as one of the pair of channels. Double click a different channel label to select a different channel as the channel that is the used in the phase computations. Drag the mouse over the EEG tracings and view the dynamic updates of the color topographic maps. Absolute phase is the square of the phase delay and ranges between 0 & 180 degrees.**



**Select First or Second Derivatives of instantaneous time-frequency analyses:**



**Compute First or Second Derivatives of the JTFA Time Series Click View > Dynamic JTFA > First or Second Derivative.**

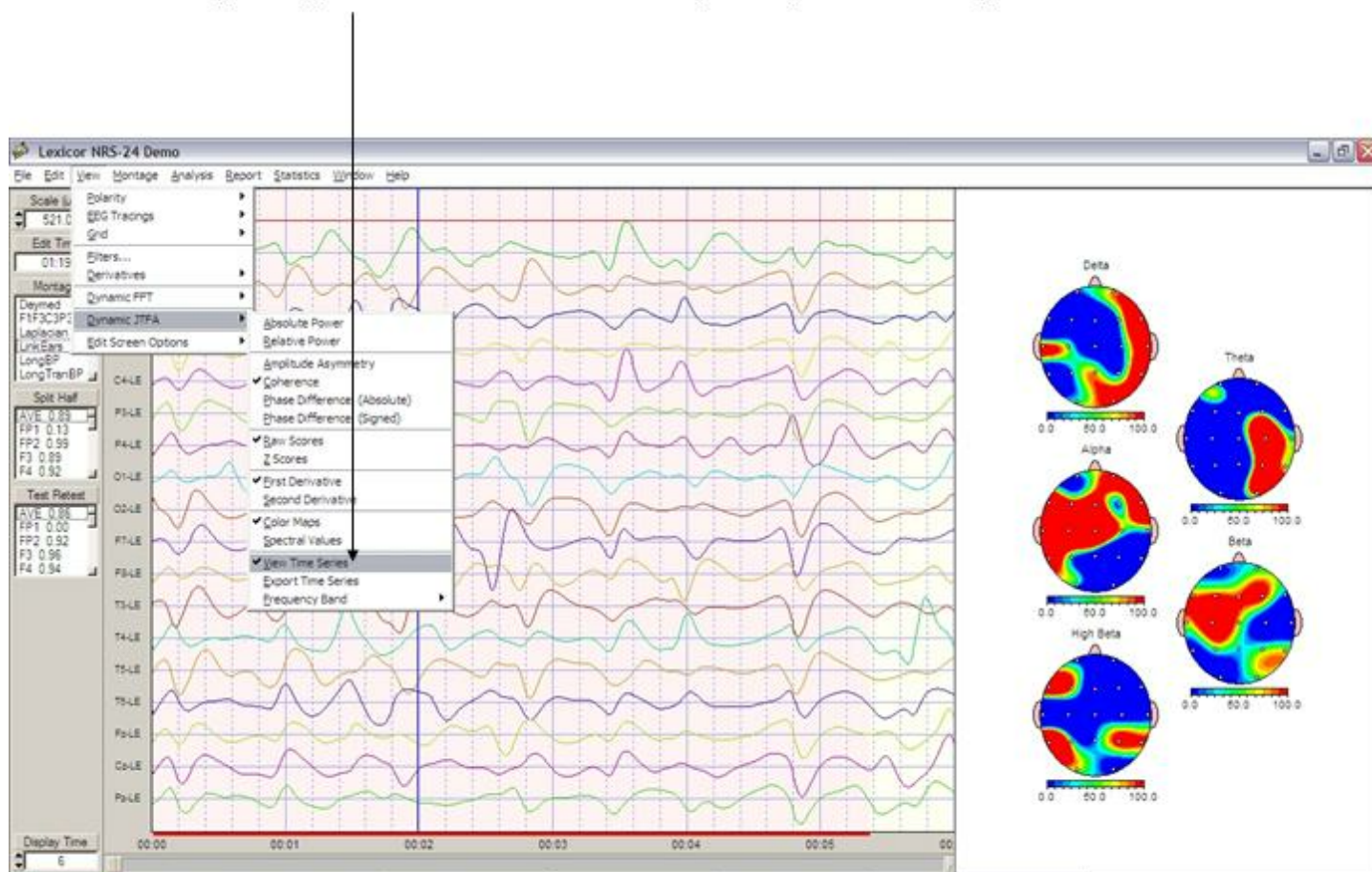


**To View the JTFA time series Click View > Dynamic JTFA > View Time Series.**





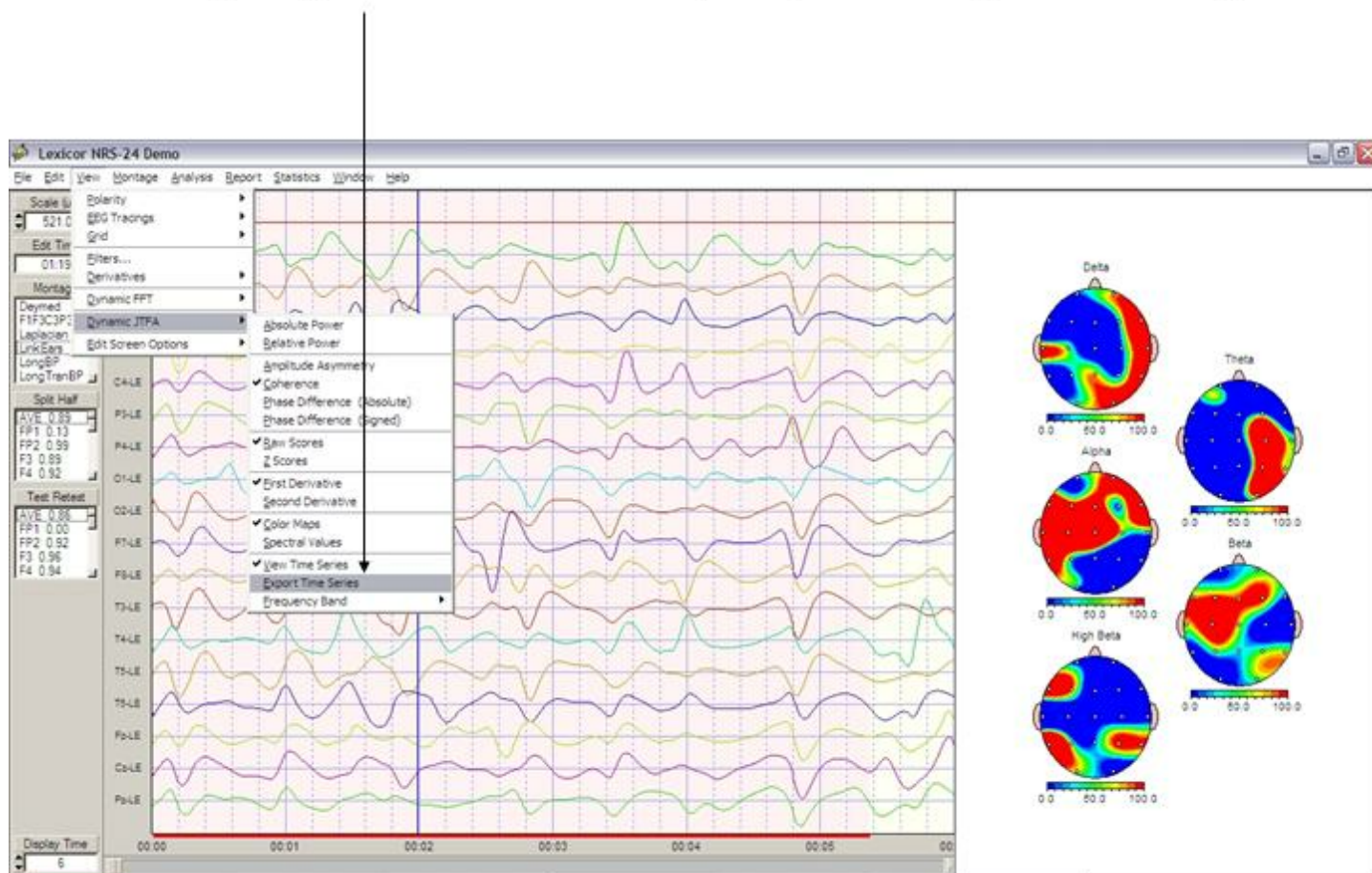
**To View the JTFA Time Series Click View > Dynamic JTFA > View Time Series.  
Click Frequency Band and then the frequency band that you want to view**



**To Export the JTFA time series in tab delimited format first click Frequency Band to select a frequency and then click View > Dynamic JTFA > Export Time Series.**



**To Export the JTFA Time Series Click View > Dynamic JTFA > Export Time Series. Click Frequency Band and then the frequency band that you want to export**



## JTFA Feature Detection

JTFA Feature Selections allow one to include or exclude different features of the EEG record and either remove or add the JTFA Selections to the Manual or Automatic Selections described previously.

To activate the JTFA Feature Detection Panel... Click Edit > JTFA Selection. Then Select one or more of the Montage Channels, then Select an EEG Measure (Absolute or Relative Power or Power Ratio), Select a Frequency Band or a Frequency Ratio (if Power Ratio was selected), Select Raw or Z Values, Select the Value Range, Select Exclude or Include and then Click OK.

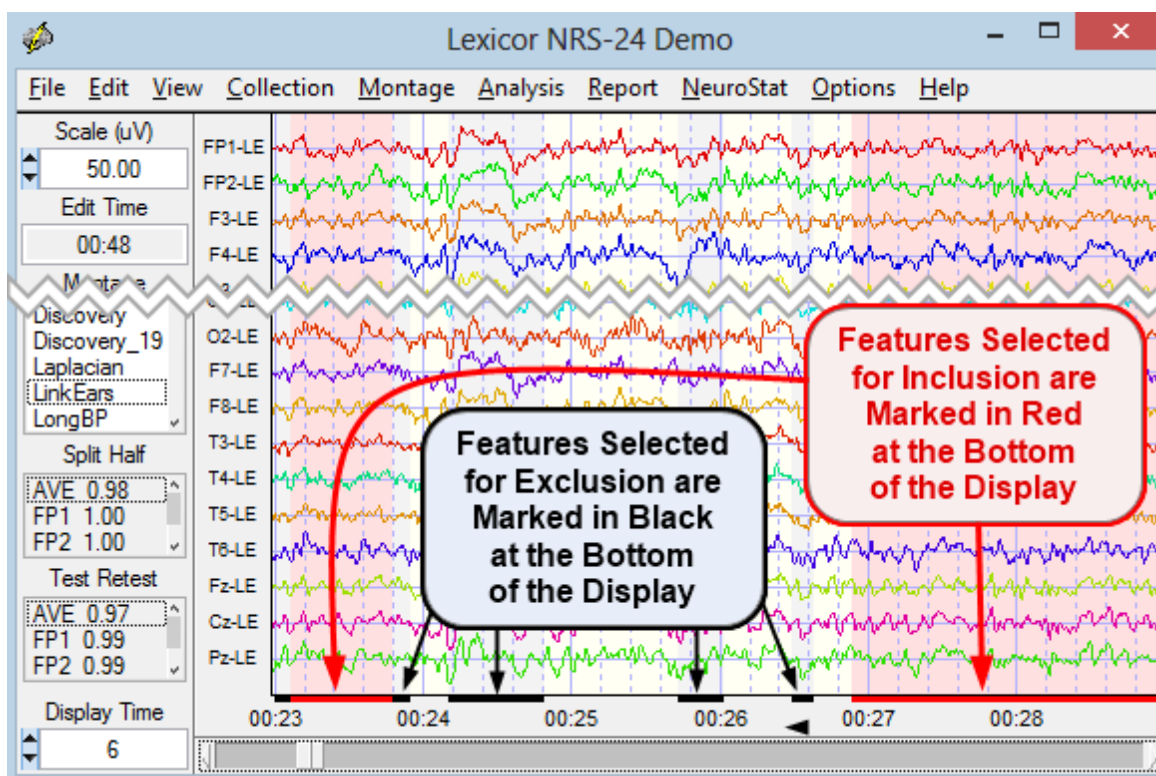
One can either continue Selecting various Features to Detect and Include or Exclude from other Channels, Measures and/or Frequencies or Click Close to view the selections.



The screenshot shows the 'JTFA Feature Detection' dialog box with the following sections and options:

- Select a Measure** (red box):
  - ☒ Absolute Power
  - ☐ Relative Power
  - ☐ Power Ratio
- Select a Frequency** (blue box):
  - ☒ Delta
  - ☐ Theta
  - ☐ Alpha
  - ☐ Beta
  - ☐ High Beta
- or Select a Frequency Ratio** (blue box):
  - ☒ Delta / Theta
  - ☐ Theta / Beta
  - ☐ Delta / Alpha
  - ☐ Theta / High Beta
  - ☐ Delta / Beta
  - ☐ Alpha / Beta
  - ☐ Delta / High Beta
  - ☐ Alpha / High Beta
  - ☐ Theta / Alpha
  - ☐ Beta / High Beta
- Montage Channels** (blue box):
  - FP1-LE
  - ☒ FP2-LE
  - F3-LE
  - F4-LE
  - C3-LE
  - C4-LE
  - P3-LE
  - P4-LE
  - O1-LE
  - O2-LE
- Select 1 or More** (yellow box) is at the bottom of the Montage Channels list.
- Select a Value Range** (purple box):
  - ☒ Greater Than: 3.00
  - ☐ And
  - ☒ Or
  - ☒ Less Than: -3.00
- Select a Value Range** (yellow box) points to the Greater Than/Less Than section.
- Raw Values / Z Values** (orange box):
  - ☐ Raw Values
  - ☒ Z Values
- Include / Exclude** (red box):
  - ☐ Include
  - ☒ Exclude
- Buttons**: OK, Close

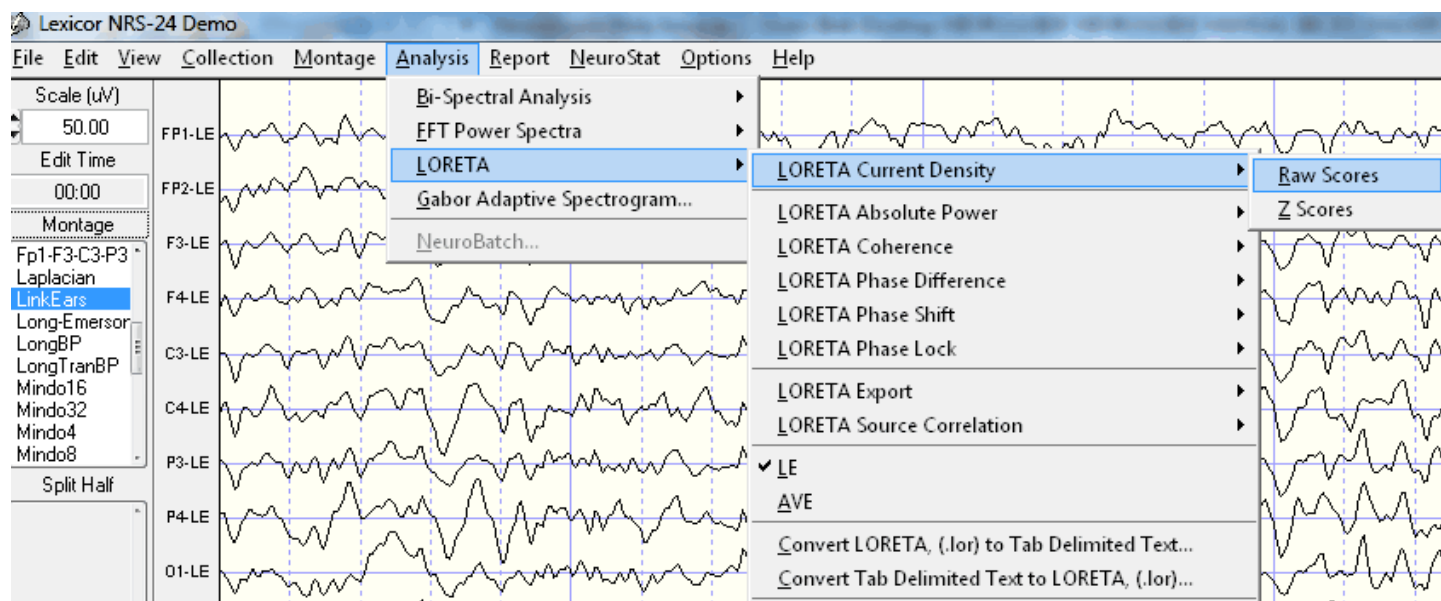
**Manual Selection or Deselection** (by dragging the Left or Right Mouse over the EEG tracings) overrides any of the previous Automatic Selections or JTFA Feature Selections (inclusions or exclusions). If Exclusion of a particular feature, e.g., Delta activity in Fp1 & Fp2 > 2 standard deviations is chosen, then a Black Bar at the bottom of the EEG display will mark the excluded segments. If Inclusion of a particular features is chosen, then a Red Bar will mark the included segments at the bottom of the EEG display.



## LORETA Key Institute Software and Viewer

Download the free Key Institute LORETA programs at ([www.unizh.ch/keyinst/NewLORETA/Software/Software.htm](http://www.unizh.ch/keyinst/NewLORETA/Software/Software.htm)) and then request a copy of the Key Institute password. Install the Key Institute LORETA in the default directory at: c:/program files(x86)/LORETA. Once the Key Institute software is installed on the users computer then the LORETA viewer program can be launched directly from the NeuroGuide edit window.

To analyze raw source current values Select artifact free EEG samples then Click Analysis > LORETA > LORETA Current Density > Raw Scores. The units for the square root transform of the squared source current vectors are amperes/meter<sup>2</sup>.



## Simultaneous NeuroGuide and LORETA Viewer



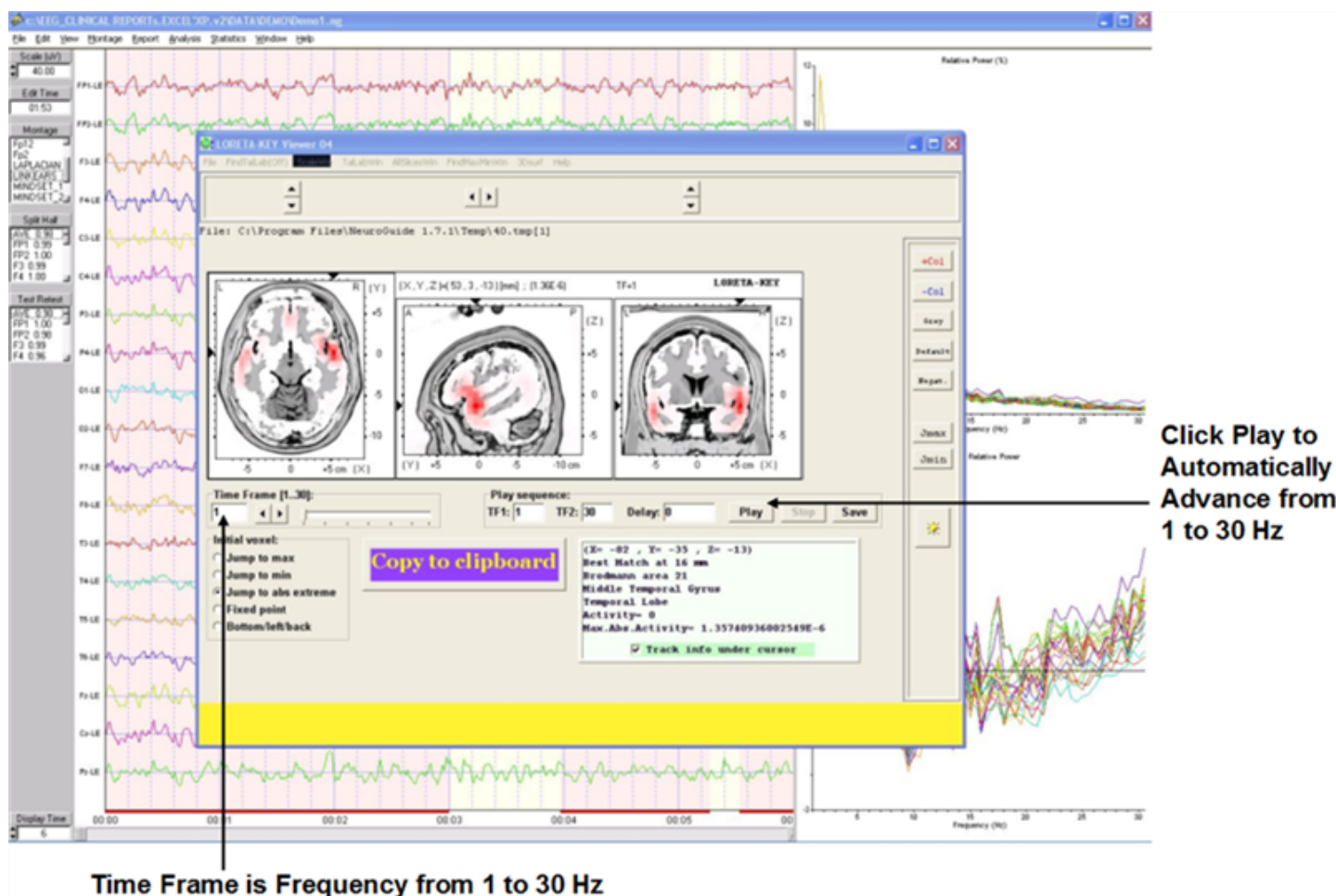


## Example of Simultaneous LORETA Viewer and NeuroGuide. Click Back and Forth between NeuroGuide and the LORETA Viewer



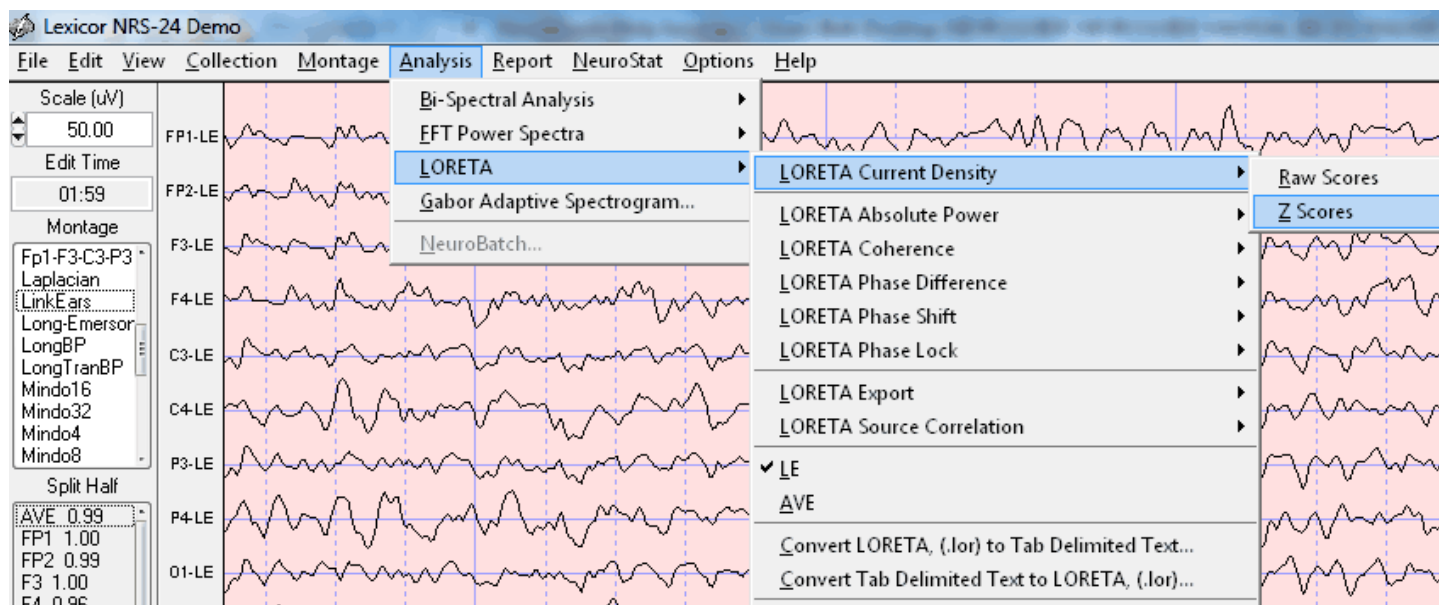
Time Frames are Frequencies from 1 to 30 Hz in 1 Hz increments.





The cross-spectral values are computed according to the equations provided by the Key Institute for frequency domain analysis (i.e., Hermitian matrix multiplication as specified in the Key Institute documentation) and the spatial localization can be independently verified by exporting the same digital EEG selections in the time domain and then manually importing the data into the Key Institute's LORETA viewer software. The automatic launching of the LORETA viewer involves the use of the electrode coordinates and T- Matrix described in Appendix D, therefore saving the user of NeuroGuide the trouble of manually importing the raw digital time domain data into the to cross-spectral steps described by the Key Institute's documentation. See the Key Institute documentation to learn how the \*.crs file and the \*.lorb are computed and then passed to the LORETA viewer by NeuroGuide.

Select artifact free EEG samples then Click Analysis > LORETA > Current Source Density > Z Scores. This procedure exports normative database Z Scores which is an add on feature of NeuroGuide. See [Appendix F](#) for details.

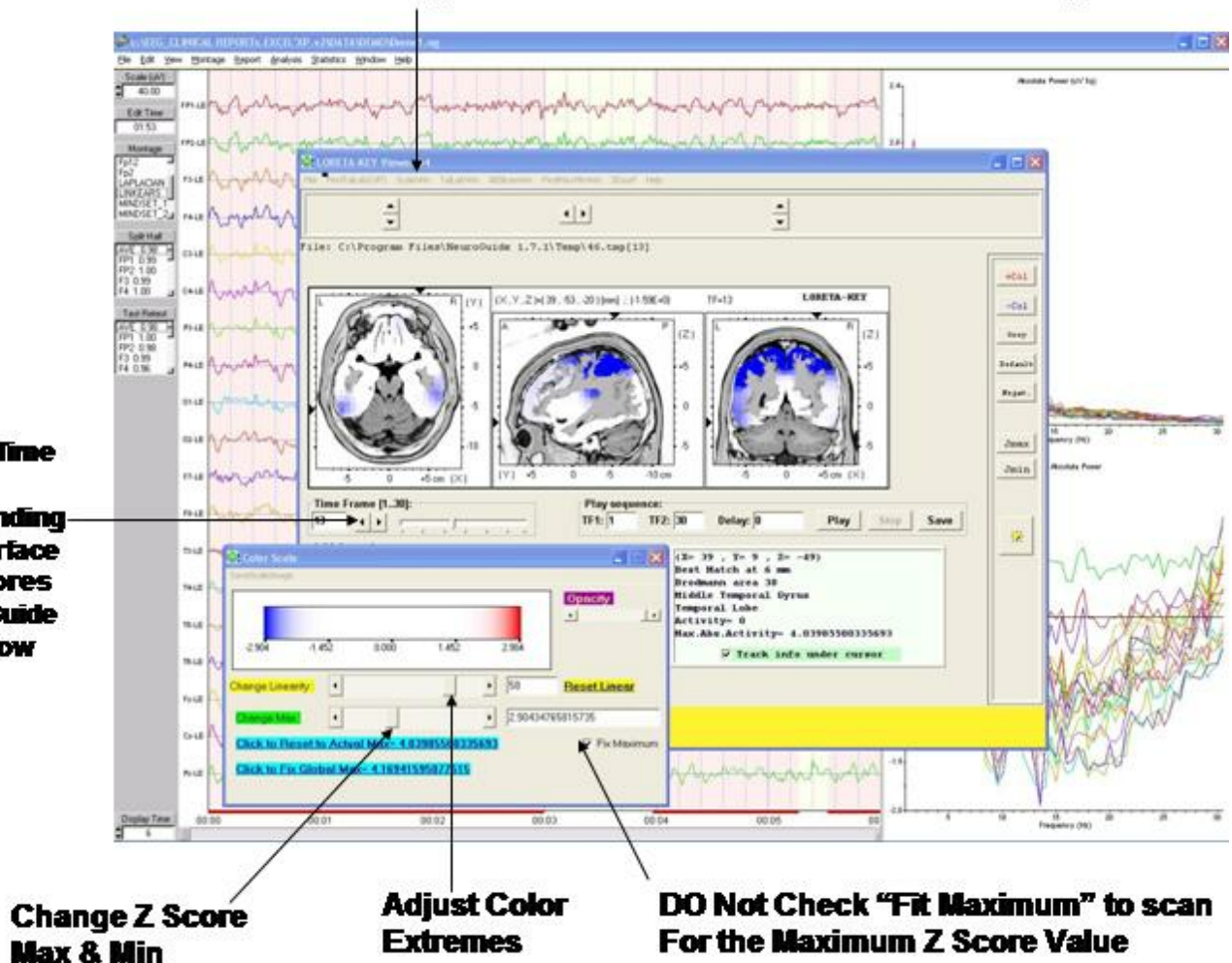


Click **ScaleWin** and then click **Time Frame >** to advance from 1 to 30 Hz and view the default maximum Z Scores. Note that the Z Scores of the maximum and minimum blue and red pixels in the MRI sequence may or may not be statistically significant (i.e.,  $Z > 2$  standard deviations). That is, the default **ScaleWin** only displays the "maximum" and "minimum" Z Scores which may or may not be  $Z > 2$  standard deviations. Click "Play" to automatically step through the entire spectrum of Z Scores and note the Z Score maxima and minima. Click the **NeuroGuide** edit window and identify the frequencies at which the maximum deviations from normal occur on the scalp surface and then type these frequencies into the **Explorer Viewer** time frame and examine the **LORETA** solution.



## Click – ScaleWin and Adjust the Color Scale and Viewer Settings

Advance Time  
Frames  
Corresponding  
To the Surface  
EEG Z Scores  
In NeuroGuide  
Edit Window

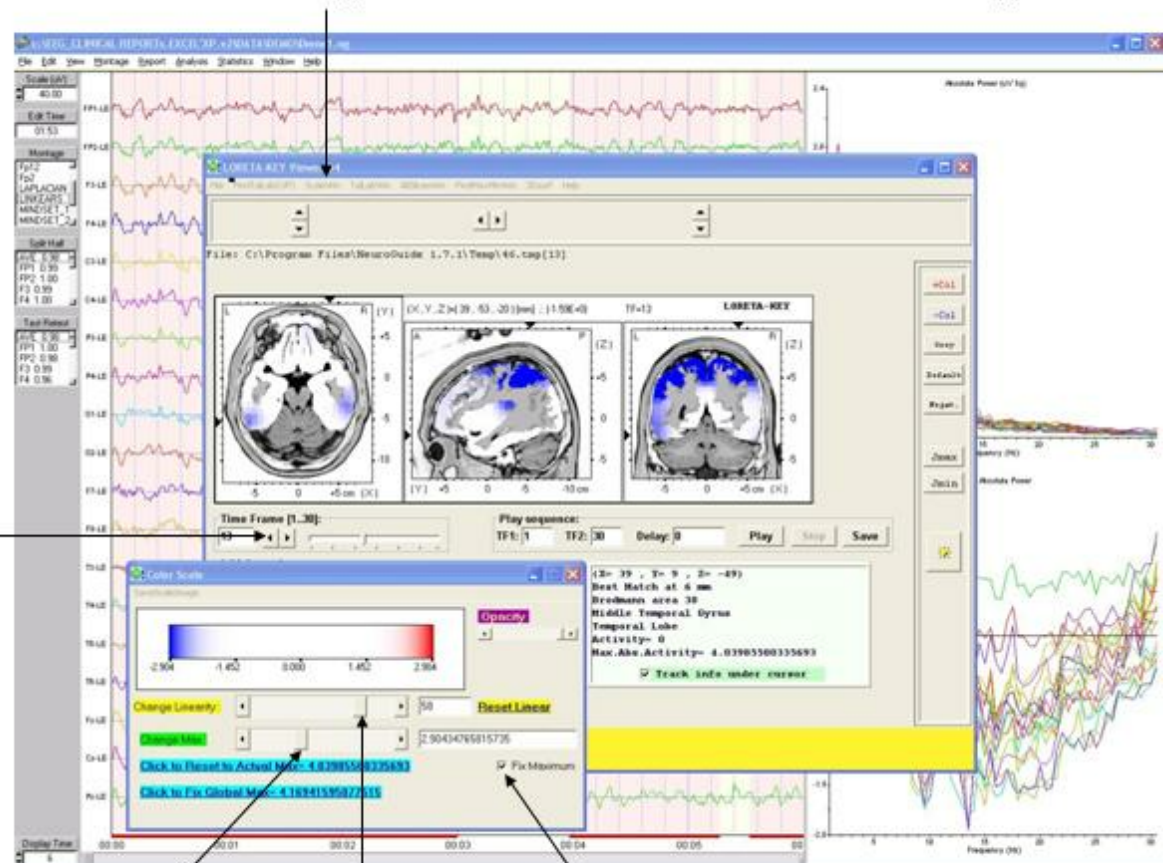


Click - ScaleWin in the Viewer and then check "Fit Maximum" and move "Change Max" wiper to adjust Z Score thresholds and move "Change Linearity" wiper to adjust color extremes. Z Scores are only valid if they correspond to the surface EEG measures in the NeuroGuide edit window. Click the NeuroGuide EEG tracing and dynamic FFT window and determine the frequencies of maximum deviance from normal and then click the LORITA Viewer and change frequency and Z Score settings accordingly. Details of normative database creation and validation using the Key Institute software and NeuroGuide computation of the Key Institute equations are provided in [Appendix F](#).



## Click – ScaleWin and Adjust the Color Scale and Viewer Settings

Advance Time  
Frames  
Corresponding  
To the Surface  
EEG Z Scores  
In NeuroGuide  
Edit Window



Change Z Score  
Max & Min

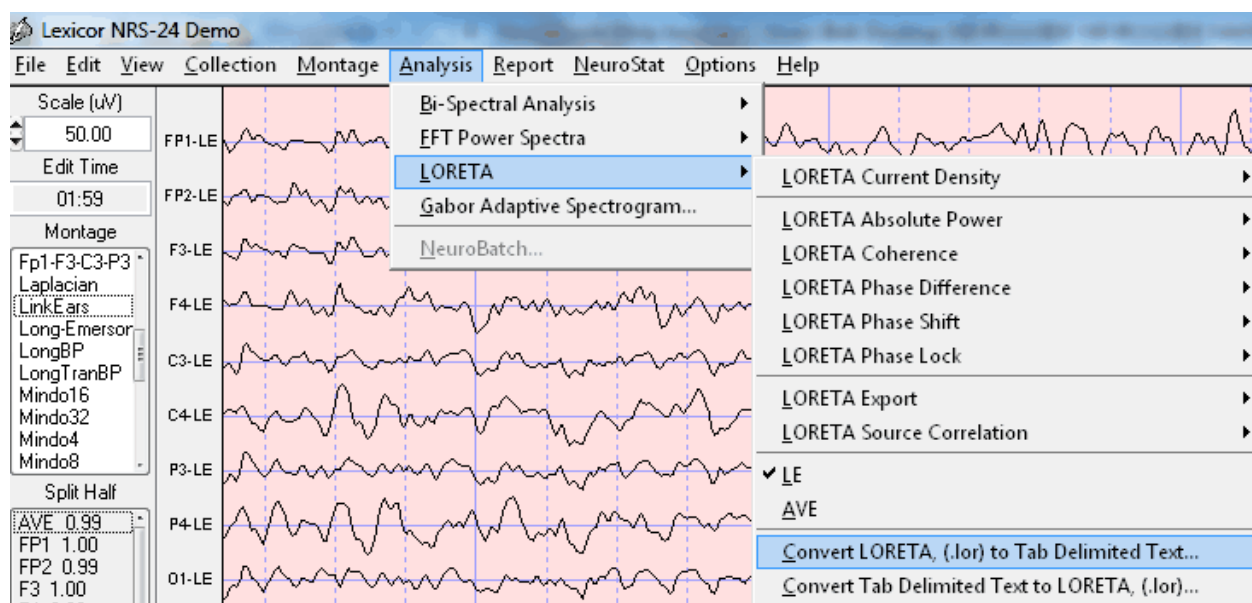
Adjust Color  
Extremes

Check "Fit Maximum" to scan  
For a Threshold Z Score Value

In the LORETA Viewer Click "3DSurf" to Open the 3-Dimensional Rendered Brain. Click "Orthoview" to Produce a Full View of the Rendered Brain and the Location of Z Scores. Click "Left" or "Right" to View the Hemispheres.

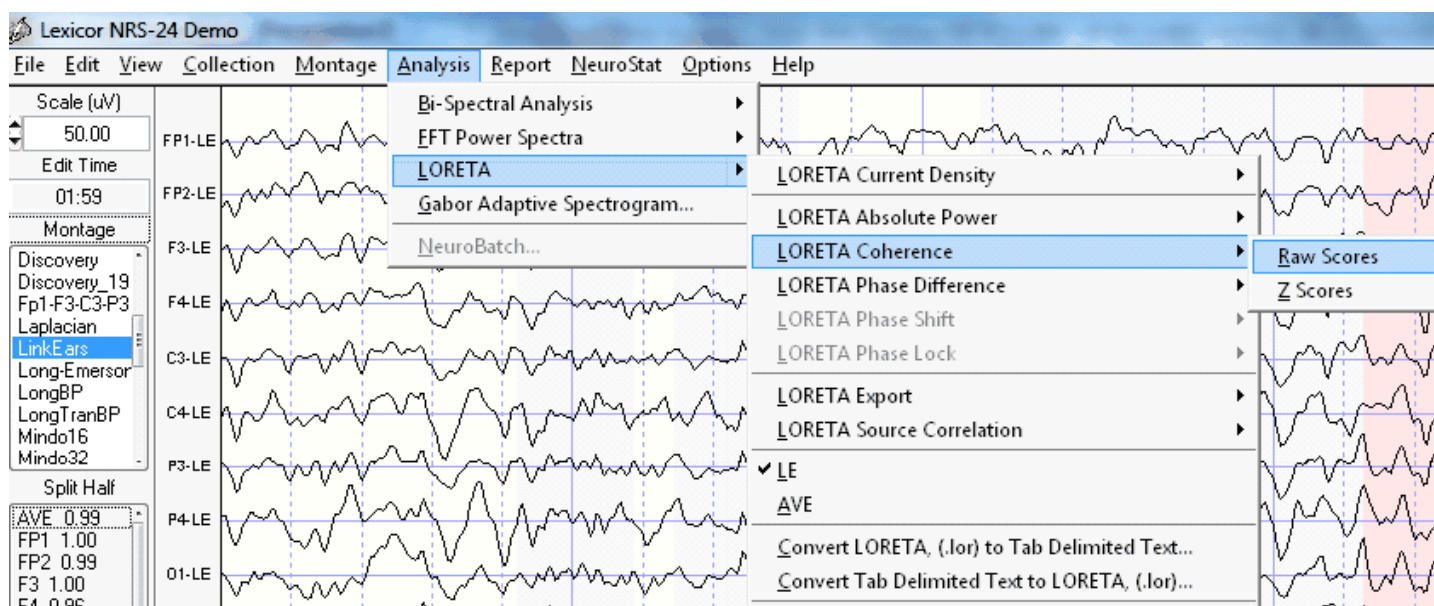
Convert .lor files for easy import into Excel and other Statistical Packages. The conversion takes 1 column and 71,820 rows (i.e., 30 Hz x 2,394 = 71,820) and transforms to 30 columns (1 to 30 Hz) and 2,394 rows (all gray matter pixels)



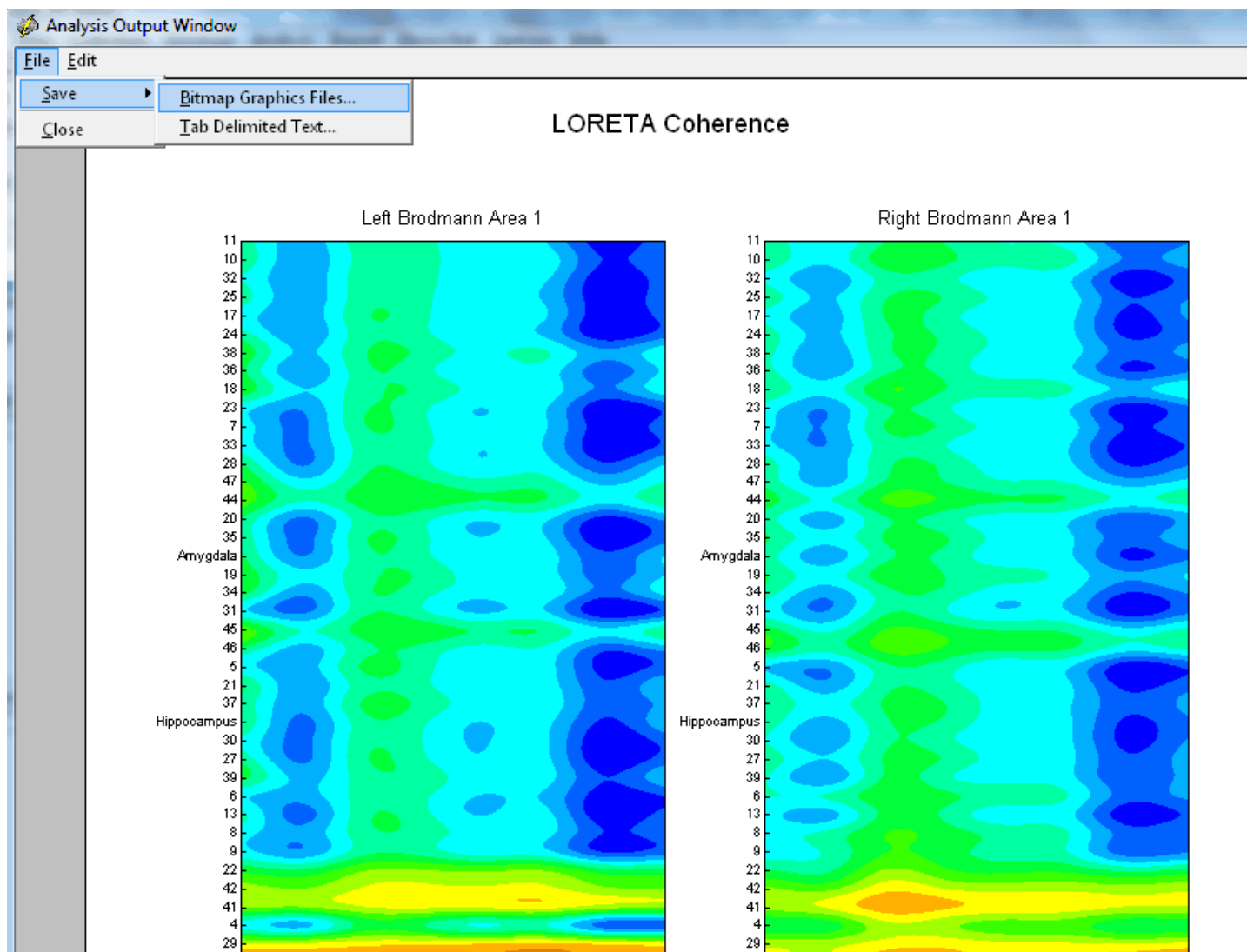


## LORETA Coherence and Phase Differences

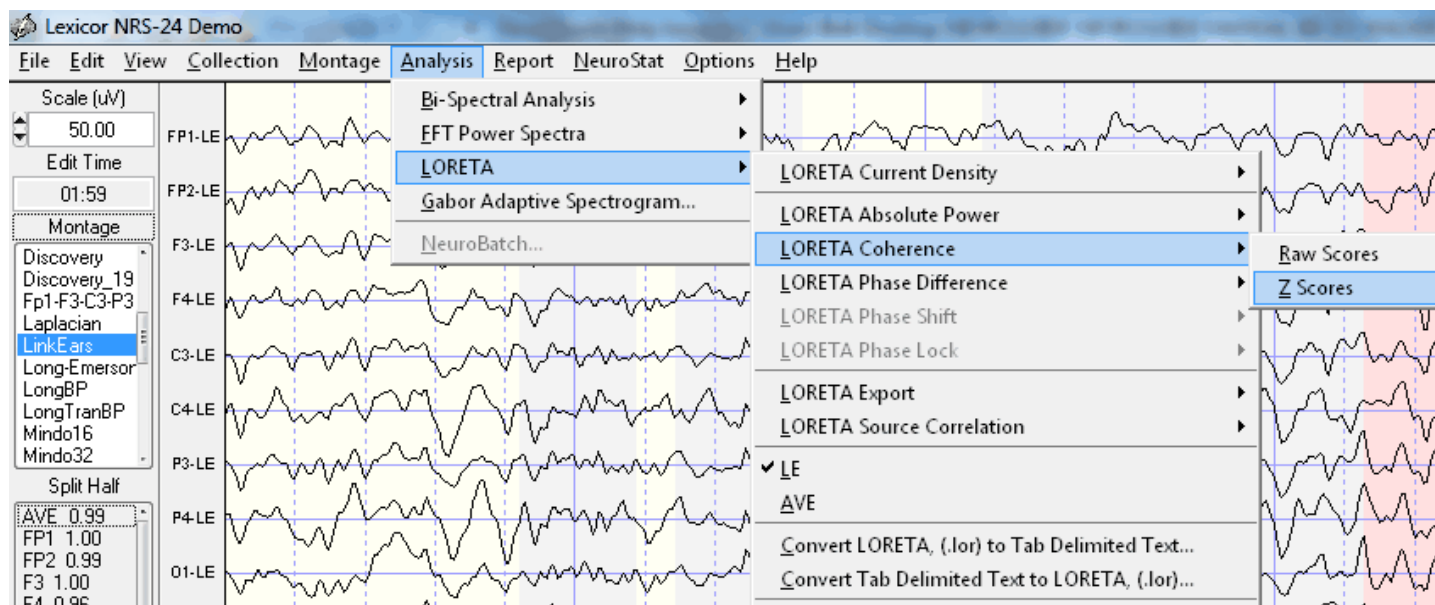
After selecting at least 30 seconds of artifact free EEG data, then click LORETA > LORETA Coherence > Raw Scores to compute the Raw LORETA Coherence values that range from 0 to 100 (i.e., coherence from 0 to 1 times 100 to scale to percent variance).



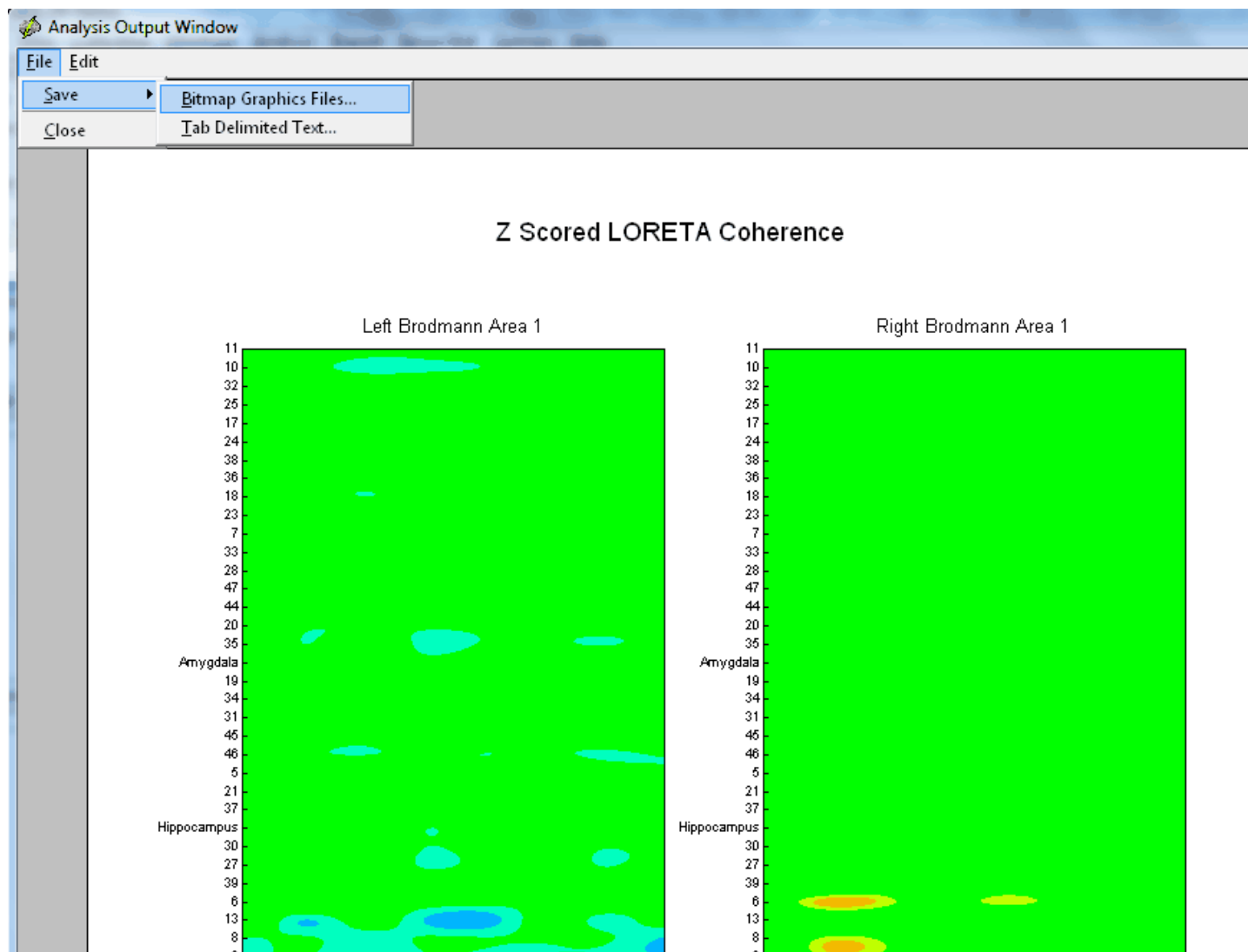
Save the bitmaps and/or tab delimited Raw LORETA Coherence data file by clicking File > Save.



To compute LORETA Coherence Z Scores click LORETA > LORETA Coherence > Z Scores

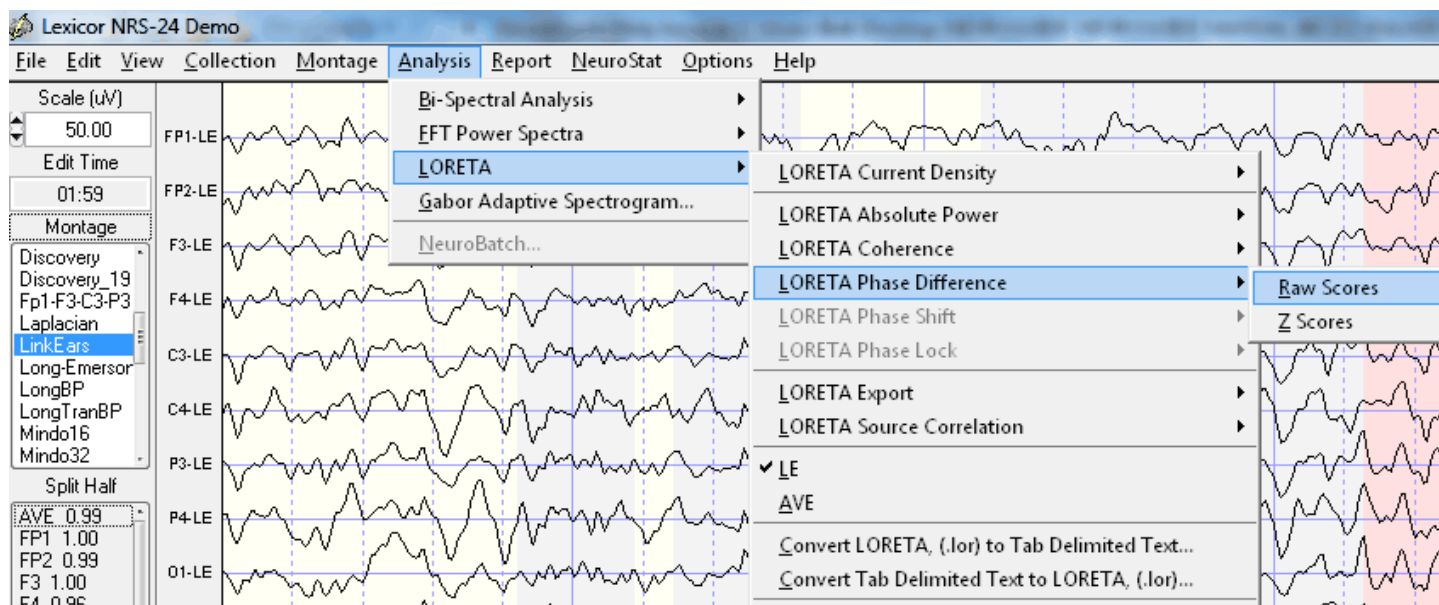


Save the LORETA Coherence Z Scores bitmaps and/or tab delimited data file by clicking **File > Save**.

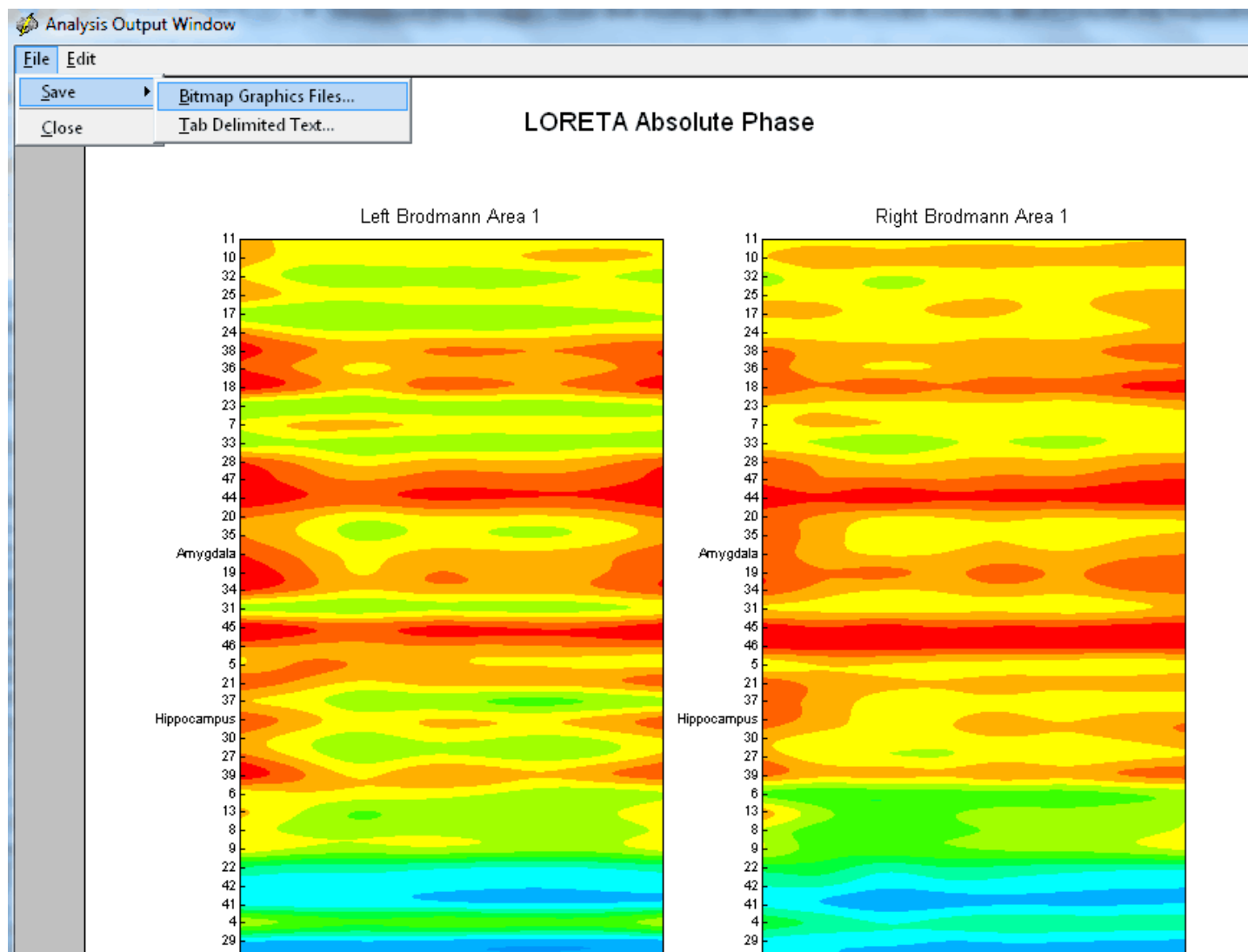


To compute LORETA Phase Differences raw scores click LORETA > LORETA Phase > Raw Scores

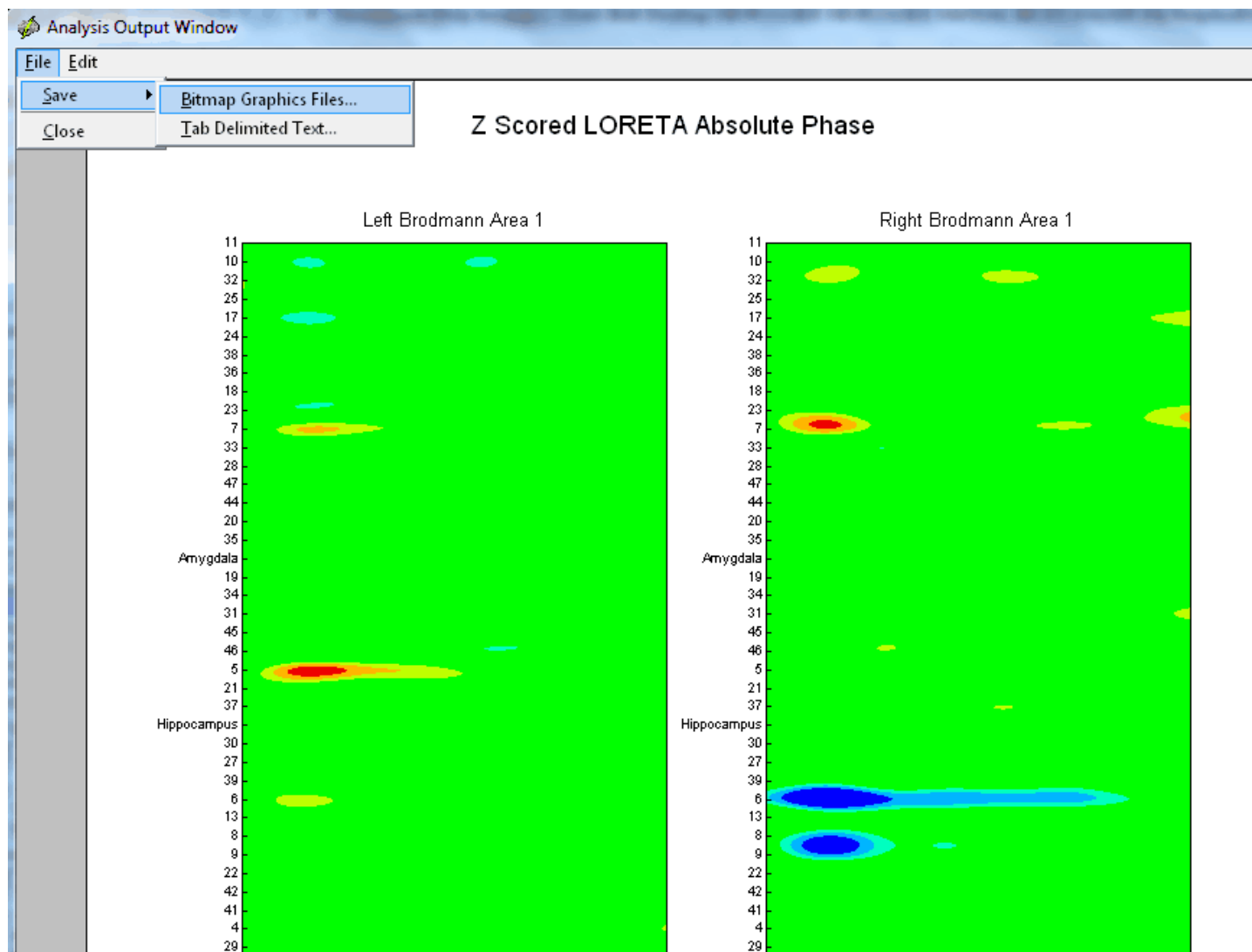




**Save the bitmaps and/or tab delimited LORETA Phase Differences Raw Scores data file by clicking File > Save.**



To compute LORETA Phase Difference Z Scores click Analysis > LORETA > LORETA Phase > Z Scores. Save the LORETA Phase Difference Z Scores bitmaps and/or tab delimited data file by clicking File > Save.



## LORETA Current Density Z Scores

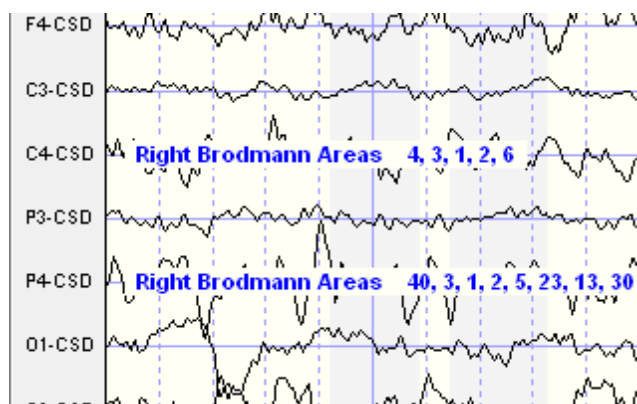
To avoid multiple comparison statistics that cause large Type II statistical error we recommend the use of planned comparison statistics based on hypotheses formed prior to launching LORETA. For example, start with patient's symptoms and then based on the scientific literature hypothesize the most likely Brodmann areas (nodes) and connections between nodes in networks linked to the patient's symptoms. For example, a patient with attention deficit disorder (ADD) then hypothesize the attention network, or anxiety symptoms with the anxiety network or depression symptoms with the depression network, etc. A google search of these networks will help identify the nodes and connections or the use of Pubmed or the Handbook of QEEG and EEG Biofeedback ([www.anipublishing.com](http://www.anipublishing.com)) are recommended.

## Hypothesis Formation and Planned Comparison Statistics

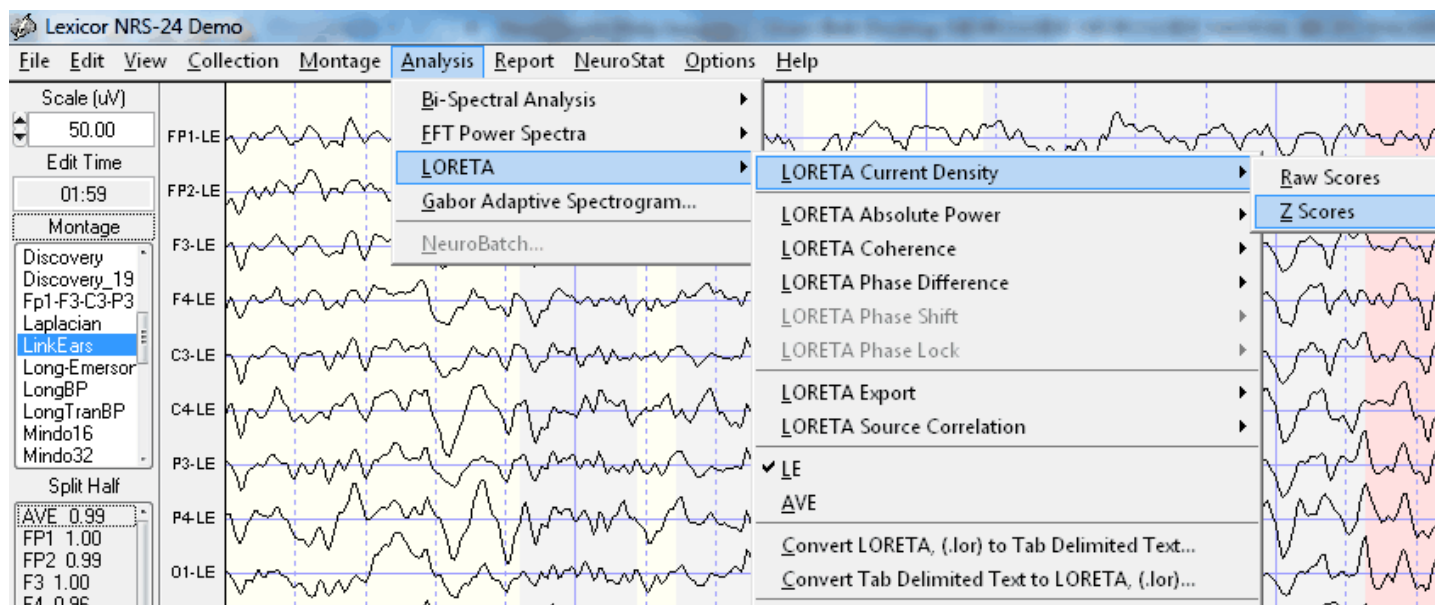


It is best to double click Laplacian in the montage window to the left of the neuroguide edit screen in order to compare the surface Laplacian to the LORETA sources. The reason is that the surface Laplacian and LORETA sources are the same measures of CURRENT in amperes and not VOLTAGE in microvolts. The scalp linked ears or other common referenced electrical fields are transformed by the 2nd spatial derivative into current density in amperes which minimizes the large spatial distribution of voltages and replaces the electrical field with focal or spatially localized gradients of change in the electrical field. The same process happens with LORETA sources, i.e., a Laplacian operator converts the surface microvolt electrical field gradients into 3-dimensional current sources in microamperes and therefore there is a much closer alliance and hypothesis testing capability when one compares the surface Laplacian to LORETA. This is why the surface Laplacian and LORETA are so powerful in minimizing medication or drug effects because they eliminate the low spatial frequencies that medications cause due to their blood stream introduction effecting widespread brain regions. Therefore, please make sure that you double click Laplacian for the montage to form hypotheses about expected deviant Brodmann areas.

To help form hypotheses, identify the frequency of deviant Z Scores in the surface Laplacian montage. Then move your mouse over the channel label with a significant Z Score at that frequency and then right mouse click prior to launching LORETA. Then confirm or disconfirm your hypotheses based on both frequency and location after launching LORETA Z Scores. Below is an example of hypotheses formed at 5 Hz for C4 and P4 in the Demo patient.



Select artifact free EEG samples then Click Analysis > LORETA > LORETA Current Density > Z Scores. This procedure uses the Key Institute 'T' matrix to calculate current sources from each voxel and each raw value is subtracted from the normative database mean divided by the standard deviation to compute a Z Score. The LORETA normative database Z Scores is an add on feature of NeuroGuide. See [Appendix F](#) for details.



Click **ScaleWin** and then click **Time Frame >** to advance from 1 to 30 Hz and view the default maximum Z Scores. Note that the Z Scores of the maximum and minimum blue and red pixels in the MRI sequence may or may not be statistically significant (i.e.,  $Z > 2$  standard deviations). That is, the default **ScaleWin** only displays the "maximum" and "minimum" Z Scores which may or may not be  $Z > 2$  standard deviations. Click "Play" to automatically step through the entire spectrum of Z Scores and note the Z Score maxima and minima. Click the **NeuroGuide** edit window and identify the frequencies at which the maximum deviations from normal occur on the scalp surface and then type these frequencies into the **Explorer Viewer** time frame and examine the **LORETA** solution.

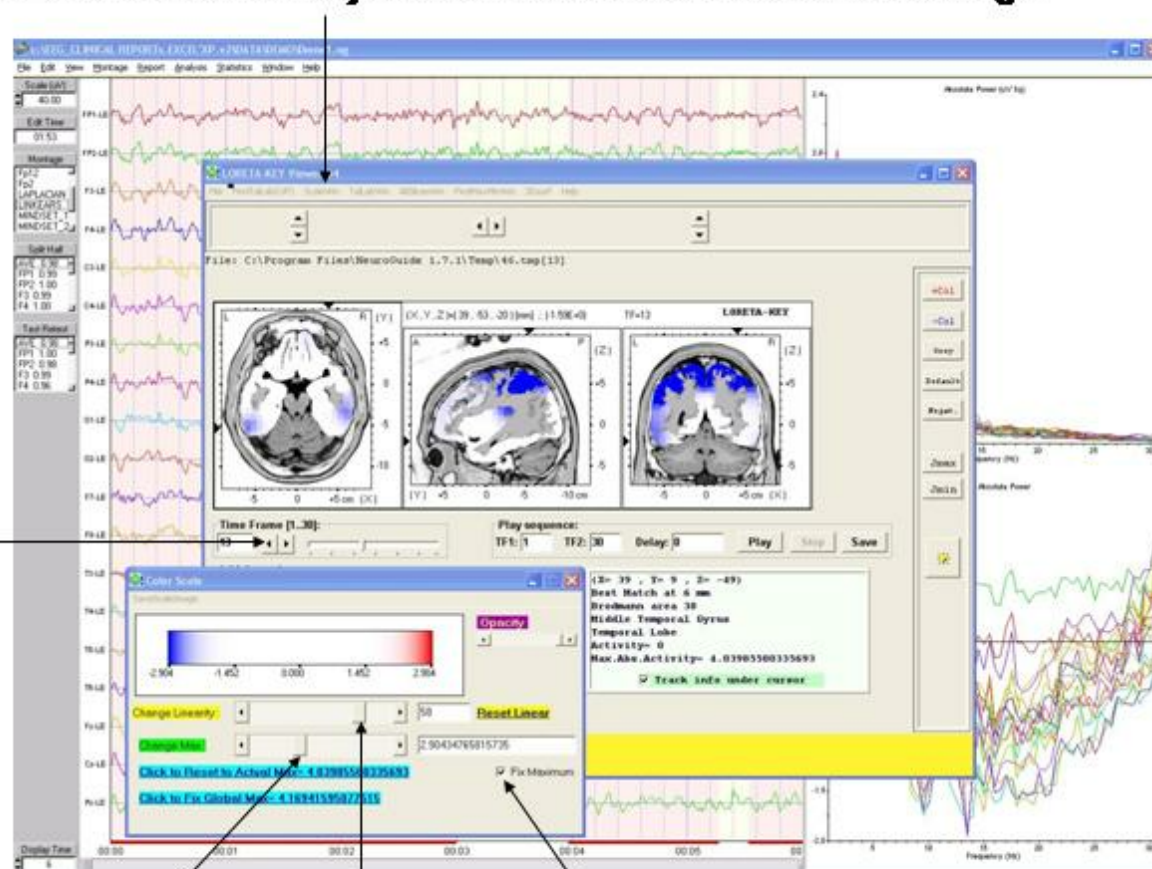






## Click – ScaleWin and Adjust the Color Scale and Viewer Settings

Advance Time  
Frames  
Corresponding  
To the Surface  
EEG Z Scores  
In NeuroGuide  
Edit Window



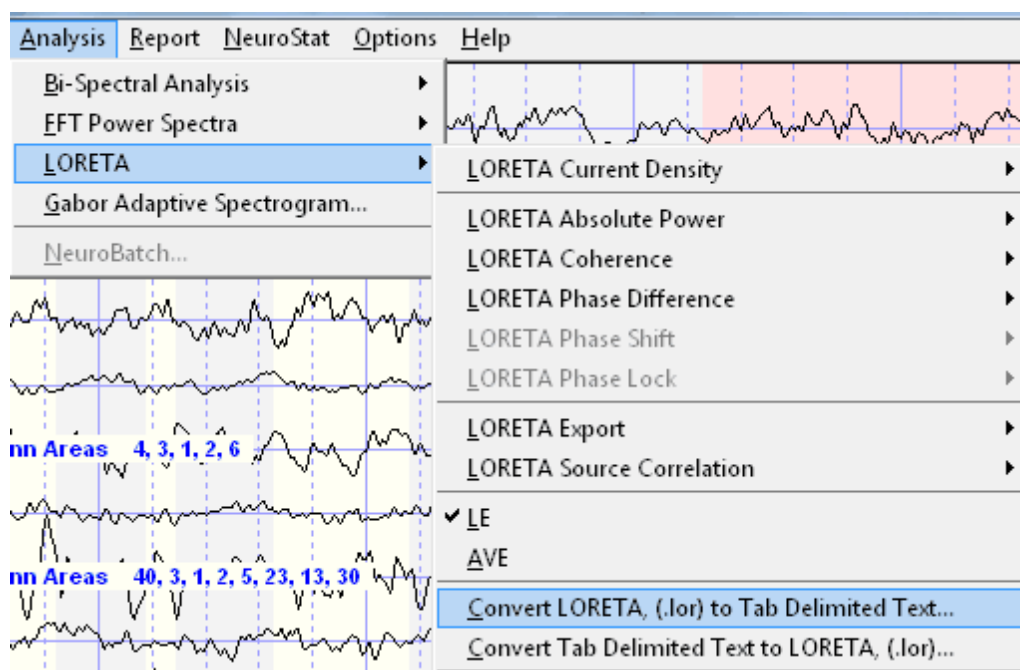
Change Z Score  
Max & Min

Adjust Color  
Extremes

Check "Fit Maximum" to scan  
For a Threshold Z Score Value

In the LORETA Viewer Click "3DSurf" to Open the 3-Dimensional Rendered Brain. Click "Orthoview" to Produce a Full View of the Rendered Brain and the Location of Z Scores. Click "Left" or "Right" to View the Hemispheres.

Convert .lor files for easy import into Excel and other Statistical Packages. The conversion takes 1 column and 71,820 rows (i.e., 30 Hz x 2,394 = 71,820) and transforms to 30 columns (1 to 30 Hz) and 2,394 rows (all gray matter pixels)



## LORETA Export of EEG Time Series in ASCII Format Easy Steps

### NEUROGUIDE TIME SERIES EXPORT

1. After editing the 19 channels of digital EEG, in the NeuroGuide menu bar select Analysis > LORETA Export and click on Overlapping Windows and the Save Export Files window will appear.
2. In the Save Export Files window Click on the create folder button and name the folder Overlap-LE
3. Double click on the new folder (i.e., Overlap-LE), name the files LE and then click Save.

### LORETA Key CROSS-SPECTRUM

1. Download the FREE Key Institute LORETA software ([www.unizh.ch/keyinst/NewLORETA/Software/Software.htm](http://www.unizh.ch/keyinst/NewLORETA/Software/Software.htm)) and then launch it and double click on EEG cross-spectrum (users must first obtain a password to use the FREE Key Inst. Software).
2. From the FREE Key Inst. EEG cross-spectral maker menu select A1EEGs -> 1Spec(aut) and navigate to where you saved the LORETA Export files from NeuroGuide (i.e., step #2). Click Add this folder and click add all sub-folders.
3. Type: Number of electrodes = 19, Number of time frames = 256, sample rate = 128, select





normalize each EEG file, select the top frequency option, click GO.

## LORETA Key 3-D IMAGES

1. Re-Activate the main LORETA window and double click LORETA Explorer for cross-spectra then in the menu bar select File > Open EEG-crs and select the crs file created in steps # 5 & 6, Open Electrode Coords and select Lex-TalairachCoord.xyz, highlight File>Open TransfMatrix and select the file LexTMatrix.tm file. These two files were created using the Key Institute Electrode Coordinates Maker and the Lexicor electrode order for the international 10/20 system of electrodes. Download the coordinate and transfer matrix files at [www.appliedneuroscience](http://www.appliedneuroscience) and click the demo webpage to download.
2. Now click on the part of the spectrum that you are interested in and create the 3-D displays that you are interested in. Try 3Dsurf and ScaleWin and please read the LORETA-Key manual pages 34 and 35.

## Details of Export of ASCII EEG as a Time Series

After making your edit selections in the NeuroGuide edit window, highlight Analysis in the menu bar and select LORETA Export. There are two options: Overlapping Windows or Successive Windows.

For purposes of this demo, select Overlapping Windows by highlighting with the left mouse button. Then click on Overlapping Windows.

### 15b Save Key Inst. Formatted Files in a Folder

Click on the create folder button and name the folder Overlap-LE (e.g., for Cross-Spectral Linked Ears montage). Open the folder & type the file name LE.txt and click save. This will save the successive ASCII files in the Key Inst. Institute format for the A1EEGs -> 1Spec(aut) option.

Selection of the Overlapping Windows option minimizes the FFT windowing effects by overlapping 256 point x 19 channel EEG segments by 75% in ASCII format (see Kaiser & Serman, J. of Neurotherapy, 4(3): 85-92, 2001). This is a standard procedure in NeuroGuide, including the method by which the normative EEG data was analyzed.

The Successive Windows method saves successive 256 point data without overlapping which is not optimal as discussed by Kaiser & Serman, 2001). The user is encouraged to compare and contrast the Successive Windows vs the Overlapping methods in order to see the effects



of the cosine taper windowing of a 256 point FFT.

## Export of ASCII EEG Time Series to LORETA EEG Cross-Spectra and LORETA Explorer

First download the Lex-Talairachcoord.xyz and the Lex-TalairachTMatrix.tm files from the Demo page of [www.appliedneuroscience.com](http://www.appliedneuroscience.com) and save these files in a convenient location. The user must download the free Key Institute LORETA Internet software by going to <http://www.unizh.ch/keyinst/NewLORETA/Software/Software.htm>). Once the Key Inst. Software is installed, launch the LORETA program and double click on EEG Cross-Spectra

Activate the EEG Cross-spectral maker > A1EEGs -> 1Spec(aut)

As described on page 34 of the Key Inst. Documentation the A1EEGs -> 1Spec(aut) option computes 1 single cross-spectral file for each and every 256 point NeuroGuide time series file that the user previously saved as described in section 11a.

Navigate to the location where you created the folder Overlap-LE described in 11a and then click Add this folder -> and add all sub-folders ->. Type 19 as the number of electrodes, type 256 as the number of time frames/EEG file, type 128 as the sampling rate (Hz), click Normalize each EEG file (deselect Force Average Reference users are encouraged to repeat these steps using Force Average to compare and experiment), click the Discrete frequency selection and set the lower end = 1 Hz and the Upper end = 30 Hz then click Go. A cross-spectral file with a \*.crs extension will be saved with the same folder name of Overlap-LE that you created in section 11a.

## LORETA Explorer for EEG Cross-Spectrum

Double click LORETA Explorer for Cross-Spectrum in the main LORETA Key Institute window. Highlight File > Open EEG crs and navigate to the folder where the \*.crs file was saved in section 15b and select the cross-spectral file that you created. Highlight File > Open Electrode Coords and navigate to select the electrode coordinate file for Lexicor. NeuroGuide uses the Lex-Talairachcoord.xyz file which was produced by the Key Inst. Talairach Electrode Coordinate Maker and is compatible with the Lexicor order of electrodes using the LORETA Export menu. Repeat this step and highlight File>Open TransfMatrix and select the file and the Lex-TalairachTMatrix.tm which was also produced by the Key Inst. Software using the Lexicor electrode order.

## Create 3-D Maps

To create 3-D LORETA maps use your left mouse button to select one of the eight frequency



bands and then click View1. 3-D LORETA source localization will appear at the top of the screen.

Click 3Dsurf at the top of the LORETA Explorer menu to activate the cortical surface images. Click Orthoview to produce 9 different views.

In the LORETA Explorer Place the Color Scale Window Below the 3-Dimensional Images. Set the Change Linearity Wiper to the far right and then move the Change Max Wiper to the right and left. Observe how the absolute power values spatially extend from the Midline Visual Cortex or the Midline Occipital Cortex (near to Visual Area 17) and then spreads to Visual Area 18 as the Change Max Wiper.

Save the LORETA Images in jpeg format. Click File and then Save As.

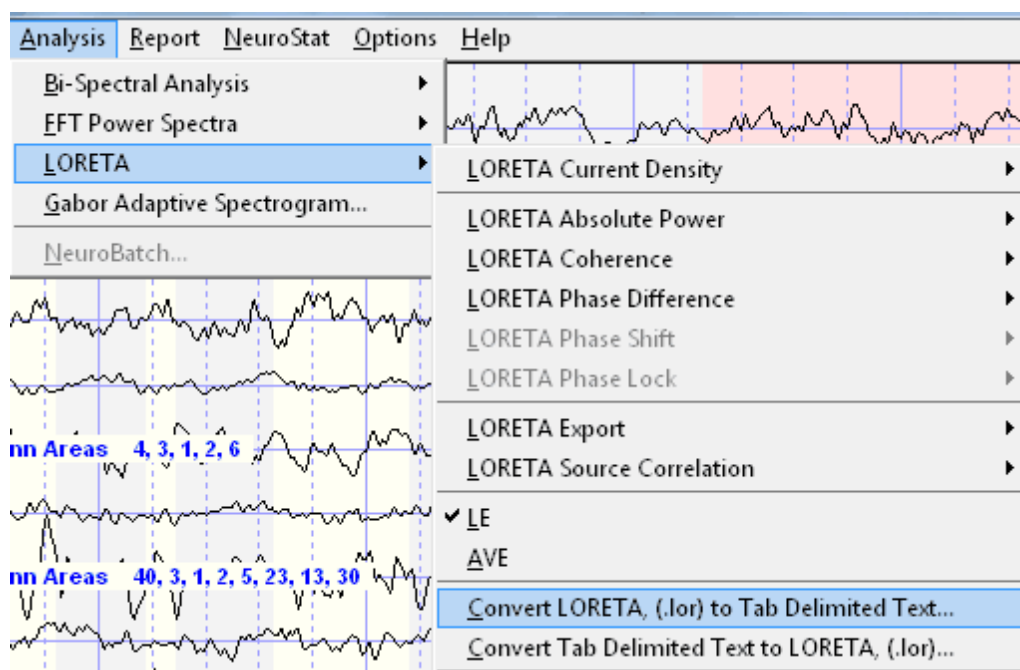
Examine All of the LORETA Slices. Click AllSlicesWin in the LORETA Explorer Menu.

Save the All Slices LORETA images in jpeg format by Clicking Save.

Repeat Step 15a to 16g by importing a different NeuroGuide Output file into the LORETA Explorer by clicking on the Open EEG/ERP menu. Repeat Steps 16b 16g with a different NeuroGuide ASCII time series output, for example, an Eyes Open condition from the same subject and explore the fine details of the 3-Dimensional Sources of the EEG. Enjoy exploring relationships between frequency and 3-D space and brain anatomy using NeuroGuides Exports to LORETA.

## **Export LORETA \*.lor files to Excel and Other Statistical Packages in tab delimited format**

The \*.lor files created by NeuroGuide are 71,820 rows and one column. That is,  $2,394 \times 30 = 71,820$ . Excel and other statistical packages often have limits to the number of rows that can be imported. In order to facilitate export to statistical programs and database programs NeuroGuide provides a tab delimited export utility that converts the NeuroGuide generated \*.lor files into a tab delimited file with 2,394 rows in the Key Institute pixel order and 30 columns of frequency from 1 to 30 Hz. A return conversion from a tab delimited file with 2,394 rows and 30 columns to a \*.lor file with 71,820 rows and 1 column is also available in NeuroGuide.



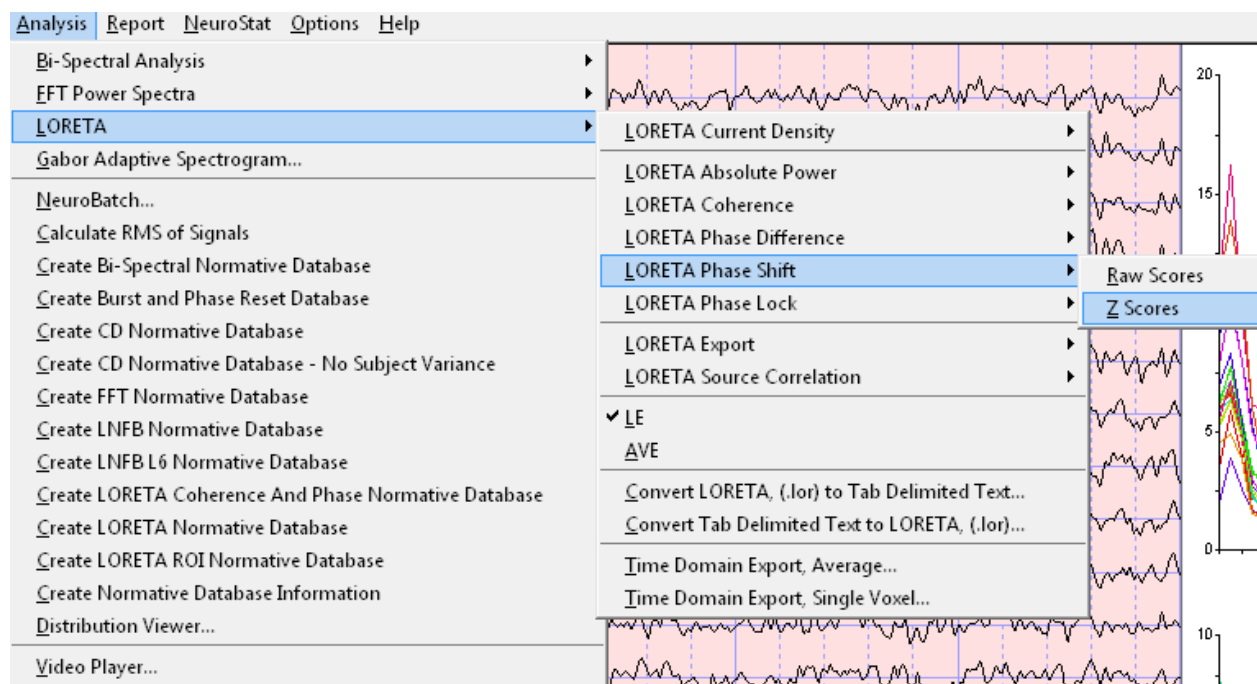
LORETA is a special and excellent program and the user needs to read the LORETA Explorer manual that is provided with the program from the Key Institute before using it.

A number of different tools are available after you launch the Key Institute LORETA programs. Validation of LORETA is necessary before one can trust the solutions that are provided.

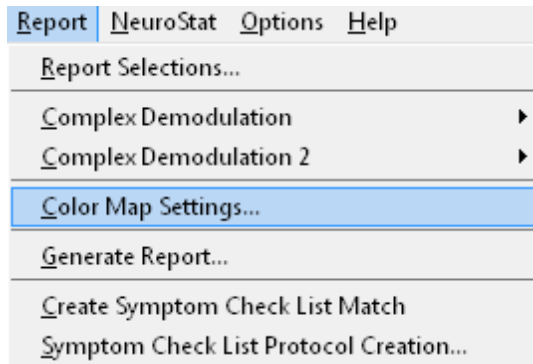
Try validating by comparing Eyes Open vs Eyes Closed changes in amplitude of the alpha rhythms. It is expected that if the visually observed alpha is maximal in O1 and O2, then it should also be maximal in LORETA in the posterior cortical regions and not in the midline Pz lead or in anterior cortical regions, etc. Users must be cautious to validate LORETA to the extent that LORETA is consistent with physiological information and the re-montaged digital EEG.

## LORETA Phase Reset

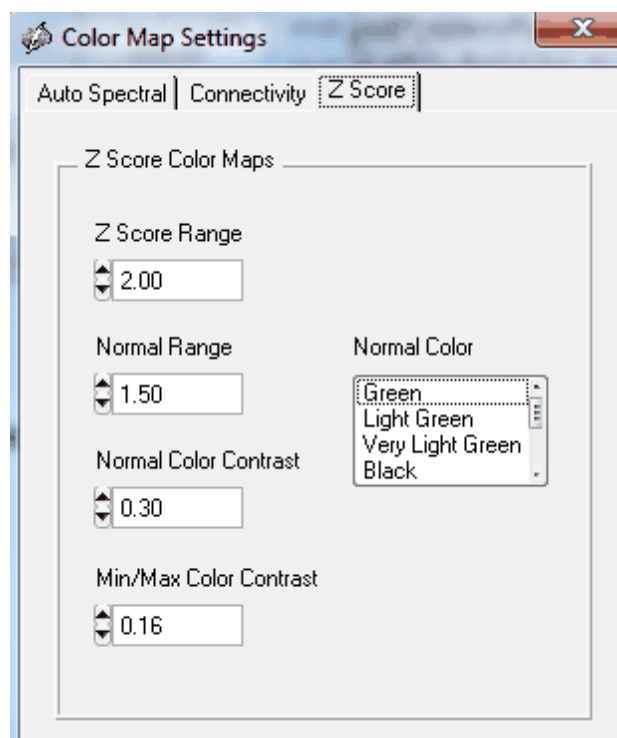
LORETA phase reset is an add on product that is made up of two parts: LORETA phase shift duration and LORETA phase lock duration. After selecting at least 30 seconds of artifact free EEG (& preferably one minute or more) then Click Analysis > LORETA > LORETA Phase Lock or LORETA Phase Shift and select Raw scores or Z Scores. Raw scores are displayed in a contour map with the x-axis as frequency and the y-axis are Brodmann area pairs with respect to each Brodmann area designated at the top of each contour map. The colors of the contour map are scaled in milliseconds as depicted by the horizontal color bar at the bottom of each contour map.



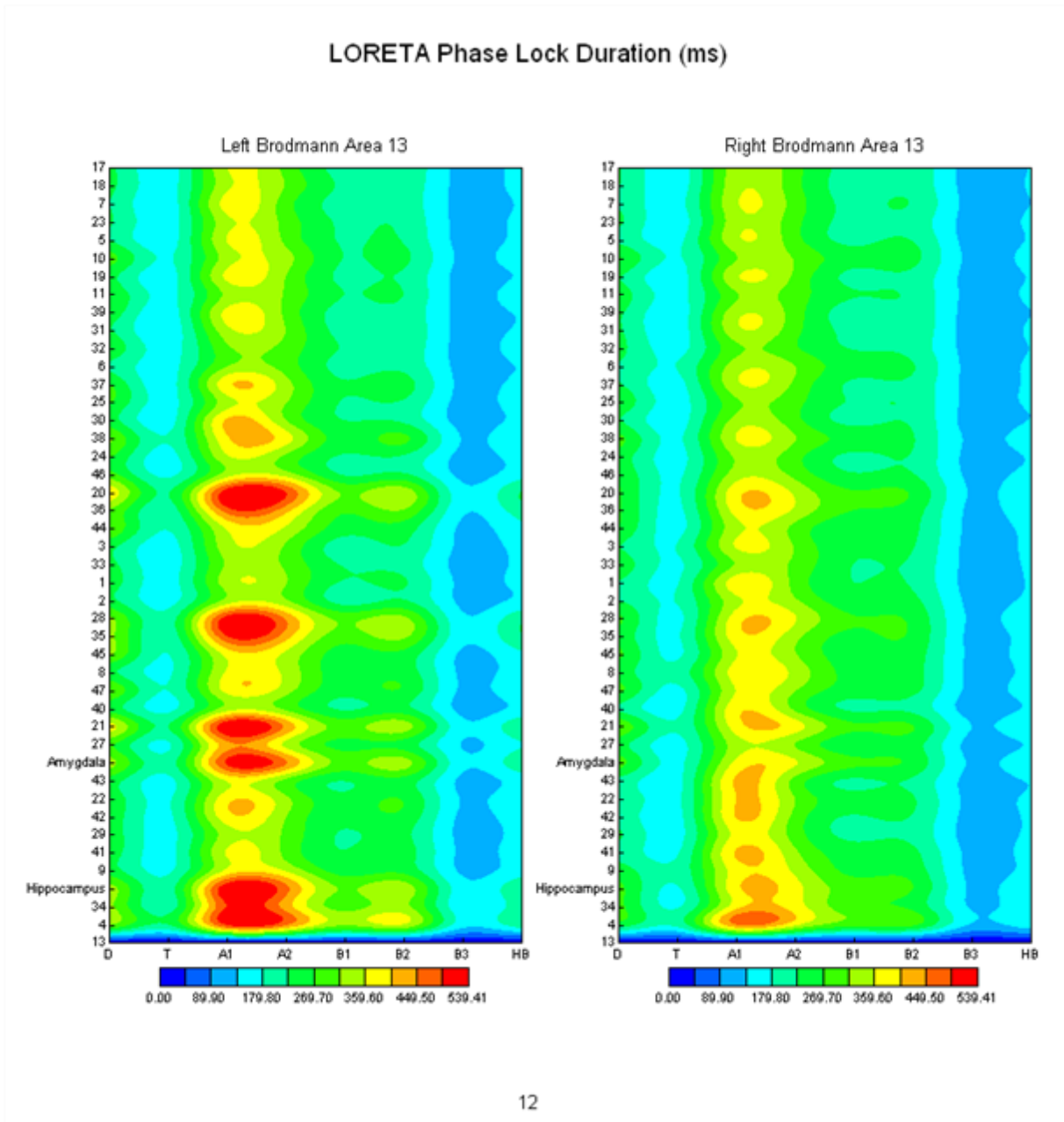
**Adjust the Z Score range for LORETA phase reset Z Scores by clicking Report > Color Map Settings**



**Click the Z Score Tab and open the Z Score color settings panel and set the normal range where the color is green and the deviant or upper Z Score range where the colors are orange to red in the contour maps**

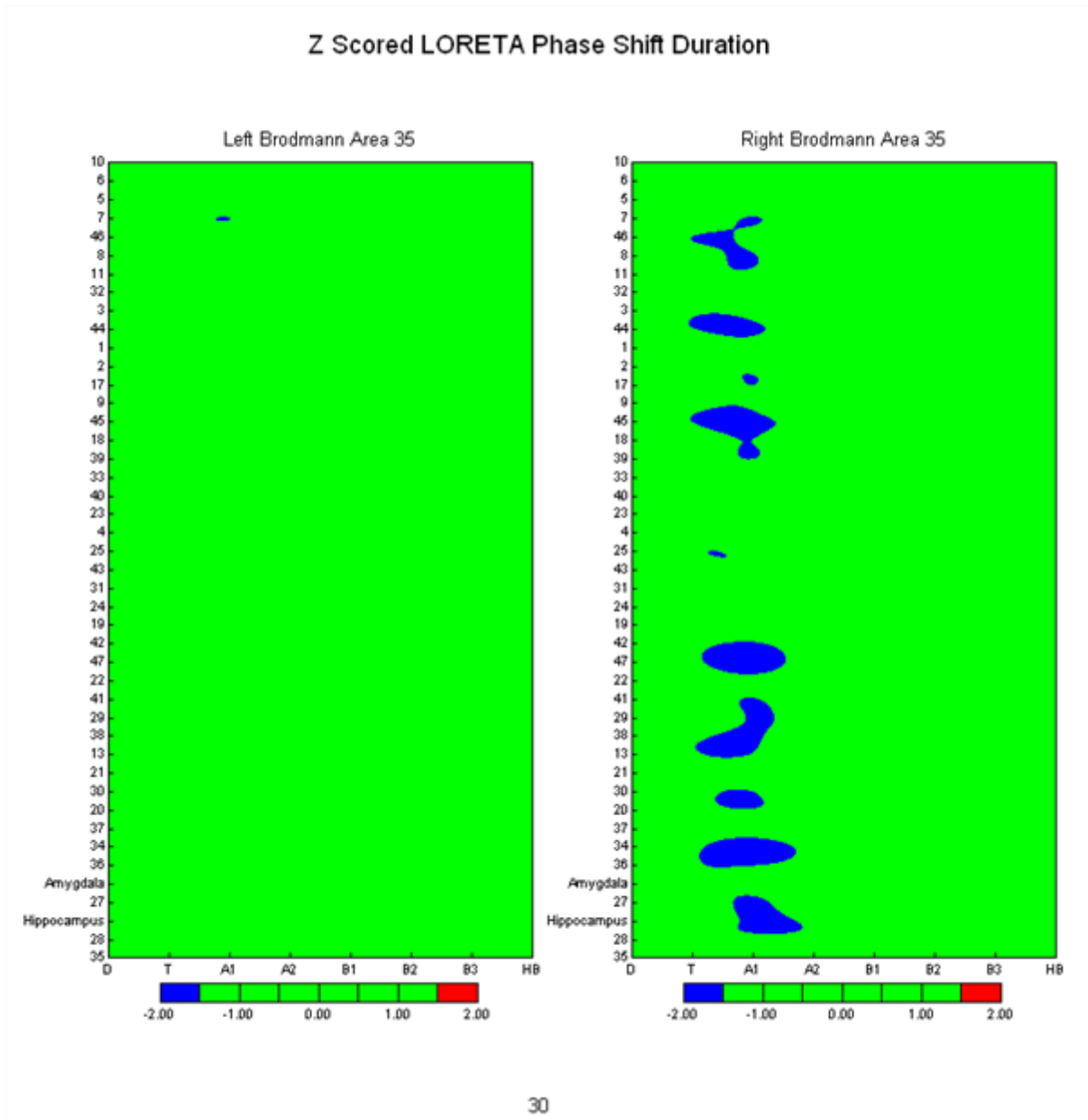


Here is an example contour map of LORETA Phase Lock Duration Raw Scores



Here is an example of LORETA Phase Shift Duration Z Scores





## LORETA Source Correlation Normative Database

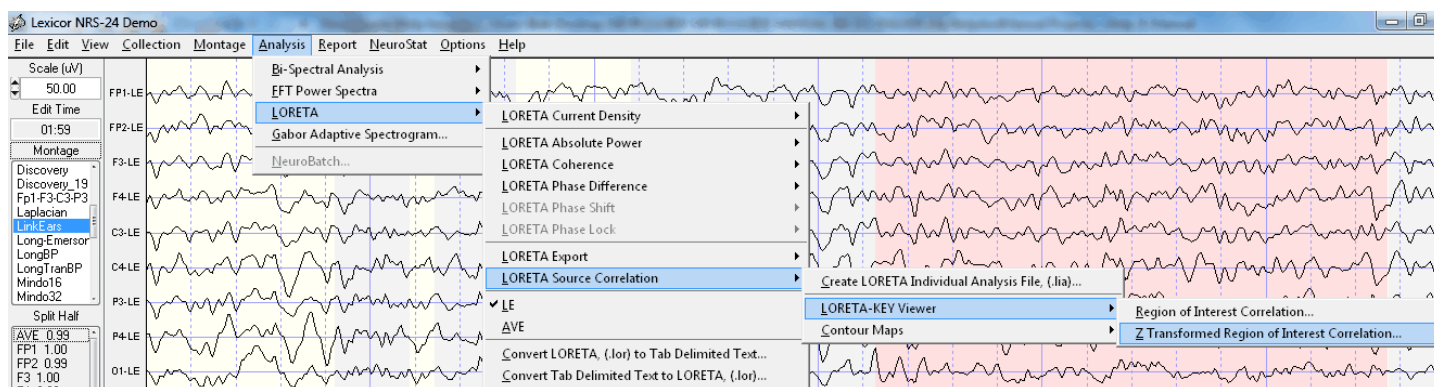
NeuroGuide computes the Pearson Product Correlation Coefficient (-1 to +1) with respect to current density in a 3-dimensional Region of Interest (ROI) and the remainder of the 2,394 LORETA Gray Matter Pixels and then displays the results in either the LORETA Viewer or using Color Contour Maps (see Appendix G). The ROI is identified by either an Anatomical Name or by Brodmann Area. The average current densities of the ROI are used in the computation of the correlation coefficient and the ROI correlation with itself = 0 in the LORETA Viewer.

The NeuroGuide Source Correlation Normative Database is an add on product and the Source

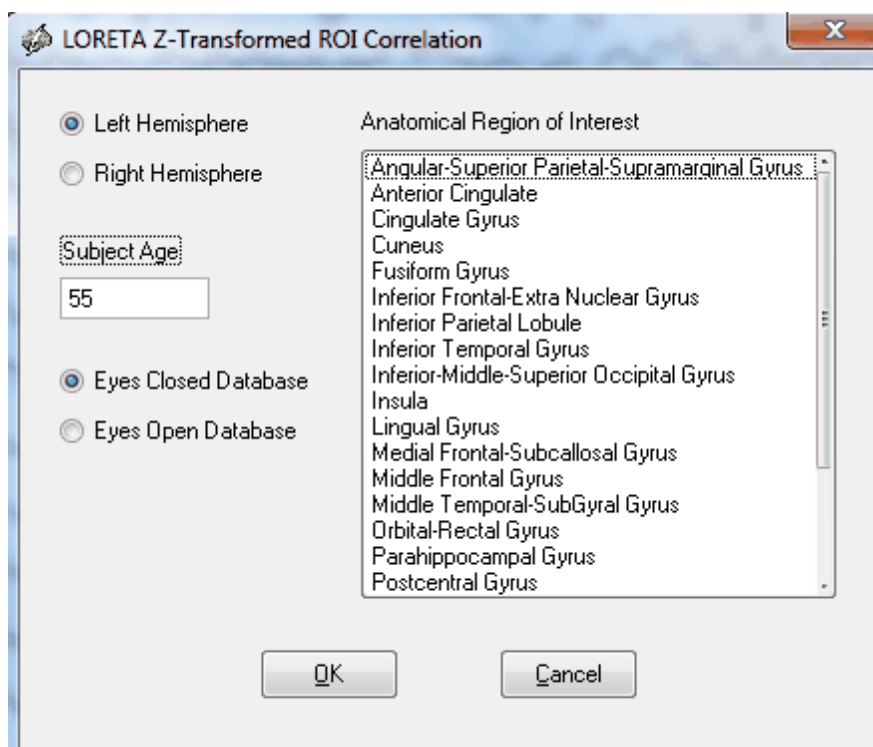


Correlation Normative Database must be [downloaded](#) and installed separately. (see [How to Install the Add-On Normative Databases](#)<sup>13</sup> located in the [Installations](#)<sup>12</sup> section of the [Getting Started](#)<sup>8</sup> part of this Manual) Use the normative database as a reference to evaluate the magnitude and direction of the LORETA source correlation from 6 months to 82 years of age. Because the correlation coefficient is bounded at +1 & -1 the distribution of scores is often kurtotic and skewed and therefore not normally distributed. In order to better approximate a normal distribution the LORETA source correlation of gray matter pixels were averaged within 46 ROIs as compared to the 66 ROIs available for the raw correlations. A table of the 46 ROIs used for the normative database is in Appendix G.

To view regions of interest, click Analysis > LORETA > LORETA Source Correlations > LORETA Key Viewer > Z Transformed Region of Interest Correlations. For raw scores, select Region of Interest Correlations and not the Z Scores



Select the Anatomical Region of Interest, age and hemisphere and click OK



**Select Left or Right or Both Hemispheres and Select Anatomical Names or Brodmann Areas and then Select the ROI to be Correlated with the Remainder of the 2,394 Gray Matter Pixels.**

**Brodmann assigned numbers to various cortical regions by analyzing each area's cellular structure starting from the central sulcus (Area No. 1). Different cell structures resulted in different Brodmann Area numbers. Below are illustrations of the Brodmann areas for the lateral sagittal surface of the cortex as well as the medial surface. Use the illustrations below to aid in deciding which Brodmann Areas and/or Anatomical Locations to be selected.**



## Symptoms, Electrodes & Brodmann Areas

**Frontal Lobe (Fp1/2; F3/4; F7/F8; C3/C4)**  
Thinking, Planning,  
Motor execution,  
Executive Functions,  
Mood Control

**Temporal Lobe (T3/5)**  
language function and  
auditory perception  
involved in long term  
memory and emotion

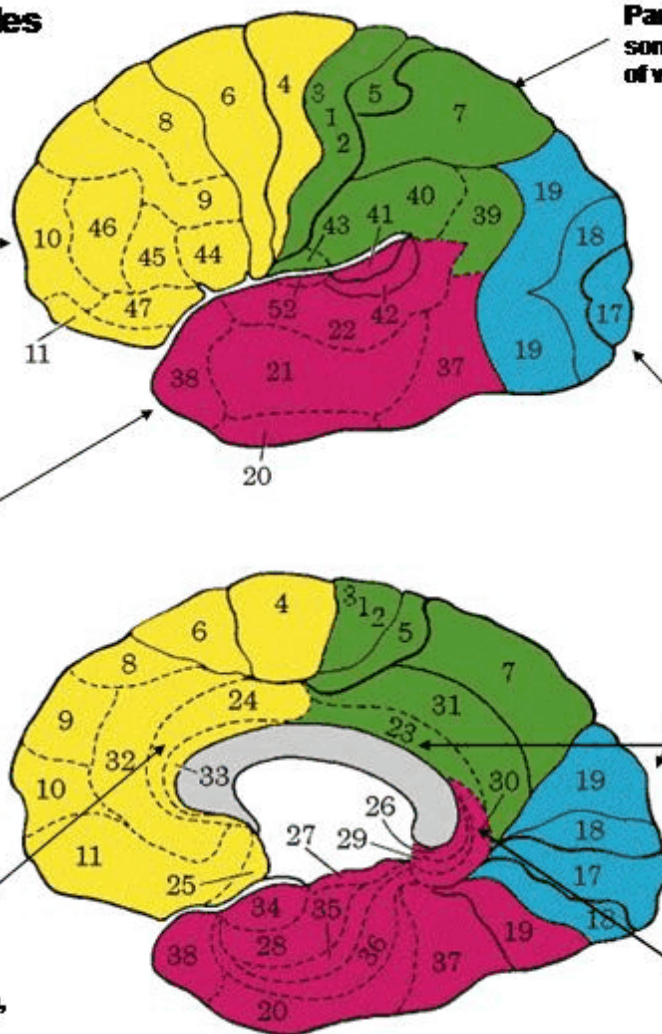
**Anterior Cingulate Gyrus (Fz,Cz,C3/4)**  
Volitional movement, attention,  
long term memory

**Parietal Lobe (P3/4,Pz)**  
somatosensory perception integration  
of visual & somatospatial information

**Occipital Lobe (O1/2,T5/6)**  
Visual perception &  
Spatial processing

**Posterior Cingulate (P3/4,Pz)**  
attention, long-term  
memory

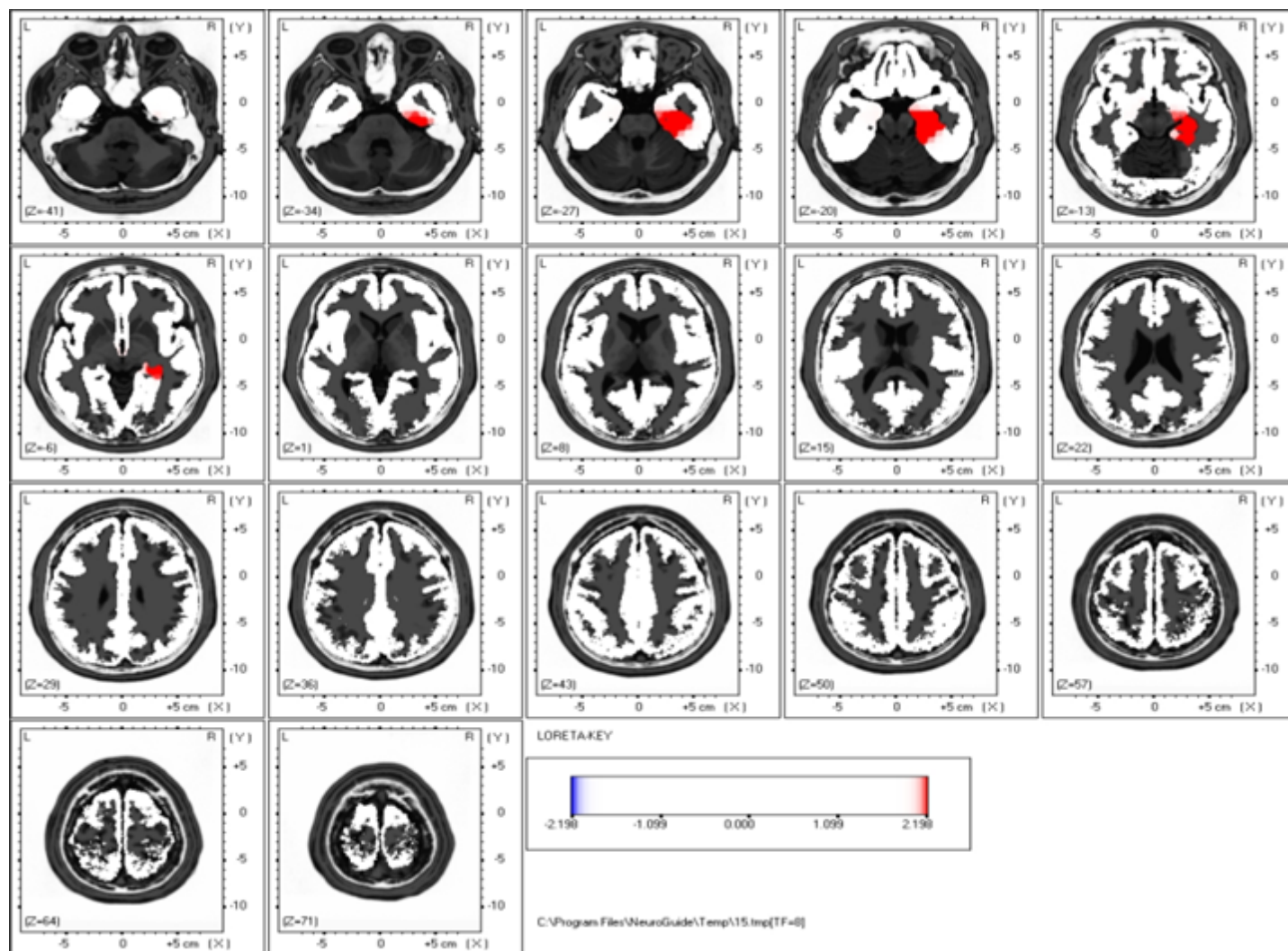
**Parahippocampal Gyrus (P3/4,T5/6,Pz)**  
Short-term memory, attention



Save the Correlation Values in .LOR Format for Later Review or Click Cancel to Launch the LORETA Viewer

After the LORETA Viewer Launches Click ScaleWin and Adjust the Change Max Wiper to the correlation value that is statistically significant based on the Degrees of Freedom (i.e., number of 2 second epochs or the edit time in seconds divided by 2). Then click Time Frame arrows to advance from 1 to 30 Hz and view the correlations between, e.g., the Right Inferior Temporal Gyrus and the remainder of the 2,394 pixels.

Click AllSlices in the LORETA Viewer to Examine Source Correlations between the ROI (e.g., Right Inferior Temporal Gyrus) and the Remainder of the 2,394 Gray Matter Pixels

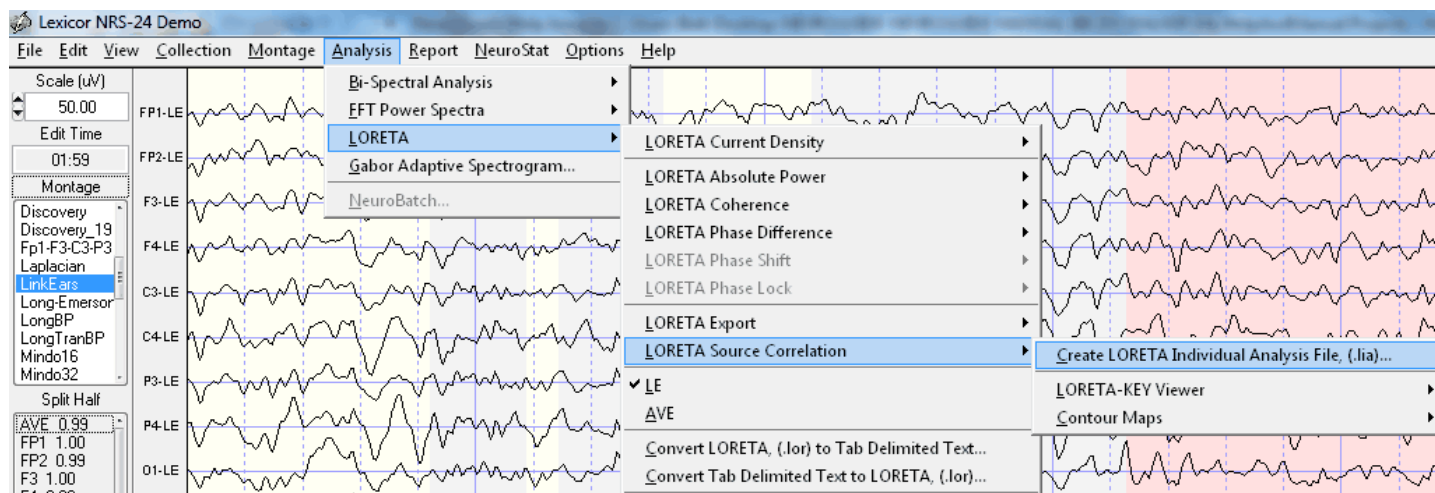


To Activate the Color Contour Maps Click Analysis > LORETA > LORETA Source Correlation > Contour Maps > Region of Interest Correlation

## Create Individual Analysis File (\*.ila)

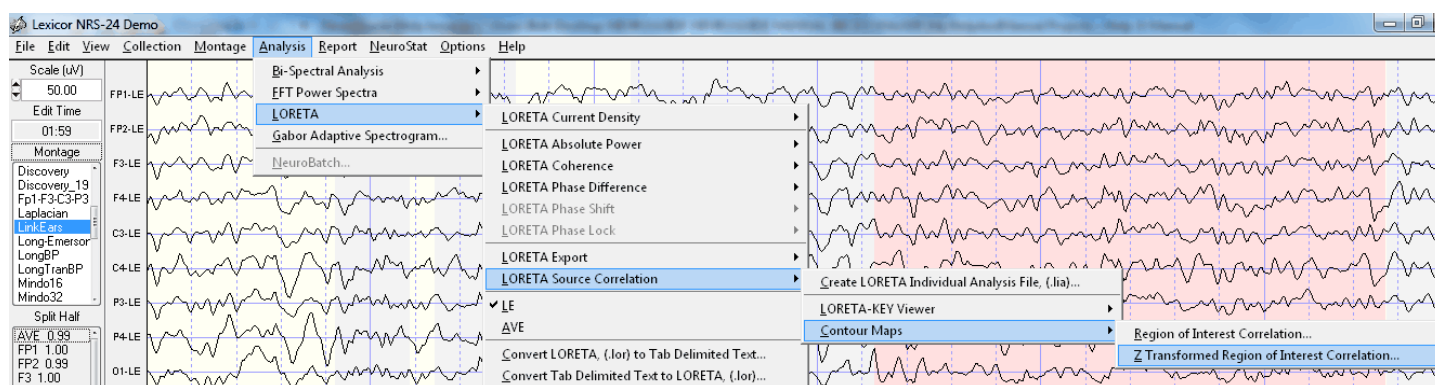
To view the Z Scores of the source correlation normative database click Analysis > LORETA Source Correlation > Create Individual Analysis File (.ila) and save the .ila file in the subject's folder.



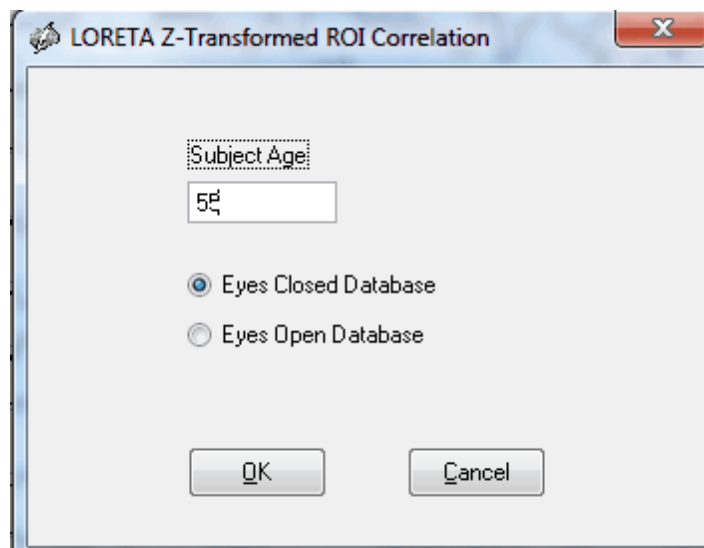


To view source correlations in a contour map, click **Analysis > LORETA Source Correlation > Contour Maps** and then either raw scores for the regions of interest or Z transformed regions of interest. Select the LORETA Individual Analysis File and then name and save the .lor file or click cancel to launch the LORETA viewer. As explained in Appendix G, there was a tendency toward a kurtotic distribution, e.g., 0.13% is expected at 3 standard deviations while the observed cross-validation percentages at 3 standard deviations were .06% and .02%. For this reason users of the LORETA source correlation normative database are recommended to use 2.5 SD or 3 SD as the alpha for clinical comparison purposes.

To View source correlation Z Scores of the normative database using the color contour maps click **Analysis > LORETA Source Correlation > Contour Maps > Z Transformed Regions of Interest Correlations**.



Enter the correct age and the correct database condition of eyes closed or eyes open and then click OK.



**Example of Z Score Color Contour Maps.** The Analysis output page contains four ROI Correlations to 23 left and 23 right hemisphere maps on each page. There are 17 pages so that all 46 ROI correlations are available (see appendix G for details of the selection of 46 ROIs). The X-Axis is frequency from 1 to 30 Hz, the Y-Axis are the 22 ROIs (see table of abbreviations in 17j and on the last page of Analysis output window). The ROIs are ordered by distance from the reference ROI using the Talariach coordinate system (square root of the sum of squares of x, y & z). The absolute distance in millimeters is the first column in the Tab Delimited output (click Save > Tab Delimited Text). The Z-Axis are Z Scores that are color scaled between + & - 3 standard deviations.





## LORETA ROI Correlation

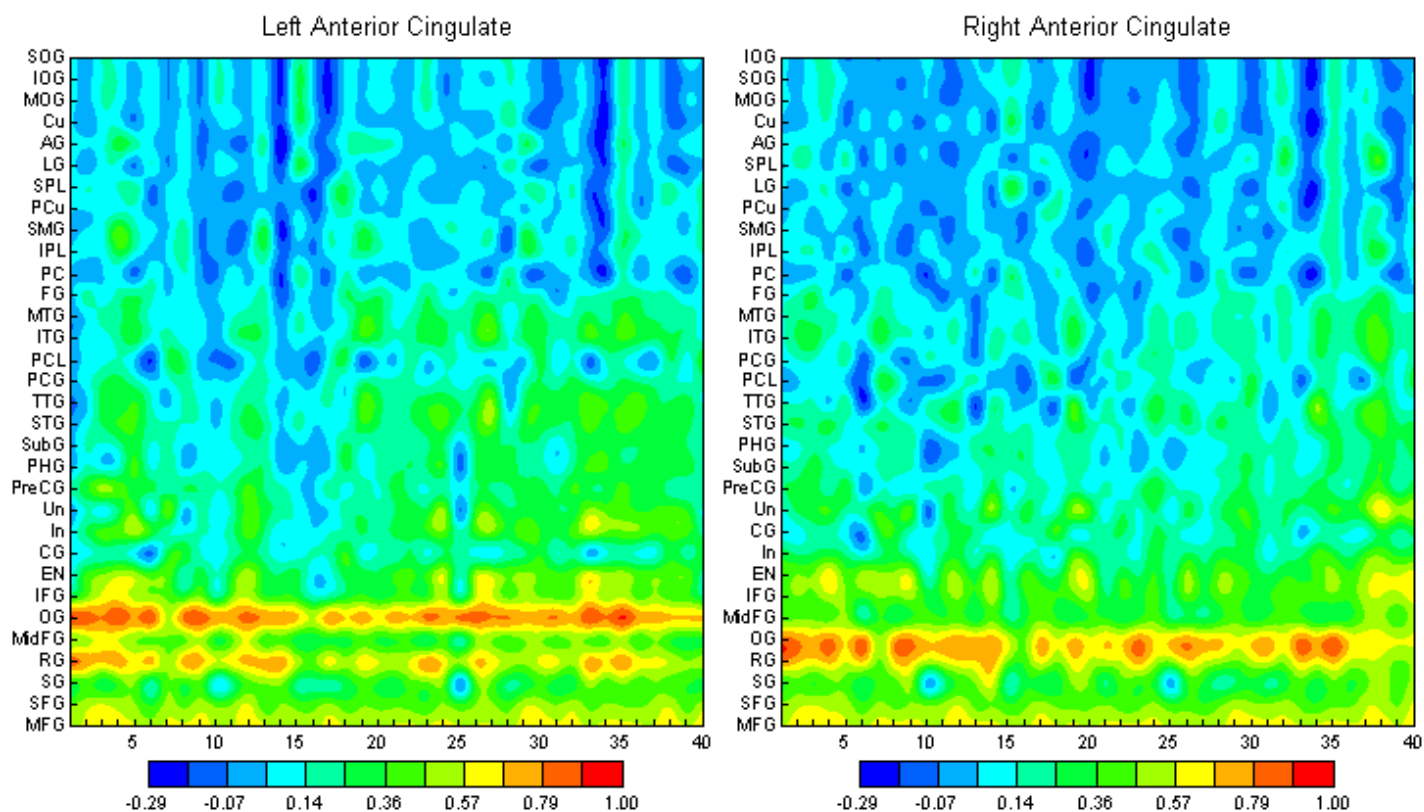


Table of abbreviations of normative database source correlation ROIs is the last page of the color maps in the Analysis Output panel. A smaller number of ROIs ( $N = 23$ ) were used for the normative database in order to achieve adequate approximation to Gaussian and high cross-validations (e.g.,  $> 95\%$ ).

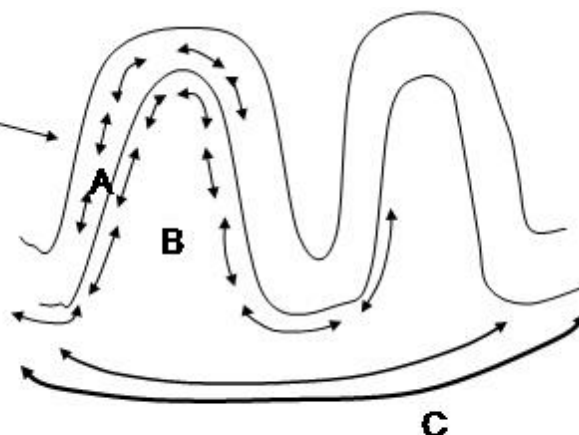


AG	Angular Gyrus
AC	Anterior Cingulate
CG	Cingulate Gyrus
Cu	Cuneus
EN	Extra-Nuclear
FG	Fusiform Gyrus
IFG	Inferior Frontal Gyrus
IOG	Inferior Occipital Gyrus
IPL	Inferior Parietal Lobule
ITG	Inferior Temporal Gyrus
In	Insula
LG	Lingual Gyrus
MFG	Medial Frontal Gyrus
MidFG	Middle Frontal Gyrus
MOG	Middle Occipital Gyrus
MTG	Middle Temporal Gyrus
OG	Orbital Gyrus
PCL	Paracentral Lobule
PHG	Parahippocampal Gyrus
PCG	Postcentral Gyrus
PC	Posterior Cingulate
PreCG	Precentral Gyrus
PCu	Precuneus
RG	Rectal Gyrus
SG	Subcallosal Gyrus
SubG	Sub-Gyral
SFG	Superior Frontal Gyrus
SOG	Superior Occipital Gyrus
SPL	Superior Parietal Lobule
STG	Superior Temporal Gyrus
SMG	Supramarginal Gyrus
TTG	Transverse Temporal Gyrus
Un	Uncus

Neurophysiological model used to explain and interpret source correlation maps is based on Braitenberg "Cortical architectonics: general and areal". In: Architectonics of the cerebral cortex, edited by M.A.B. Brazier and H. Petsche, New York, Raven Press, 1978, pp. 443-465 and Schulz, A. and Braintenberg, V. "The human cortical white matter: Quantitative aspects of cortico-cortical long-range connectivity". In: Cortical Areas: Unity and Diversity, edited by A. Schultz and R. Miller, Conceptual Advances in Brain Research, London, 2002, pp. 377-386. See Thatcher et al "[Spatial-Temporal Current Source Correlations and Cortical Connectivity](#)" (*Clinical EEG and Neuroscience*, 2007 Vol. 38(1): 35-48. To download copy visit [www.appliedneuroscience.com](http://www.appliedneuroscience.com) and highlight Articles & Links and click on Articles).

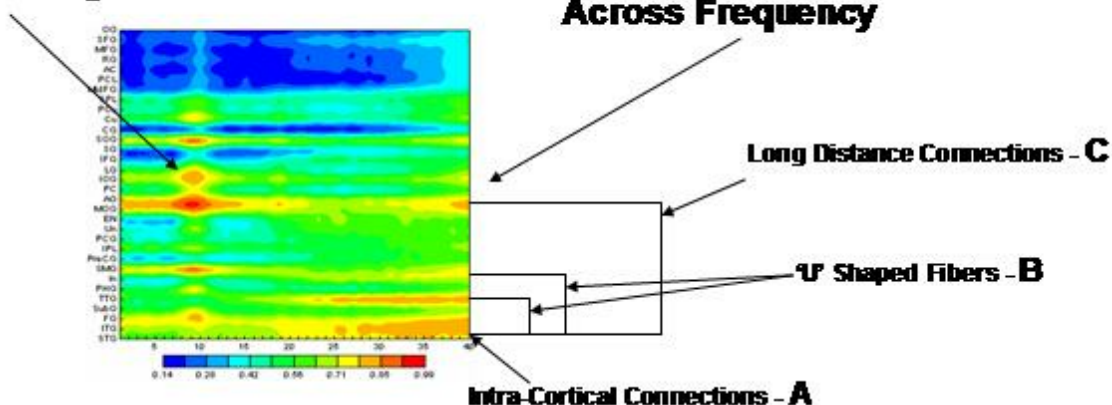


### Braitenberg's Cortico-Cortical Connection Model



### Vertical Features = Frequency Multiplexing to Multiple ROIs

### Horizontal Features = Cortico-Cortical Fiber System Across Frequency



Red = High Correlations, Green = Small Correlations and Blue = Near Zero and Negative Correlations

**Example of Color Contour Maps.** The Analysis output page contains four ROI Correlations to 32 left and 32 right hemisphere maps on each page. There are 17 pages so that all 66 ROI correlations are available. The X-Axis is frequency from 1 to 40 Hz, the Y-Axis are the 32 ROIs (see table of abbreviations in 17j and on the last page of Analysis output window). The ROIs are ordered by distance from the reference ROI using the Talariach coordinate system (square root of the sum of squares of x, y & z). The absolute distance in millimeters is the first column in the Tab Delimited output (click Save > Tab Delimited Text). The Z-Axis are correlation coefficients that are color scaled between the maximum and minimum values.

ROI Abbreviation Table is on the last page of the Analysis Output

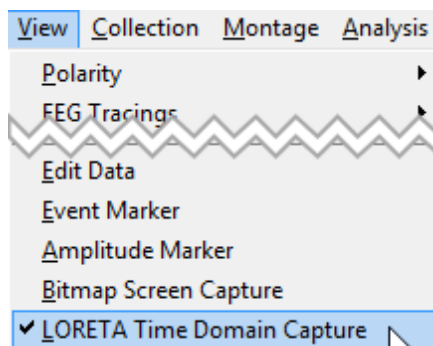


An-SP-PG	Angular-Super Parietal-Supramarginal Gyrus
AC	Anterior Cingulate
CG	Cingulate Gyrus
Cu	Cuneus
FG	Fusiform Gyrus
IF-EnG	Inferior Frontal-Extra Nuclear Gyrus
IPL	Inferior Parietal Lobule
ITG	Inferior Temporal Gyrus
IMS-OG	Inferior-Middle-Superior Occipital Gyrus
In	Insula
LG	Lingual Gyrus
MF-SG	Medial Frontal-Subcallosal Gyrus
MFG	Middle Frontal Gyrus
Mt-SG	Middle Temporal-SubGyral Gyrus
Or-RG	Orbital-Rectal Gyrus
PHG	Parahippocampal Gyrus
PCG	Postcentral Gyrus
PC	Posterior Cingulate
PCu	Precuneus
Pre-PCL	Pre-Para Central Lobule-Gyrus
SFG	Superior Frontal Gyrus
S-TTG	Superior-Transverse Temporal Gyrus
Un	Uncus

To Save the Color Contour Maps in Bitmap Format Click Save > Bitmaps Graphics Files. Then create a folder and name the files and then save them. Click Save > Tab Delimited Text to save the raw correlation files in text format.

## LORETA Time Domain Capture

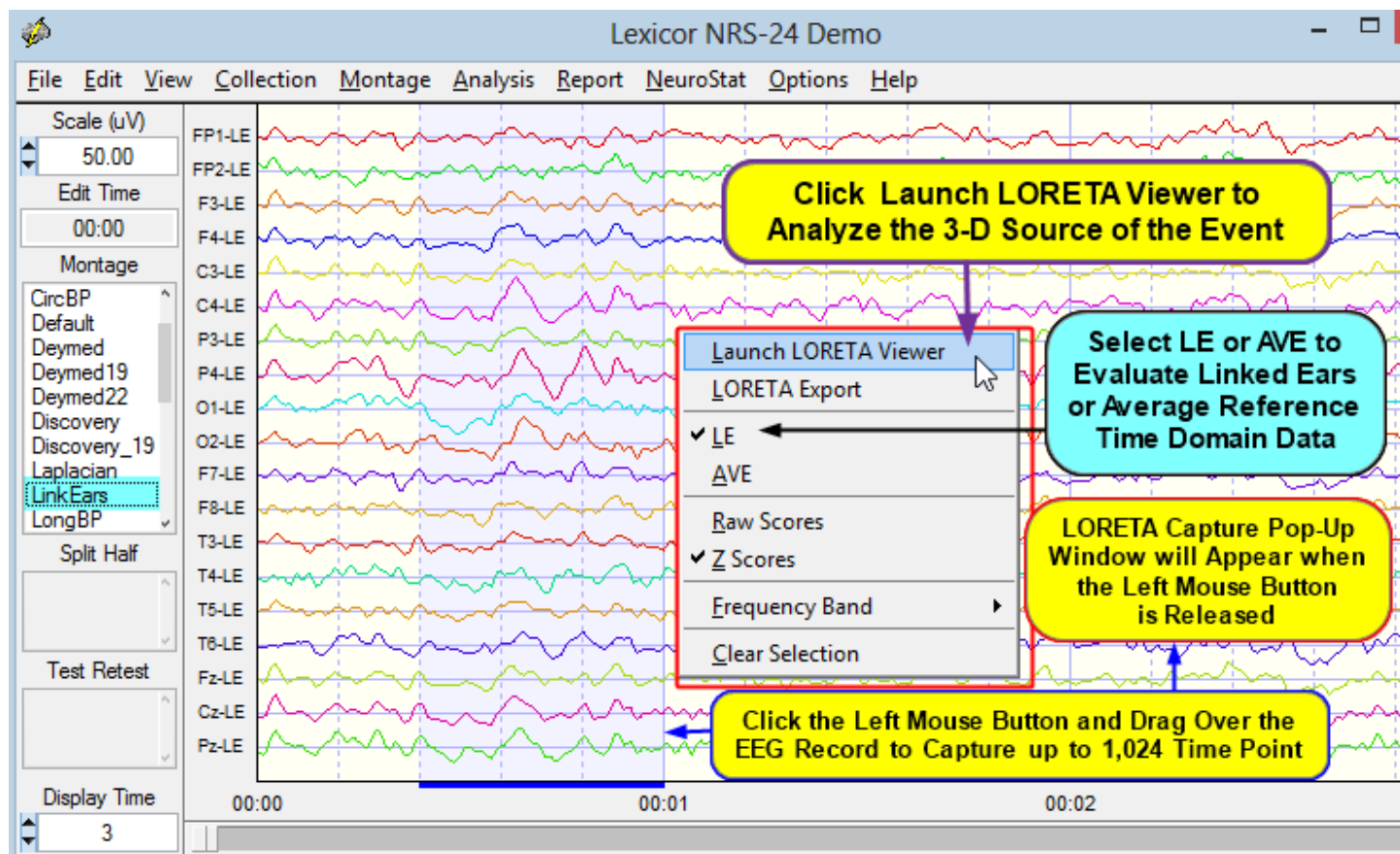
LORETA Time Domain Capture tool allows for 3-Dimensional source analysis of a selected time series (1,024 maximum number of time points). For example, the source localization of a theta or beta burst or a spike & wave event in the EEG traces can be exported to the Key Institute LORETA program for rapid analysis of an EEG event. The LORETA Time Domain Capture tool is activated by Clicking View > LORETA Time Domain Capture. Note this feature will only work after you install the Key Institute's LORETA-Key Software package (see the [Installation](#)<sup>12</sup> section of the Getting Started Manual & Tutorial).



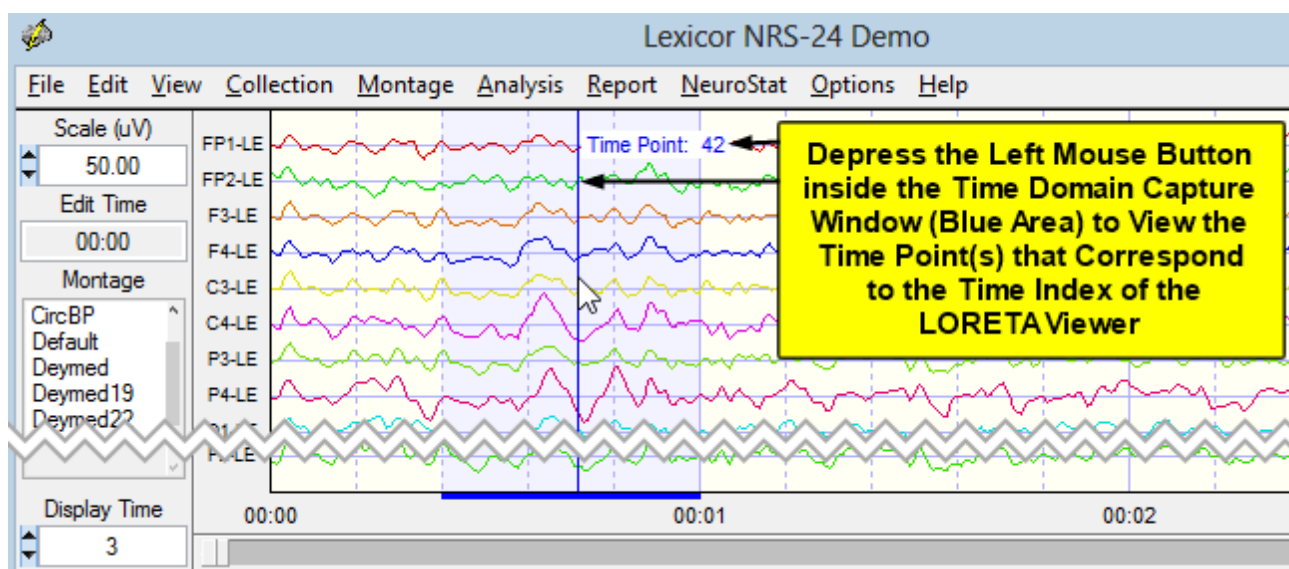
Capture up to 1,024 time points to be exported to the Key Institute LORETA software by clicking the Left Mouse button and dragging over the EEG record. Release the mouse button



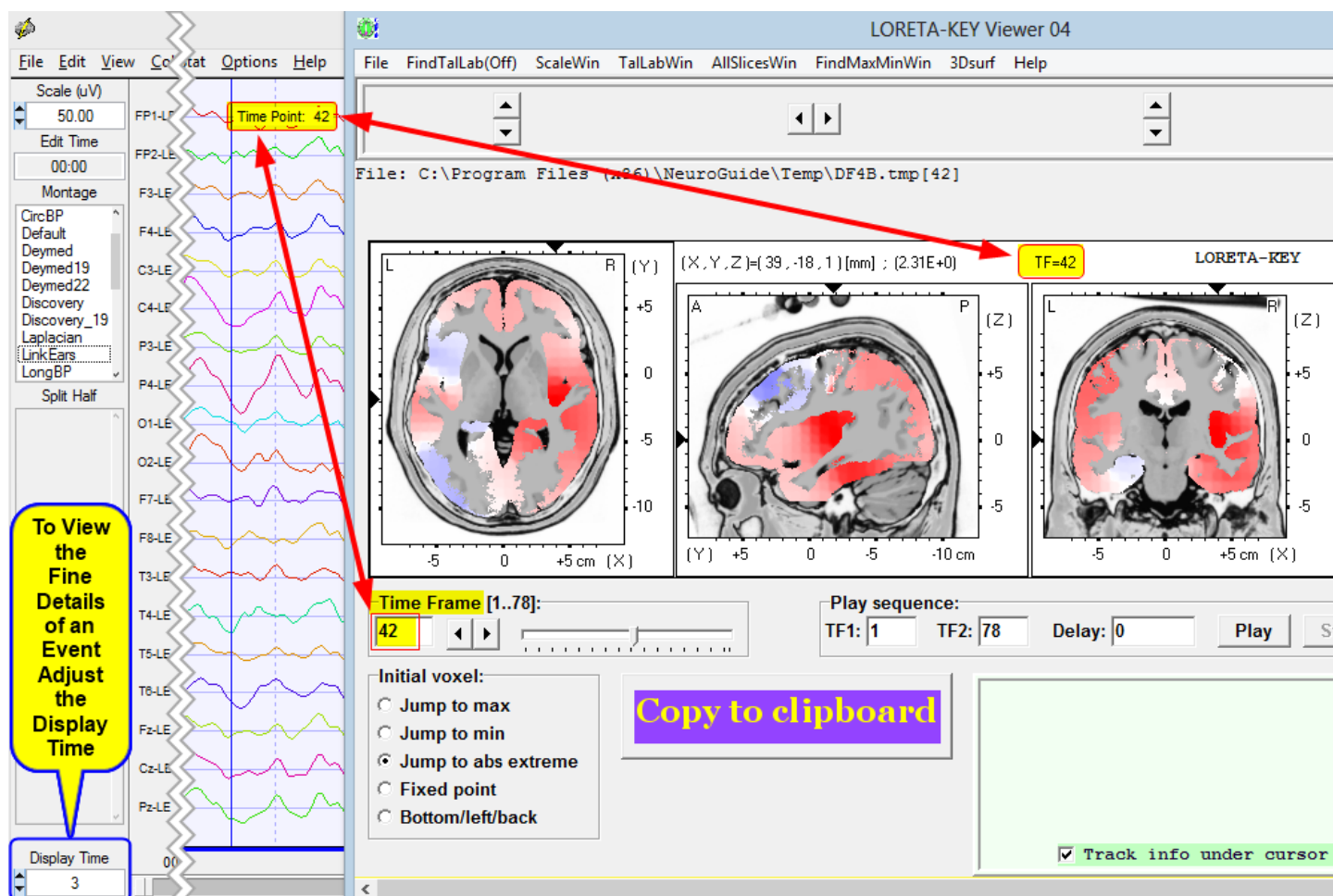
and the LORETA capture pop-up window will appear. Select Launch LORETA Viewer to analyze the 3-D sources of the events. Select LE or AVE to evaluate linked ears or average reference time domain data.



Depress the Left Mouse Button inside of the Time Domain Capture Window ( Light Blue area) to view the Time Index which corresponds to the Time Index of the LORETA Viewer. This allows one to match the Time Point-by-Time Point Analysis of the Raw Digital EEG and the Time Domain 3-D Sources produced by LORETA.

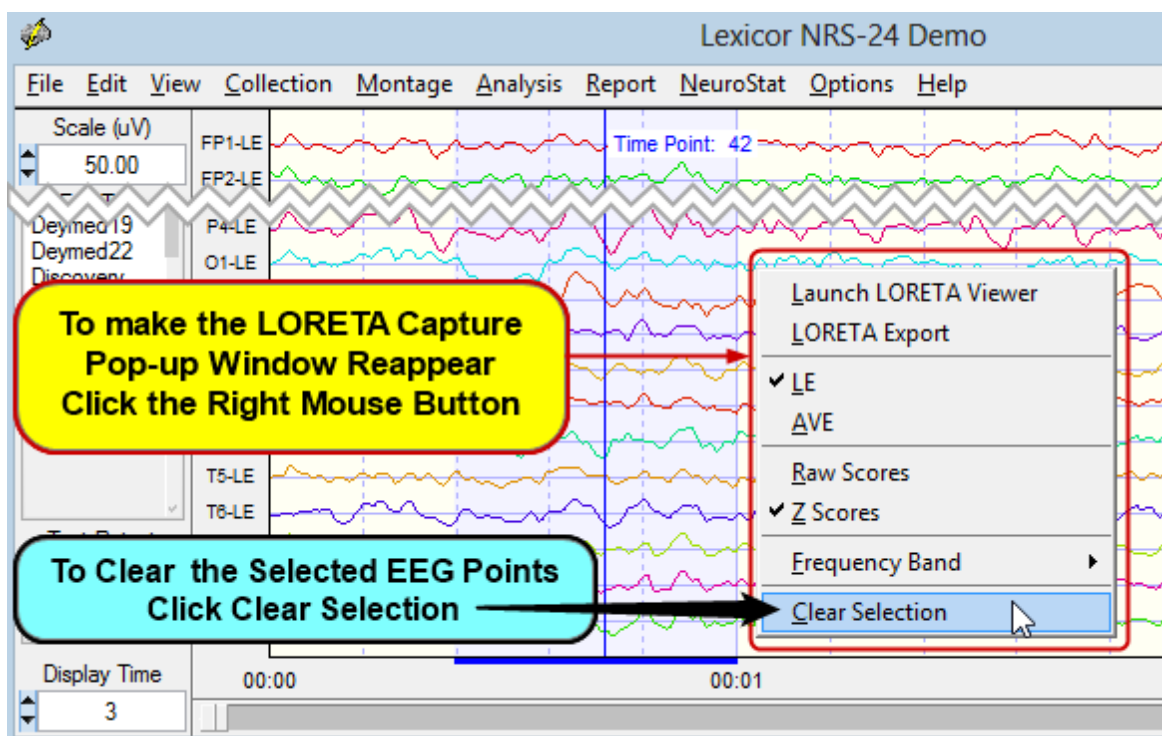


**Example of LORETA Time Domain Analyses.** This is Time Point #42 as Indexed by the Left Mouse Button and the Key Institute's LORETA Viewer at Time Frame #42. Adjust the Display Time to 3 Seconds in order to better view the fine temporal details of a Theta Burst. The time point of an event of interest depends upon the start and ending point of the selection of the EEG record by depressing the left mouse button and dragging the mouse to create the selection. Therefore, the exact time point for an event will change if a different selection window is created.



Click the Right Mouse Button to make the LORETA Capture Pop-up Window reappear. Click Clear Selections to clear the selected EEG points. Now you are ready to select different digital time points by depressing the Left Mouse Button and dragging it over a different EEG Event or Selection.





## Create and Label Montages (1 to 85 channels. Up to 128 channels for customized electrode placements)

Click Montage > Select Montage in the Montage Menu to view the locations and channel labels used in NeuroGuide.

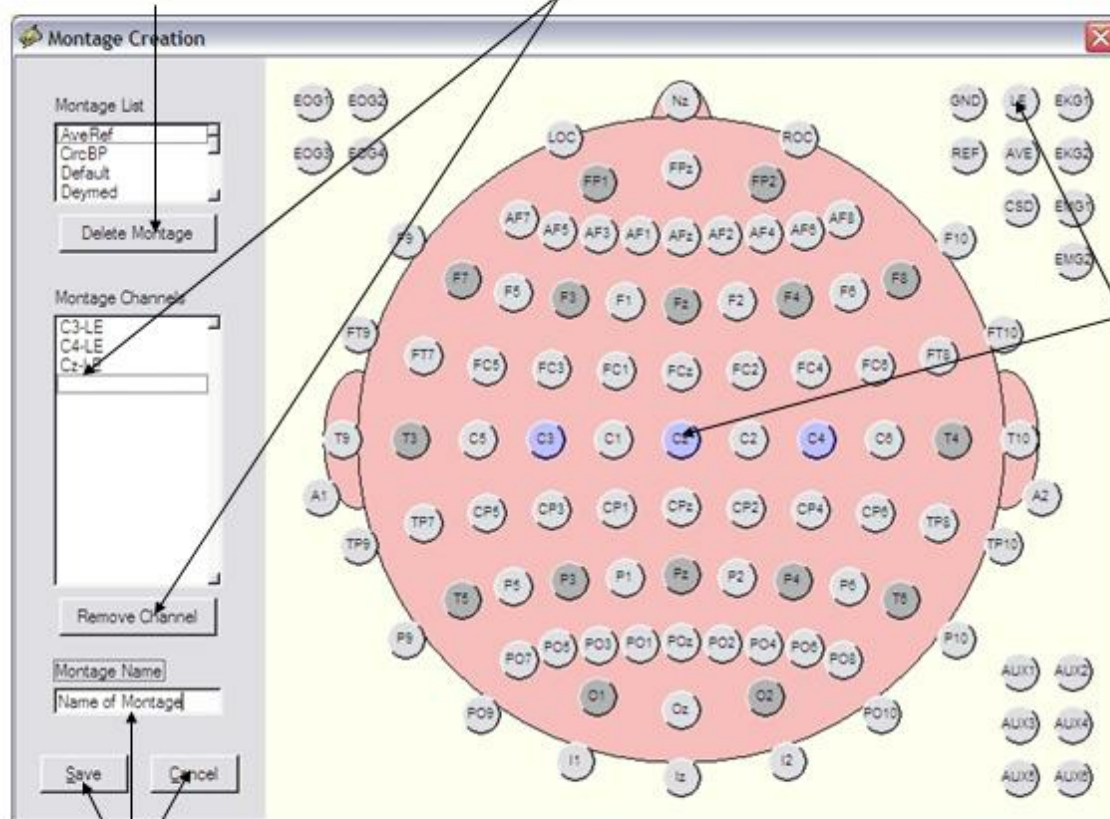
Click a Montage in the Montage List to view the electrode order and references that are present in the left column of the EEG View screen





**To Delete a Montage**  
Select and then click  
Delete Montage

**To correct mistakes click**  
Channel and then click  
Remove Channel



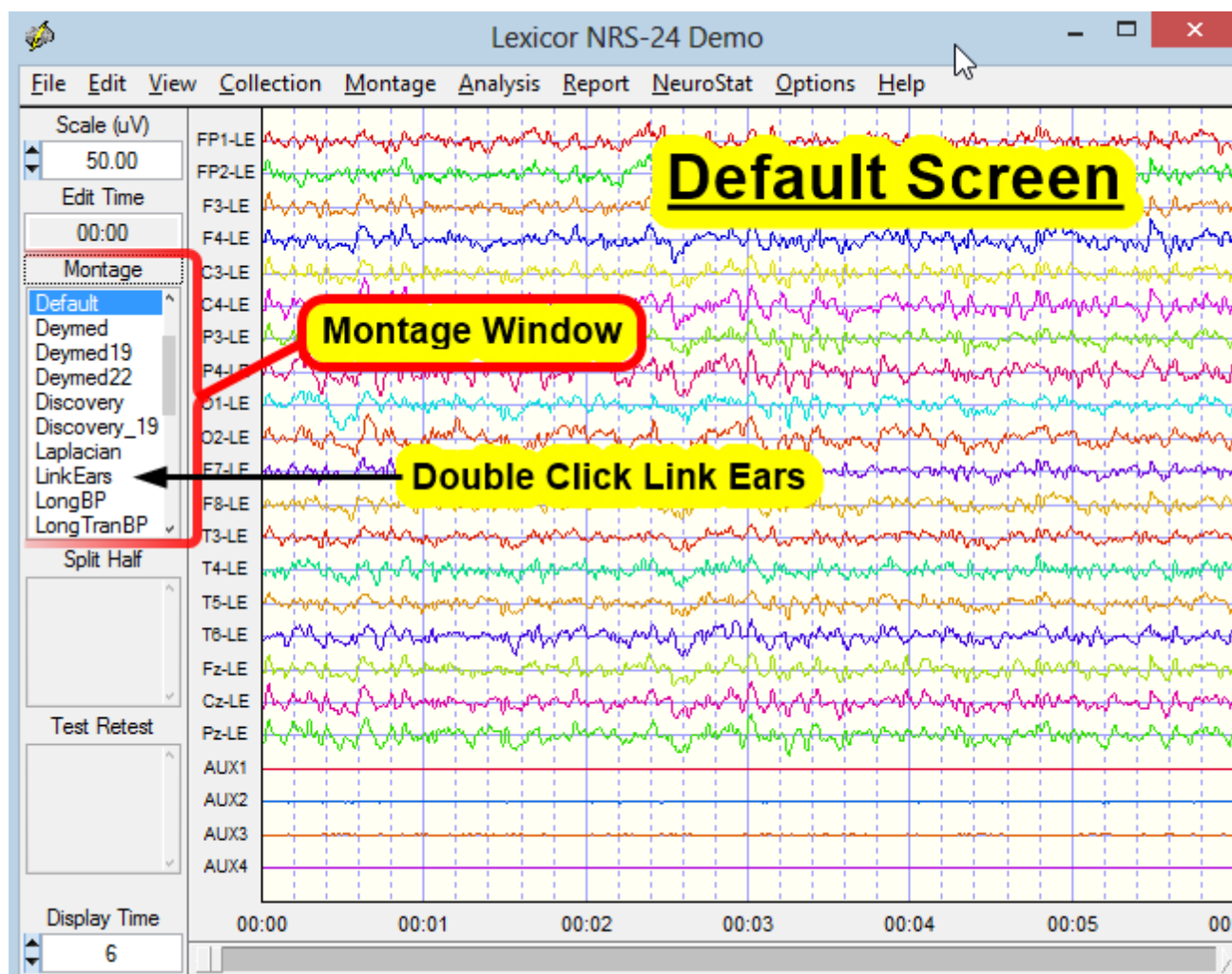
**Click on a channel**  
and then a reference

**Name the Montage**  
Then click Save and Close

If You Make a Mistake or Want to Remove an Electrode Selection, Double Click on the Electrode and then Click Remove Channel. To Delete a Previously Created and Saved Montage, Click on the Montage and then Click Delete Montage. Click Close to Return to the EEG Display or Create and Save A New Montage.

**Re-montage, Scale and Visually Scan the EEG and then further visually scan the EEG for Artifact, Epoch Length and the General Status of the EEG.**

Default Screen Contains Linked Ears Reference Digital EEG, Colored EEG Tracings, 6/sec vertical grid lines, and Polarity = Positive Up.



**Double Click different montages, Average Reference, Longitudinal Bipolar, Transverse Bipolar, Circular Bipolar, Laplacian, etc.**

## **Neurofeedback - 1 to 19 Channel Surface EEG**

Nineteen scalp electrodes distributed according to the 10/20 system measures the scalp electrical field generated by cortical pyramidal neurons rhythmically modulated by thalamo-cortical, cortico-thalamic and cortico-cortical connections. Therefore, the design of the NeuroGuide Neurofeedback module (NF1) is to compute Z Scores of the EEG 10/20 electrical field of 19 channels referenced to linked ears (mathematically linked and/or physically linked). In this way one can select and use the autospectral and cross-spectral measures such as absolute power, phase shift duration, phase lock duration, coherence, phase differences and amplitude asymmetry. In addition, with 19 channels there are approximately 8,000 EEG measures that can be computed. In order to reduce the number of variables to a logical and practical first "guess" of the most optimal variables NeuroGuide uses a Hypothesis-Test



process. The process is based on the goal to facilitate the user's ability to link symptoms and complaints to "Hubs" or "Functional Modules" by use of a symptom check list and QEEG Z Scores. The symptom check list is used to create "hypotheses" as to the most likely scalp locations related to functional systems in the brain based on modern neuropsychological, neurological, electrophysiological and functional imaging neuroscience. The hypotheses are then tested by running a quantitative EEG analysis to match and mismatch the hypothesized scalp locations to the "observed" locations of deviant Z Scores. Scalp locations of deviant EEG Z Scores are divided into two categories:

- 1) Match to Symptom Locations; and
- 2) Mismatch to Symptom Locations.

The match to symptom locations are considered to represent the "weak" systems related to the symptoms and complaints while the mismatch locations are considered to represent "compensatory" systems as part of the homeostatic balance of dynamically linked "Hubs" and "Functional Modules". Based on this logic a drastically reduced number of EEG variables (e.g., 20) are automatically selected as a Neurofeedback Protocol out of a universe of approximately 8,000 measures.

**There are six steps that must be followed to use the symptom check list and automatic Z Score protocol generator:**

1. Import an edited \*.ng EEG file by clicking File > Open
2. Click Report > Symptom Check List Match
3. Click Collection > Setup & Monitor > OK
4. Click Collection > Neurofeedback > Surface EEG
5. Click Symptom Check List in the Surface EEG Control Panel
6. Select the Symptom(s) that best represent the patient's symptoms and assign a severity from 1 to 10 for each symptom, then click OK.

There are three 10/20 scalp displays with the one labeled "Hypotheses" created by the Symptom Check List. The size of the green circle expands as a function of a relative severity index (average of the sum of channels x severity score and then scaled to the largest value). The top right 10/20 scalp display shows the symptom check list match to QEEG Z Scores from steps 1 and 2 above. The size of the green circles is scaled according to the largest average Z Score for a given scalp location and is considered as an estimate of the "weak" functional

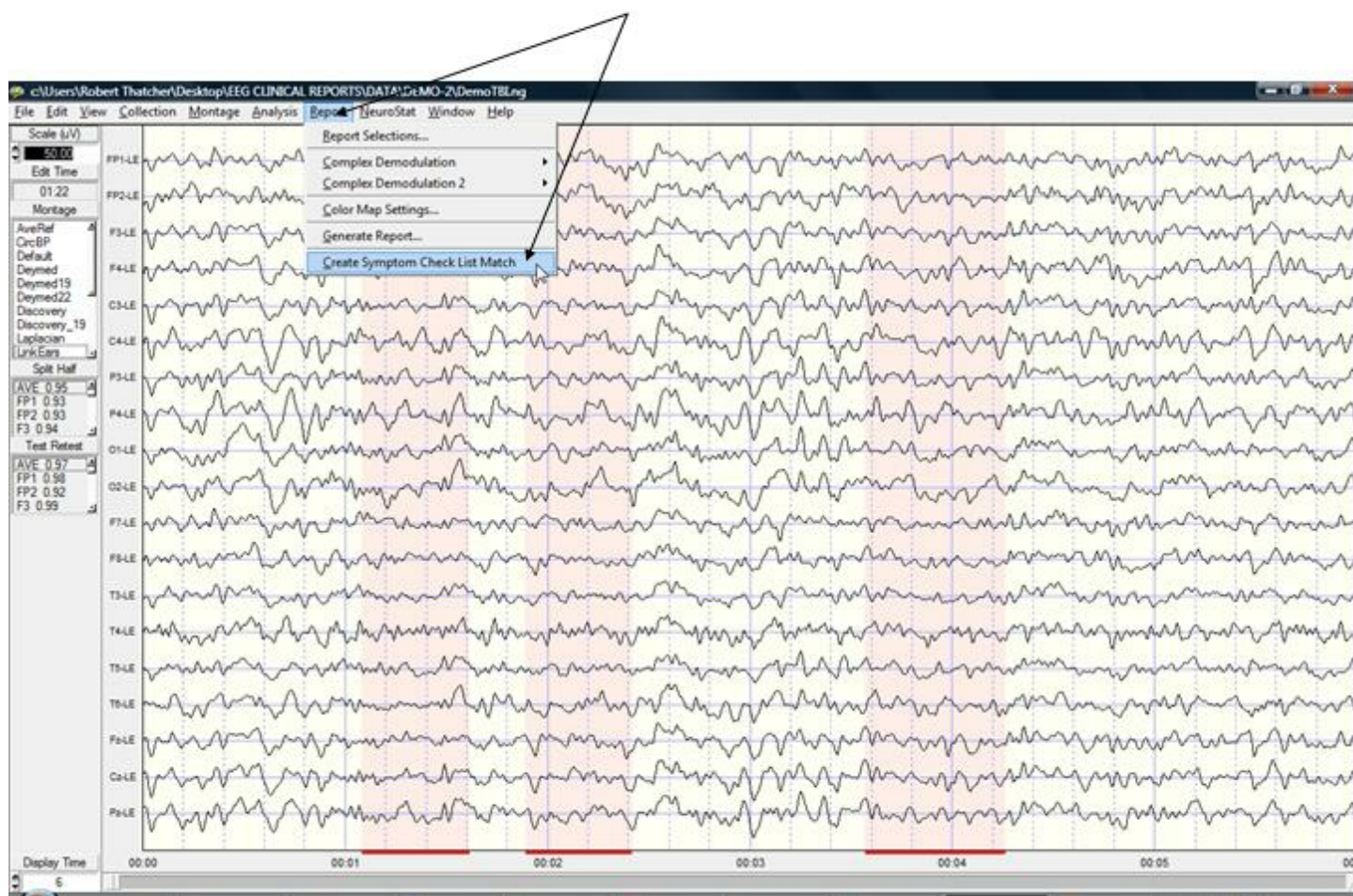




systems. The lower right 10/20 scalp display shows the mismatches and is considered an estimate of the "Compensatory" systems. The absolute Z Score control can be varied from 0 to 10 standard deviations. As Z Scores increase then the number of matches in the top right head display is reduced and vice versa. Default is  $Z = |Z|$  (absolute Z).

First Import the Patient's Edited EEG samples and click Report > Create Symptom Check List Match to generate temporary Z Score files to be used in the Hypothesis testing and construction of a Neurofeedback Protocol

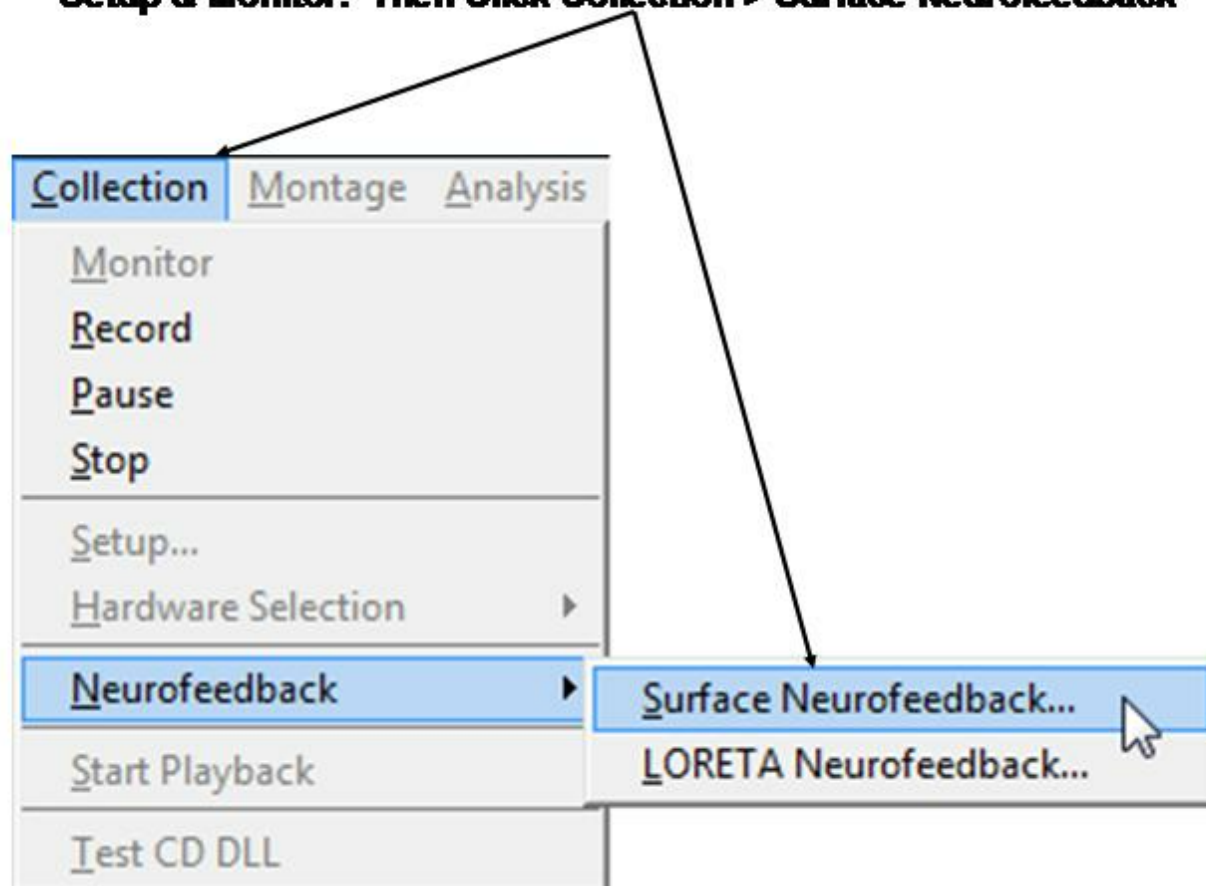
**To activate the Symptom Check List in the Neurofeedback Module, Import the Patient's edited EEG data, then Click Report > Create Symptom Check List Match**



Then Select the Acquisition Hardware and Setup and Monitor the Hardware in Preparation for Neurofeedback. Click OK in the setup and monitor screen to begin EEG collection. Then Click Collection > Neurofeedback > Surface Neurofeedback



**To activate 19 Channel Neurofeedback, first setup the Hardware and Setup & Monitor. Then Click Collection > Surface Neurofeedback**



19 channel Z Score Neurofeedback includes Power, Power Ratios, Coherence, Phase and Amplitude Asymmetry as Well as Linked Ears, Average Reference and Laplacian Montages. Four different frequencies can be activated and 1 to 19 channels can be selected. The Z threshold determines Z Scores that will be reinforced if they are equal to or less than the threshold value. The strategy is to reinforce Z Scores that move the EEG toward  $Z = 0$ . For example, if a client has elevated Theta and reduced Beta then the goal is to suppress Theta (4 - 7 Hz) and simultaneously reinforce Beta (13-25 Hz). To achieve this goal select the two frequency bands (Theta & Beta) and set the Z Score threshold at a value that is easy at first, e.g.,  $Z = 2.0$ . Set the event integration interval = 250 msec and monitor how the client achieves a continually larger number of Green circles on the head display. The appearance of Green circles in the head display or the bell or chime means that the threshold of  $Z < 2.0$  was reached in 50% of the events that occurred in a 250 msec. interval. As the client becomes more skilled at achieving the threshold, then lower the Z Score threshold to 1.5 standard deviations and again monitor the client's progress. The goal is to shape the client by making the initial feedback easy and then as the client learns to control his/her EEG then make the criteria more





difficult to slowly shape the client toward a  $Z = 0$ . This procedure will simultaneously lower Theta and reinforce Beta as the EEG moves toward  $Z = 0$ .

Increase the difficulty by changing the threshold and time window, e.g., 1- Lengthen the event interval, and/or 2- Lower the Z Score threshold. To make neurofeedback easier, then shorten the event interval and/or raise the Z Score threshold.

## Z Score Neurofeedback Panel

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

Settings or Progress Chart Tabs

Select Power or Coherence, Phase Amp. Asym

Select Montage Laplacian, Ave. Ref & Linked Ears

Z Score Threshold Reward if Less Than Or greater than

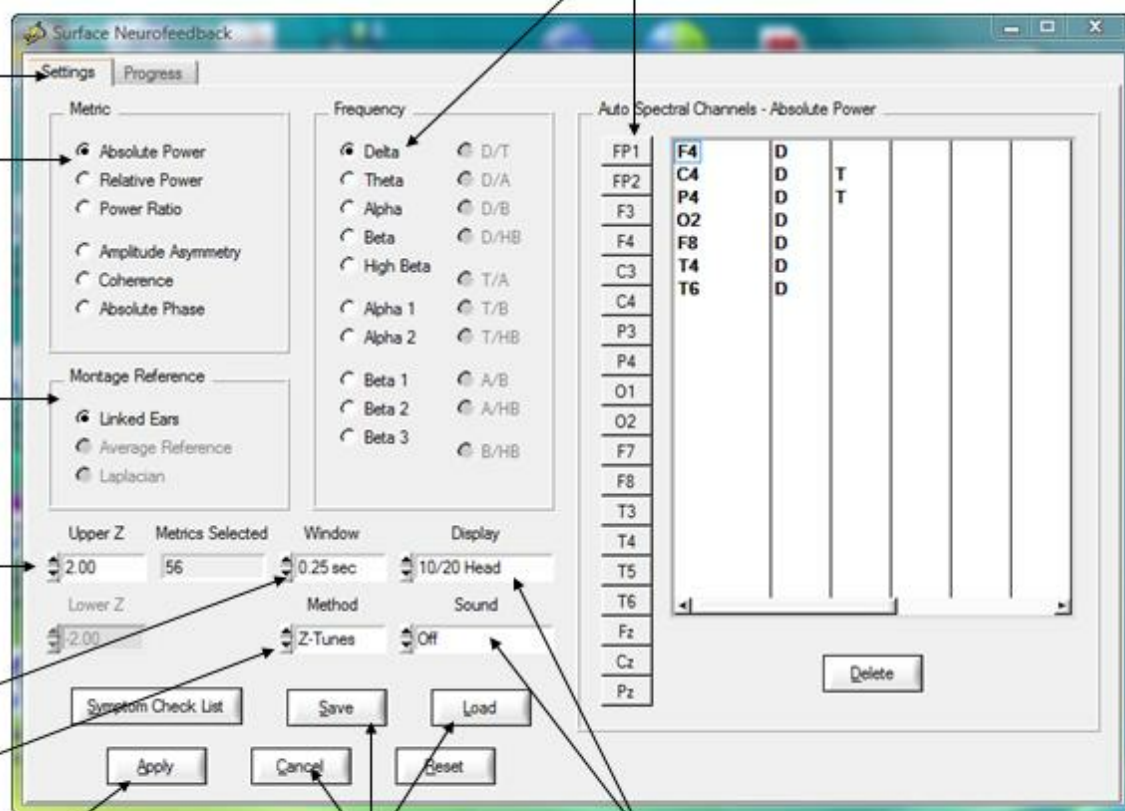
Event Integration Interval (Variability)

Z Tunes is the Reward Default

Symptom Check List

Save, Load & Cancel

Sound on/off & Visual Displays & DVD/Flash



The event integration interval is a time window that varies from 250 msec to 1 sec. There are three reward options, the default is "Z Tunes" which is a Gaussian Adaptive filter that weights Z Scores near zero higher than outliers. Average is a reward option that averages the Z Scores in the reward window of time (e.g., 250 msec to 1 sec). The All-or-None method requires that 100% of the time events within a window must reach the Z Score criteria. By lengthening the window time then one will simultaneously reinforce reduced variability. Thus, the time window provides a variability feedback method. Click sound on for the eyes closed condition and/or use both visual and auditory feedback with eyes open.



Once one has selected the channels, frequencies, EEG features and montage then click OK to activate the 10/20 Reward display or select the Progress chart as a display. If dual monitors are used then enable the monitor in the control panel > Display Settings and depress the left mouse button over the 10/20 reward display and move it to the 2nd monitor.

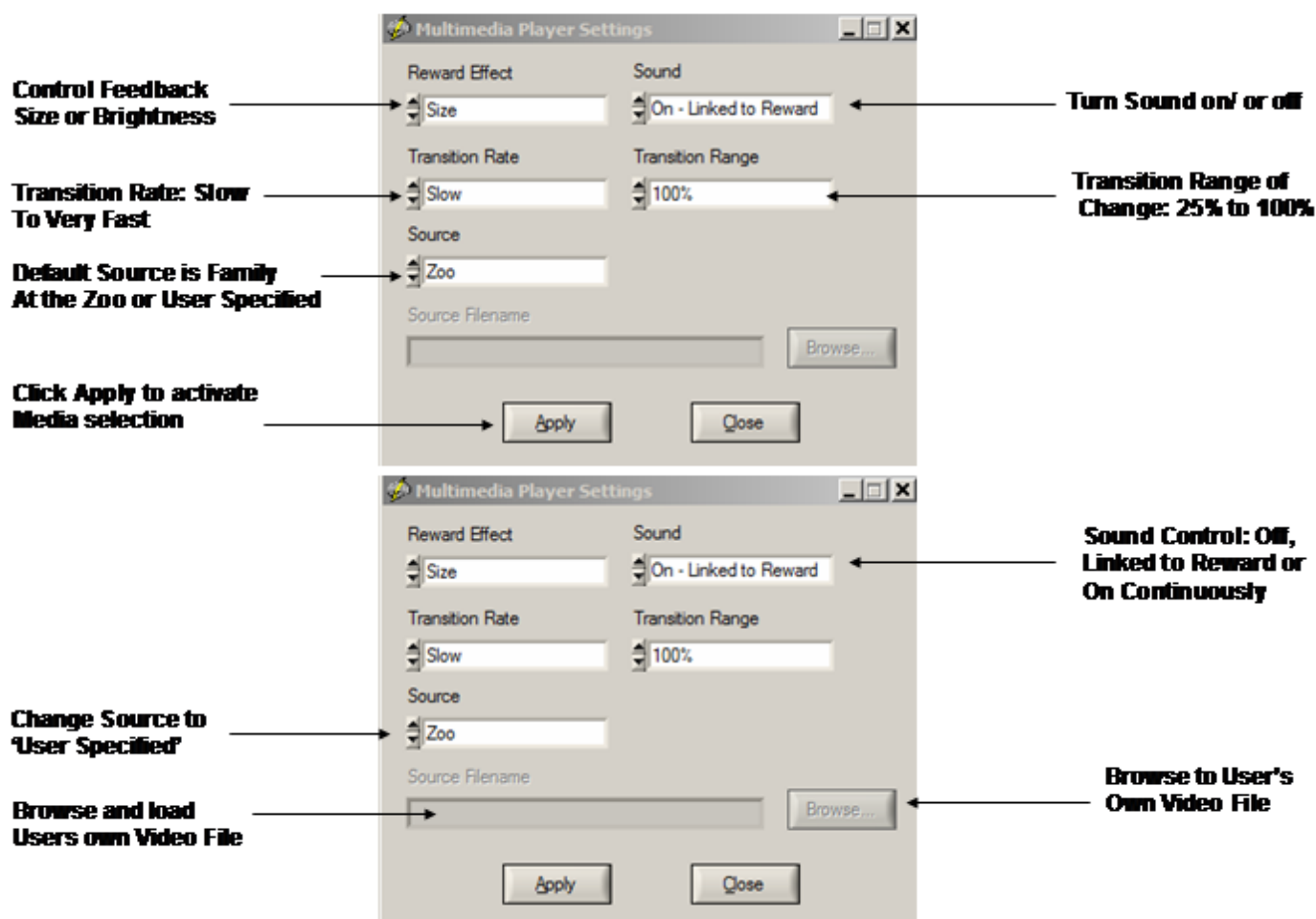
If the criteria is met for all time points in a window (e.g.,  $Z < 2.0$ ) then a reward is the color green in the 10/20 locations selected in the Z Score neurofeedback panel. The goal is to make the 10/20 head display show green as often as possible. Start with an easy reward criteria, e.g.,  $Z < 2.0$  and then adjust the reward criteria to lower Z values (e.g.,  $Z < 1.0$ ) in order to shape the client/patient EEG features toward  $Z = 0$ .

## Visual and Sound Feedback Control

Click the Display control to select different visual displays. The 1st is a green dot in the center of a head display panel than can be moved to a 2nd monitor. Other options include Brainmaster Multimedia and Deymed 3D displays that users must purchase from Brainmaster or Deymed before the display controls are visible inside of NeuroGuide. A free NeuroGuide multimedia player for videos can be selected. The NeuroGuide multimedia player control panel is shown below. The default video is a family trip to the zoo. If users want to use their own video then select User Specified in the Source control. Then browse to the location of the video and click apply to start the video. Select the feedback transition mode where brightness or size change when threshold is achieved. Turn sound off, or on linked to the reward or on continuously. Select the range of transition change where 100% is complete disappearance of the display to 25% of size reduction or brightness dimming, etc.



## Multimedia Control Panel Activated by Selecting Multimedia In the Protocol or Settings Panel under Visual Displays



## Symptom Check List Hypotheses and QEEG Z Score Tests

Identify the symptom(s) exhibited by the patient/client and double click the severity score to activate the symptom. Enter a severity score from 1 to 10. This will create red circle on the 10/20 scalp display and the size of the circle increases as a function of the severity value. As more symptoms are selected then NeuroGuide automatically weights the symptom locations and scales the size of the green circles to represent "hypotheses" of "weak systems" or "loss of function" systems (Luria, 1973).

The top right 10/20 scalp display will change depending on the symptom check list and the match of the QEEG Z Scores to the hypothesized locations. The location of green circles in the "Match" 10/20 display represents a match between hypothesized scalp locations and observed QEEG Z Scores. The radius of a green circle is produced by scaling with respect to the maximum average Z Score greater than the threshold for a given scalp location. The larger



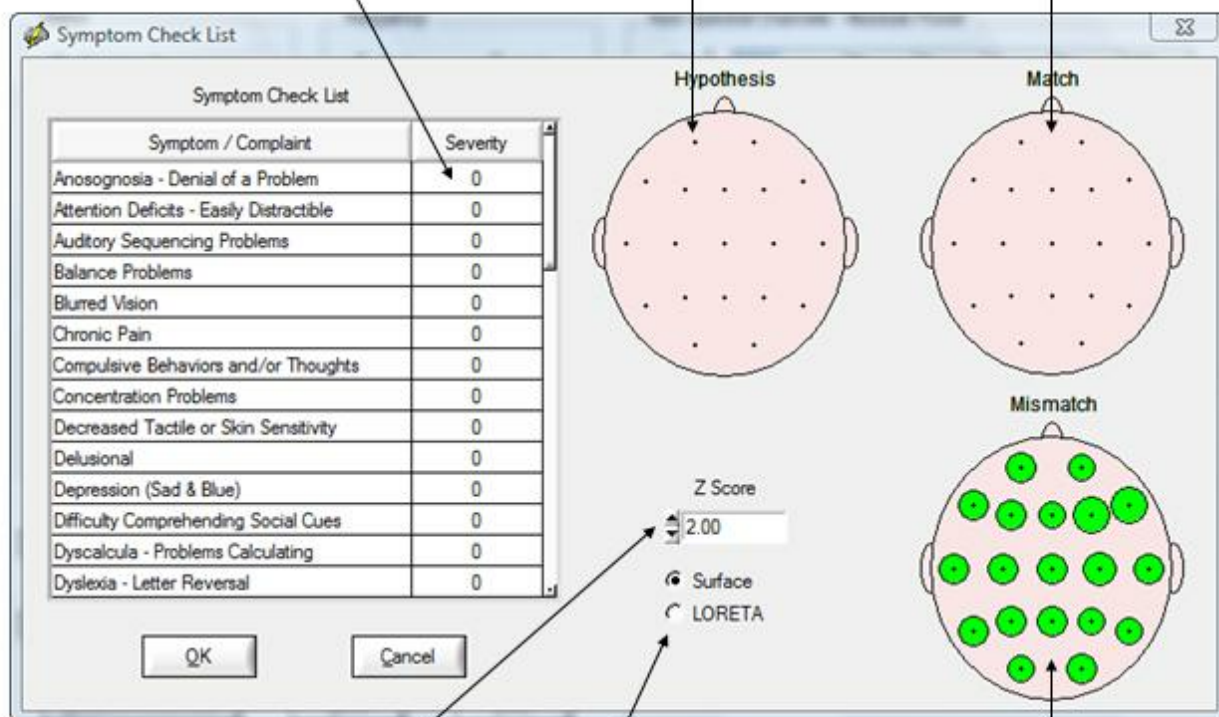
the average Z Score then the larger the radius of the circle. After the user finds an optimal link to hypothesized locations, then click OK to automatically generate a Neurofeedback Protocol.

The automatic protocol is produced by the cross-product of the symptom severity and the average Z Score in a given location or  $S \times Z$  where  $S$  = the severity index (1 to 10) from the symptom check list for that location and  $Z$  = the sum of the absolute Z or  $|Z|$  scores equal to or greater than the threshold as determined by the user (Default is  $|Z| = 2$ ). The user can veto or modify the automatically produced protocol by clicking metrics, frequencies, auto-spectrum and cross-spectrum selections in the Surface EEG panel.

**Double click the Severity of a Symptom and Grade Severity 1 to 10.**

**Symptom Check List Hypotheses**

**Match to Symptoms & QEEG Z Scores**



**Set the Z score threshold from the QEEG Analyses**

**Surface (NF1) &/or LORETA Z (NF2)**

**Mismatch of Symptoms & QEEG Z Scores**



**Example of a Slow Reader Symptom Check List Hypotheses and the Test Of the Hypothesis using QEEG Z Scores. Note how the mismatch items Move to the match 10/20 head display as Symptoms are matched**

Symptom / Complaint	Severity
Anosognosia - Denial of a Problem	0
Attention Deficits - Easily Distractible	10
Auditory Sequencing Problems	0
Balance Problems	0
Blurred Vision	0
Chronic Pain	0
Compulsive Behaviors and/or Thoughts	0
Concentration Problems	0
Decreased Tactile or Skin Sensitivity	0
Delusional	0
Depression (Sad & Blue)	0
Difficulty Comprehending Social Cues	0
Dyscalculia - Problems Calculating	0
Dyslexia - Letter Reversal	0

Z Score: 2.00

☒ Surface  
☐ LORETA

Click OK in the Symptom Check List Panel to Return to the Surface Neurofeedback Panel and View the Automatic Selections based on the Symptom Check List as Hypotheses and QEEG Z Scores as Tests of the Hypotheses. Click OK if satisfied or modify by selecting or deselecting variables or click Clear to start over. Then click OK in the surface EEG Neurofeedback panel to activate the Neurofeedback reinforcement display.





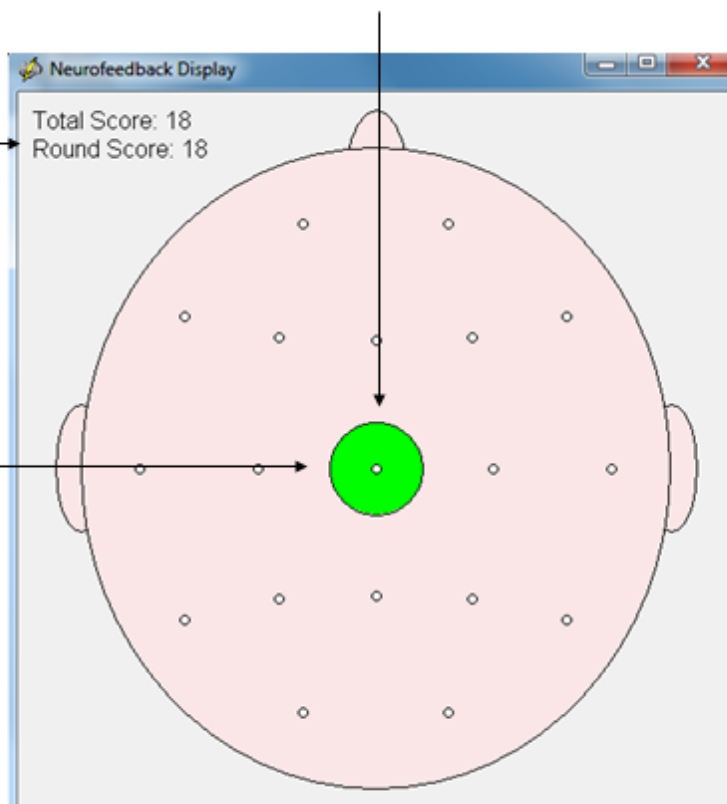
## Biofeedback Feedback Display Window – Can Be Moved to a 2<sup>nd</sup> Monitor

**Green = Threshold was Reached**

**Real-time feedback  
Session Progress**

**Threshold is < Z values set in  
The Surface NF Window**

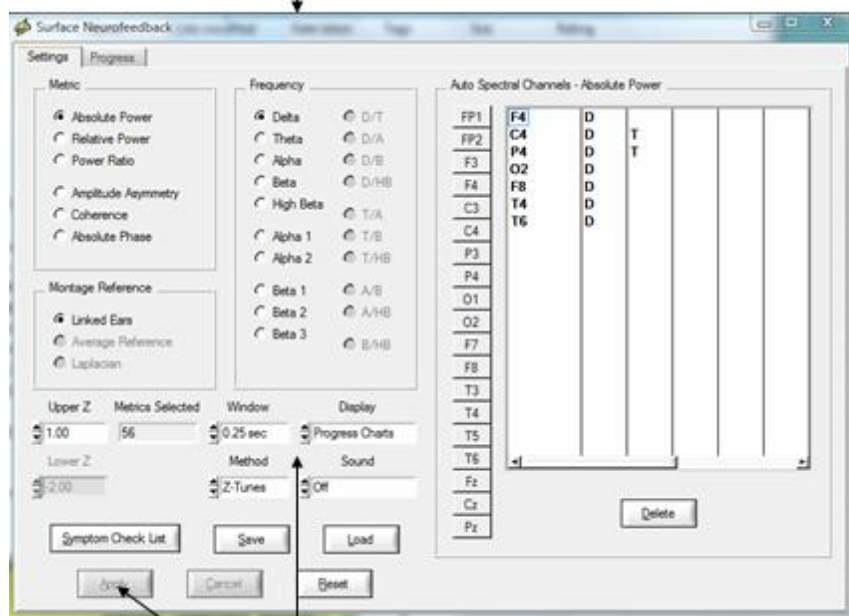
**Reinforcement requires that  
Instantaneous Z Scores are  
Less than the Threshold in a  
250 msec to 3 sec. Window  
Of Time**



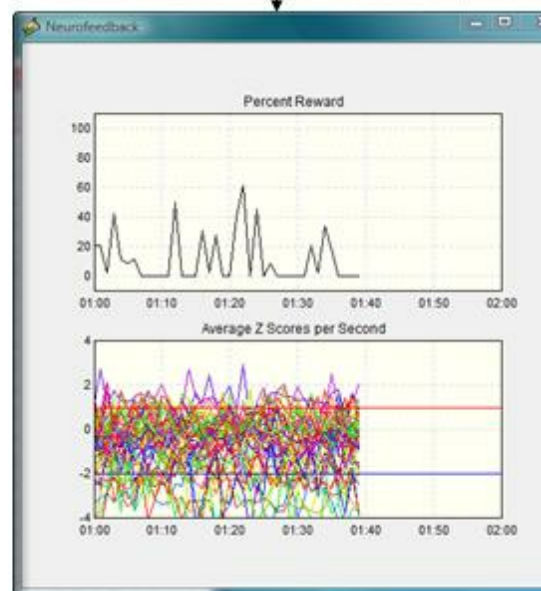


## Use the Progress Chart as a Feedback Display and Move the Display to the Client's Monitor

### Neurofeedback Setup Panel



**Select Progress Charts as Feedback to A Client and then Click Apply**



**Move to the Client's Monitor**

Toggle between the Surface Neurofeedback Panel and the Progress Charts by clicking the Settings Tab or the Progress tab. If a setting is changed then in order for the new settings to be activated click Apply and then click the Progress tab and view the instantaneous Z Scores and % reward with the new settings. A red vertical line marks the point in time when the settings change occurred.

## Session Rounds Panel

Click Session Rounds tab in the protocol panel to activate the session rounds panel. The total training duration = number of rounds x round duration. For example, 8 rounds each at 5 minute duration = 40 minutes. Session duration = total training duration + inter-round delays. For example, 8 rounds each with 30 second delays between rounds = 43 minutes and 30 seconds for the session duration. Round restart method can be automatic or manual and all of the round settings can be changed. When the Apply button is clicked in the settings panel then





the Begin Session button will become active. To start the training session click Begin Session in either the session round panel or the protocol panel.

**Click Session Rounds**

**Number of Rounds x Round Duration = Training Duration**

**Session Duration = Training Duration + Inter-Round Delays**

The screenshot shows the 'Surface Neurofeedback' window with three tabs: 'Protocol', 'Session Rounds', and 'Progress'. The 'Session Rounds' tab is active, showing a 'Session Setup' section with the following controls:

- Total Training Duration**: 40:00
- Total Session Duration**: 43:30
- Number of Rounds**: 8
- Round Duration**: 5 min
- Inter-Round Delay**: 30 sec
- Restart Method**: Automatic

Below the setup section is the 'Session Progress' section, which includes:

- Round Counter**: Current Round Number: 1
- Start Round** button

At the bottom of the window are three buttons: **Begin Session**, **End Session**, and **Close**.

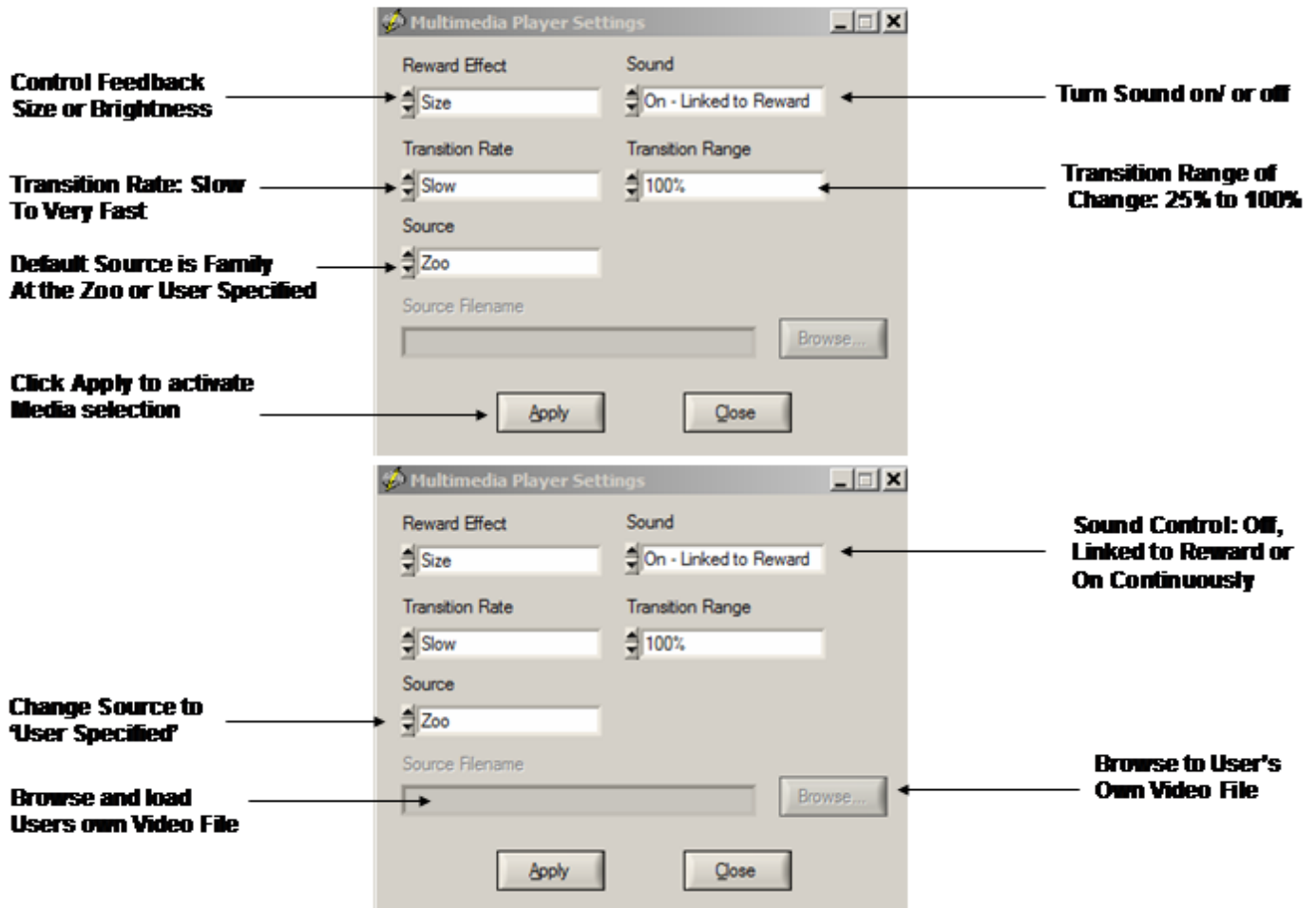
## Visual and Sound Feedback Control

Click the Display control to select different visual displays. The 1st is a green dot in the center of a head display panel that can be moved to a 2nd monitor. Other options include Brainmaster Multimedia and Deymed 3D displays that users must purchase from Brainmaster or Deymed before the display controls are visible inside of NeuroGuide. A free NeuroGuide multimedia player for videos can be selected. The NeuroGuide multimedia player control panel is shown below. The default video is a family trip to the zoo. If users want to use their own video then select User Specified in the Source control. Then browse to the location of the video and click apply to start the video. Select the feedback transition mode where brightness or size change when threshold is achieved. Turn sound off, or on linked to the reward or on



continuously. Select the range of transition change where 100% is complete disappearance of the display to 25% of size reduction or brightness dimming, etc.

### Multimedia Control Panel Activated by Selecting Multimedia In the Protocol or Settings Panel under Visual Displays

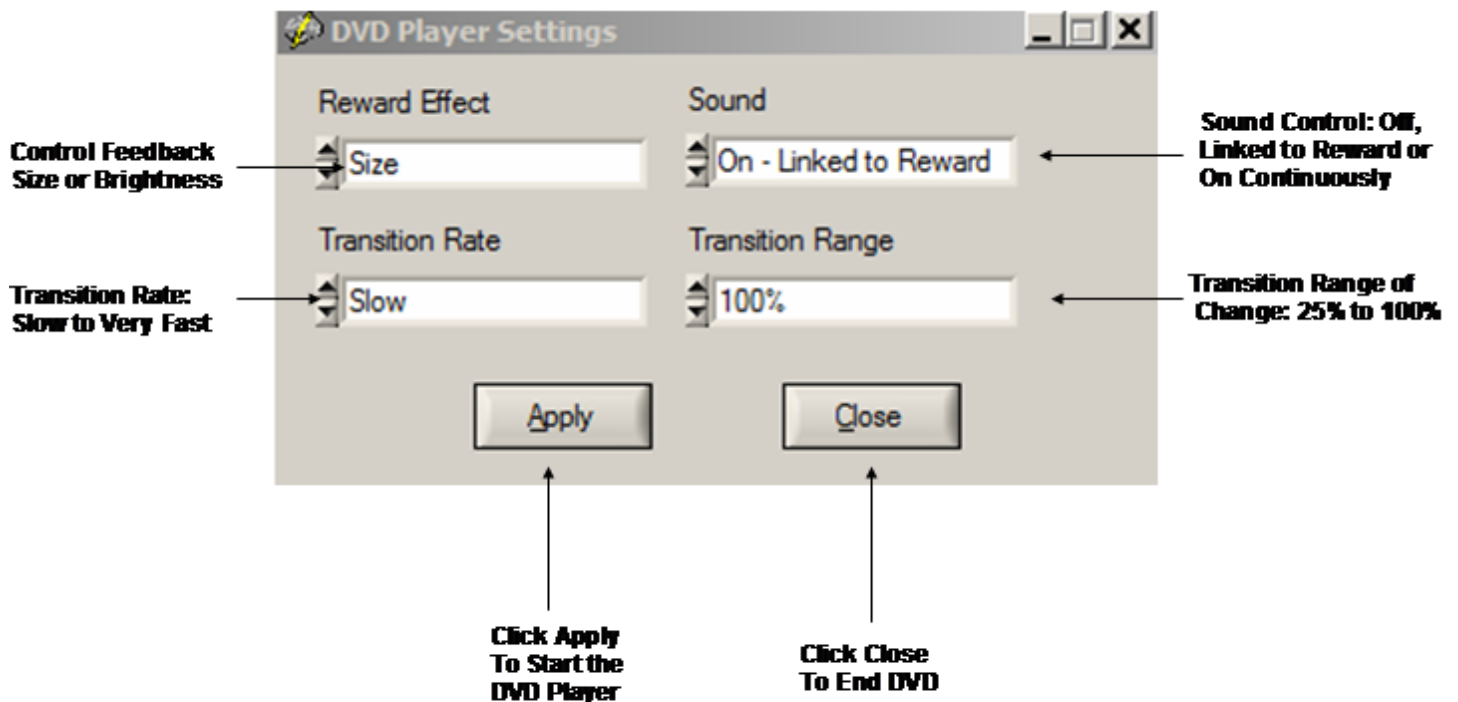


## DVD Player Controls and Activation

Click the Display control to select the NeuroGuide DVD Player. The NeuroGuide DVD player control panel is shown below. Insert a DVD into the DVD/CD drive on the computer. Select the feedback transition mode where brightness or size change when threshold is achieved. Turn sound on continuously, linked to reward or off. Select the transition rate at which the DVD appears or disappears based on the reward. Control the transition range of change from only a small size change to a large size change based on a reward.

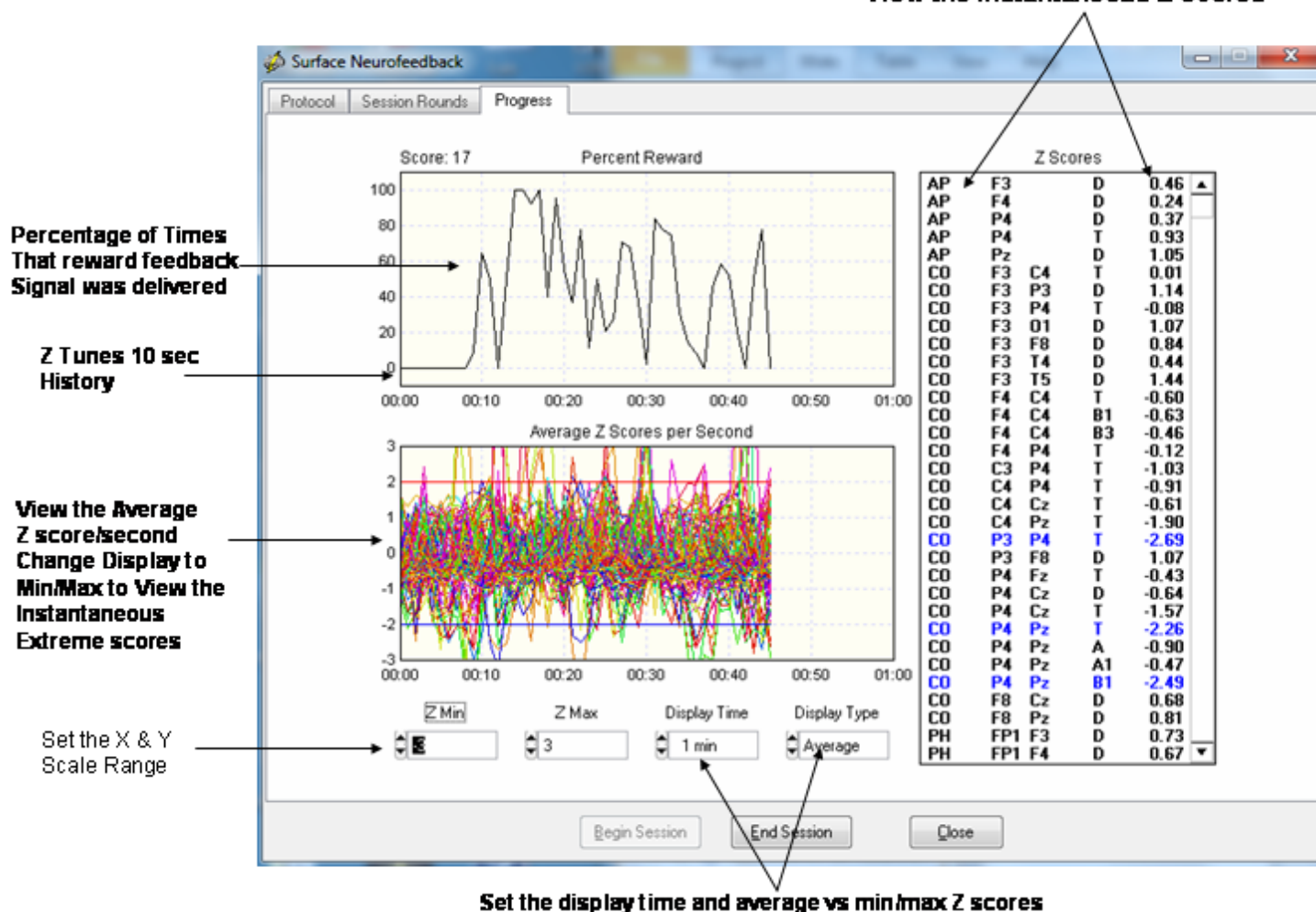


## DVD Control Panel Activated by Selecting DVD Player in the Protocol or Settings Panel under Visual Displays

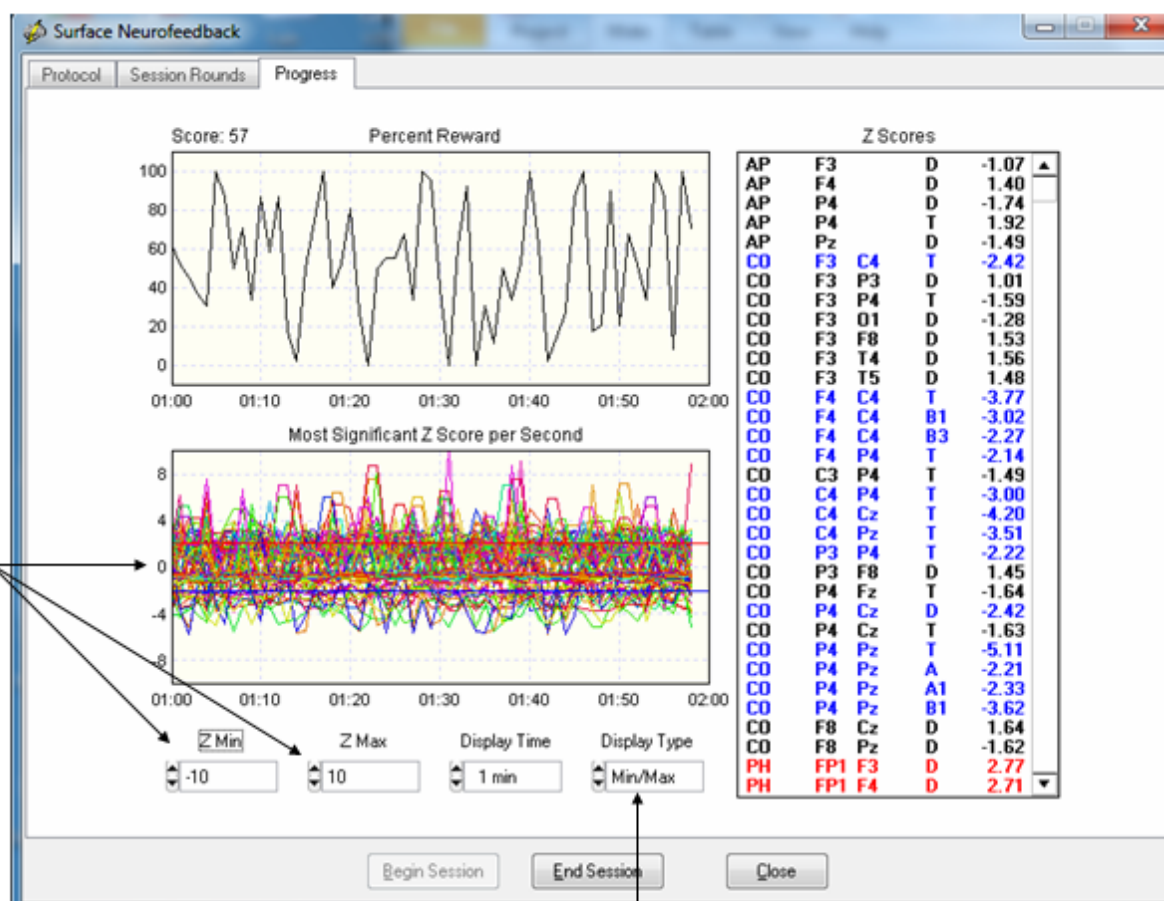


## Intra-Session Progress

View the progress of Neurofeedback by clicking OK in the Surface EEG Neurofeedback Panel

**View the Instantaneous Z Scores**

Change the display setting to Min/Max to view the extreme instantaneous Z Scores and not the average Z Score per second. The average Z Score/second may be small because 32 Z Scores were averaged over a one second period and some Z Scores may be small.



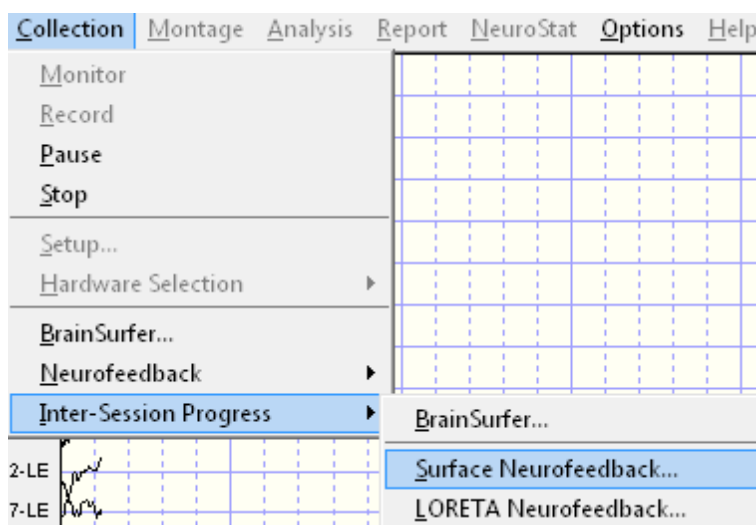
**Set Display Type to Min/Max to view the Extreme Instantaneous Z Scores**

## Inter-Session Progress Charts

After each Neurofeedback session close the session and then save the session in the client's folder. The session files end in the extension \*.nfb and will be automatically selected and used to generate an Inter-Session Progress chart based on the chronological order of the sessions.

It is important that subject's sessions not be mixed with different clients and to save each session in the same subject's folder.

Click Collection > Inter-Session Progress > Surface Neurofeedback and then navigate to the Patient/Subject Folder where the sessions were saved and click Done

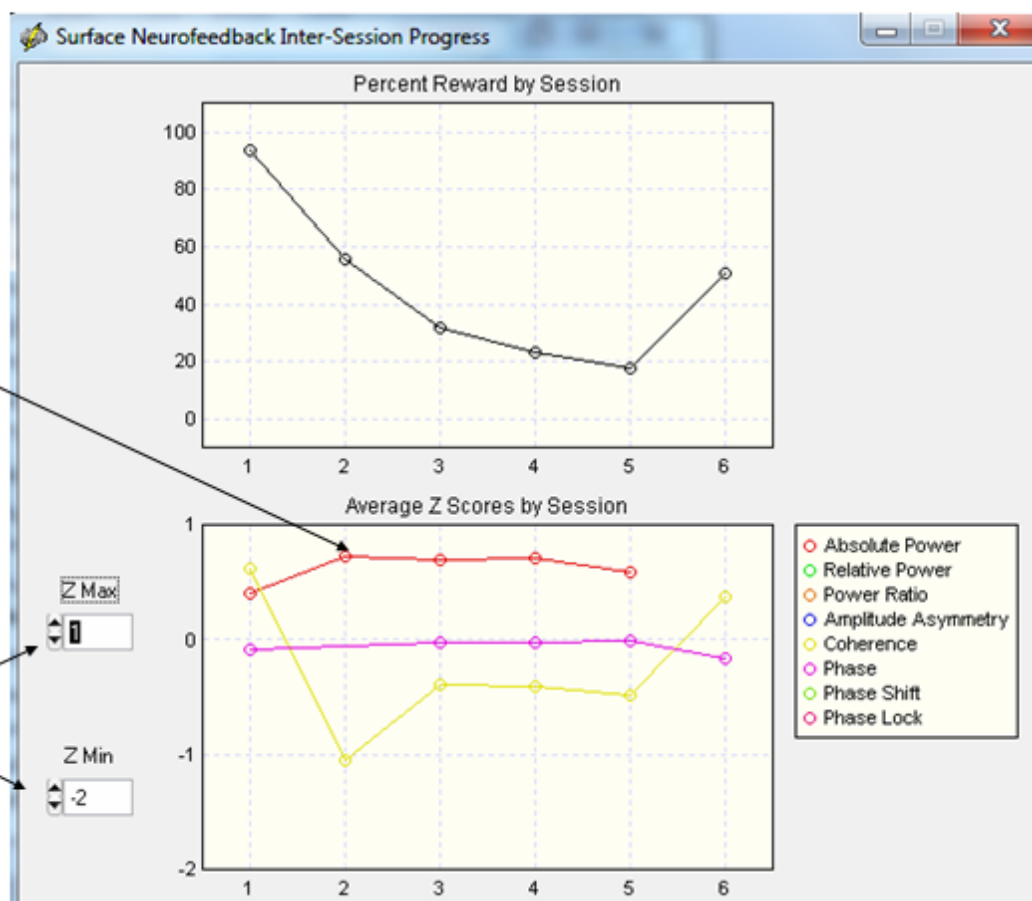


**Click Collection > Inter-Session Progress > Surface Neurofeedback**

**Top chart is Percent Reward by Session and Bottom Chart is Average Z Scores/Session**

**Move mouse over  
Session to view the  
EEG metric & Location**

**Adjust the Y  
and X axis  
scales**





## Neurofeedback LORETA Z Score Neurofeedback

LORETA Z Score Biofeedback uses similar controls as for the surface Neurofeedback. To activate LORETA Z Score Biofeedback first conduct a qEEG analysis on the patient and after editing click Report > Create Symptom Check List Match in order to link the patient's symptoms and complaints to functional systems in the brain. Activate the EEG collection software and begin recording the EEG as described above. Then click Collection > Neurofeedback > LORETA Neurofeedback to activate the LORETA Neurofeedback Protocol panel.

The screenshot shows the LORETA Neurofeedback software window with the following annotations:

- Click Tabs to Access other Panels:** Points to the 'Protocol', 'Session Rounds', and 'Progress' tabs at the top.
- Select Metrics:** Points to the 'Metric' section on the left, which includes radio buttons for Power, Coherence, Phase, Phase Shift, and Phase Lock.
- Select Frequency:** Points to the 'Frequency' section on the left, which includes radio buttons for D, A, B, HB, A1, A2, B1, B2, and B3.
- Select Regions of Interest:** Points to the 'Region of Interest' list in the center, which includes checkboxes for various brain regions like Amygdala, Angular Gyrus, Anterior Cingulate, Cingulate Gyrus, Cuneus, Extra-Nuclear, Fusiform Gyrus, Hippocampus, and Inferior Frontal Gyrus, each with 'Left' and 'Right' options.
- Select & View Brodmann Areas & Frequencies:** Points to the 'Brodmann Area' list on the right, which includes checkboxes for areas 1 through 18, each with 'Left' and 'Right' options.
- Select Z Score Threshold, Window Of Time & Display:** Points to the 'Z Threshold' (1.00), 'Metrics Selected' (0), 'Window' (0.25 sec), and 'Display' (Cz Head) fields.
- Click Symptom Check List to Access the .SCL File:** Points to the 'Symptom Check List' button.
- Save & Load Protocol Selections:** Points to the 'Save' and 'Load' buttons.
- Click Reset To Clear All Selections:** Points to the 'Reset' button.

Other visible buttons include 'Apply', 'Cancel', 'Begin Session', 'End Session', and 'Close'.

'Live' LORETA Coherence and Phase Difference Z Scores are selected by clicking Coherence or Phase and then select pairs of Brodmann Areas out of the universe of 88 Brodmann Areas. Once a Brodmann Area pair is selected then select the frequency bands. Of course one can use the Symptom Check list which will automatically select Brodmann Areas and frequencies





linked to the patient's symptoms.

If the qEEG Z Scores were generated by Report > Create Symptom Check List Match, then click Symptom Check list to open the Symptom Check List panel. If no prior qEEG was conducted or no Z Scores transferred then select the Brodmann Area(s) and frequencies and feedback settings and thresholds and click Apply and skip the symptom check. Here is a view of the symptom check list to help link a patient's symptoms and complaints to functional systems of the brain.

**LORETA Symptom Check List**

**LORETA Z Score Threshold for Symptom Match**

**Symptom Check List**

Symptom / Complaint	Severity
Anosognosia - Denial of a Problem	10
Attention Deficits - Easily Distractible	0
Auditory Sequencing Problems	0
Balance Problems	0
Blurred Vision	0
Chronic Pain	0
Compulsive Behaviors and/or Thoughts	0
Concentration Problems	0
Decreased Tactile or Skin Sensitivity	0
Delusional	0

**Z Score** 2.00

**Symptom Check List Hypotheses**

Hypothesis	Match	Mismatch			
Brodmann	Hem	Brodmann	Hem	Brodmann	Hem
7	Right	7	Right	1	Right
18	Right	18	Right	2	Right
19	Right	19	Right	3	Right
39	Right	39	Right	4	Left
40	Right	40	Right	4	Right
				5	Left
				5	Right
				6	Left
				6	Right
				7	Left

**Match of LORETA Z Scores to Hypotheses**

**Mismatch of Symptom Check List & Possible Compensatory Systems**

After testing the symptom check list hypotheses to LORETA Z Scores then click OK to return to the setup panel and select the threshold and type of feedback displays. Click Apply to begin the Neurofeedback session. The visual and auditory displays are the same for the surface EEG Z Scores and the LORETA Z Scores.



## Symptom Check List Hypotheses and QEEG Z Score Tests

Identify the symptom(s) exhibited by the patient/client and double click the severity score to activate the symptom. Enter a severity score from 1 to 10. This will create red circle on the 10/20 scalp display and the size of the circle increases as a function of the severity value. As more symptoms are selected then NeuroGuide automatically weights the symptom locations and scales the size of the green circles to represent "hypotheses" of "weak systems" or "loss of function" systems (Luria, 1973).

The top right 10/20 scalp display will change depending on the symptom check list and the match of the QEEG Z Scores to the hypothesized locations. The location of green circles in the "Match" 10/20 display represents a match between hypothesized scalp locations and observed QEEG Z Scores. The radius of a green circle is produced by scaling with respect to the maximum average Z Score greater than the threshold for a given scalp location. The larger the average Z Score then the larger the radius of the circle. After the user finds an optimal link to hypothesized locations, then click OK to automatically generate a Neurofeedback Protocol.

The automatic protocol is produced by the cross-product of the symptom severity and the average Z Score in a given location or  $S \times Z$  where  $S$  = the severity index (1 to 10) from the symptom check list for that location and  $Z$  = the sum of the absolute Z or  $|Z|$  scores equal to or greater than the threshold as determined by the user (Default is  $|Z| = 2$ ). The user can veto or modify the automatically produced protocol by clicking metrics, frequencies, auto-spectrum and cross-spectrum selections in the Surface EEG panel.



**Double click the Severity of a Symptom and Grade Severity 1 to 10.**

**Symptom Check List  
Hypotheses**

**Match to Symptoms &  
QEEG Z Scores**

Symptom Check List

Symptom / Complaint	Severity
Anosognosia - Denial of a Problem	0
Attention Deficits - Easily Distractible	0
Auditory Sequencing Problems	0
Balance Problems	0
Blurred Vision	0
Chronic Pain	0
Compulsive Behaviors and/or Thoughts	0
Concentration Problems	0
Decreased Tactile or Skin Sensitivity	0
Delusional	0
Depression (Sad & Blue)	0
Difficulty Comprehending Social Cues	0
Dyscalculia - Problems Calculating	0
Dyslexia - Letter Reversal	0

OK Cancel

Hypothesis

Match

Mismatch

Z Score

2.00

☒ Surface

☐ LORETA

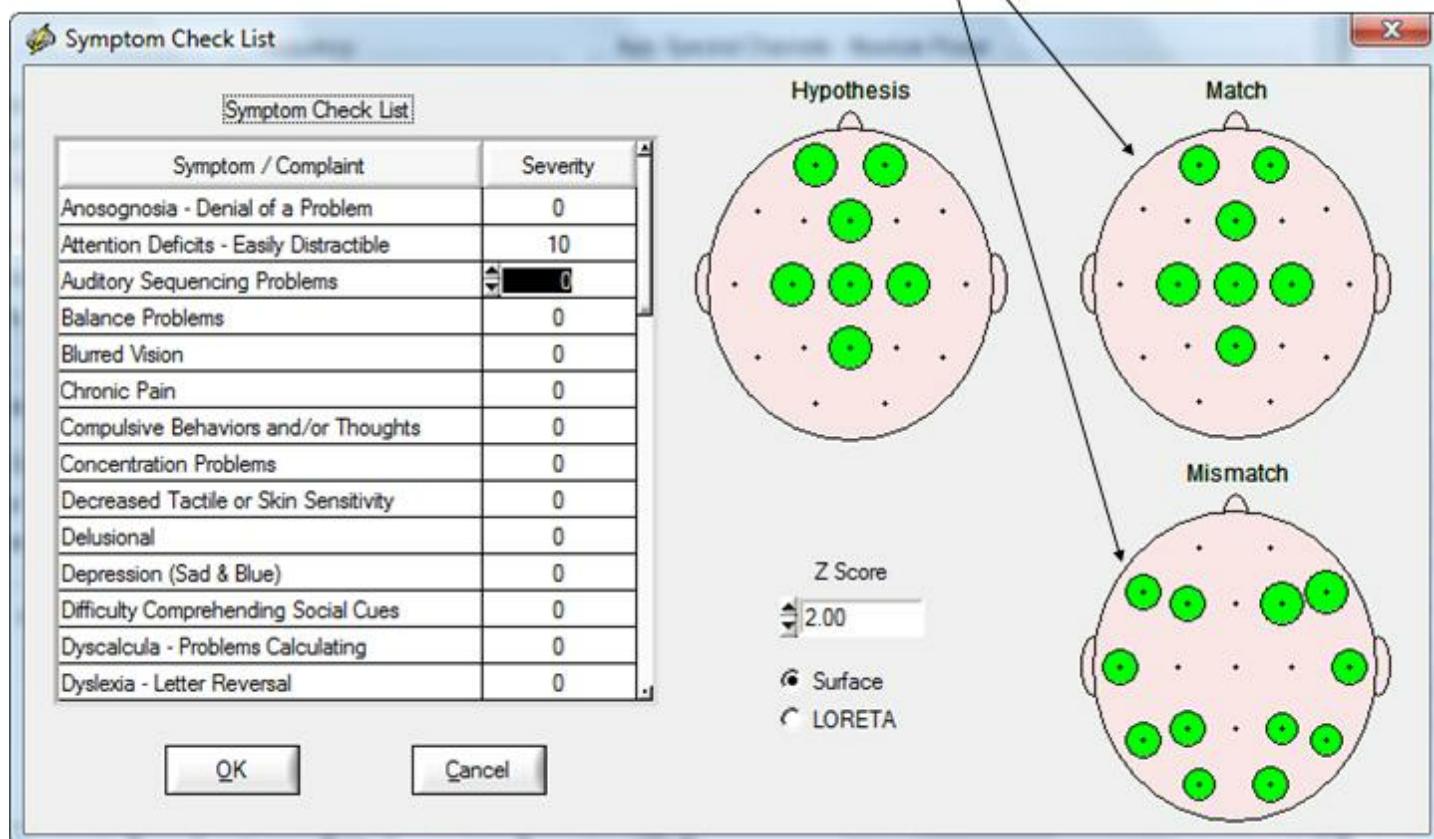
**Set the Z score  
threshold from  
the QEEG Analyses**

**Surface (NF1) &/or  
LORETA Z (NF2)**

**Mismatch of Symptoms  
& QEEG Z Scores**



**Example of a Slow Reader Symptom Check List Hypotheses and the Test Of the Hypothesis using QEEG Z Scores. Note how the mismatch items Move to the match 10/20 head display as Symptoms are matched**



Click OK in the Symptom Check List Panel to Return to the Surface Neurofeedback Panel and View the Automatic Selections based on the Symptom Check List as Hypotheses and QEEG Z Scores as Tests of the Hypotheses. Click OK if satisfied or modify by selecting or deselecting variables or click Clear to start over. Then click OK in the surface EEG Neurofeedback panel to activate the Neurofeedback reinforcement display.



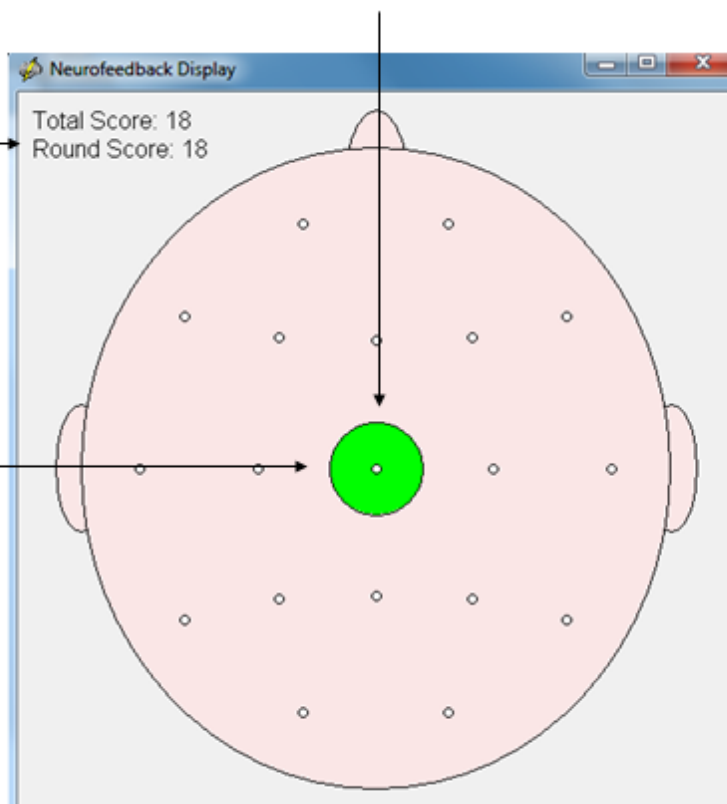
## Biofeedback Feedback Display Window – Can Be Moved to a 2<sup>nd</sup> Monitor

**Green = Threshold was Reached**

**Real-time feedback  
Session Progress**

**Threshold is < Z values set in  
The Surface NF Window**

**Reinforcement requires that  
Instantaneous Z Scores are  
Less than the Threshold in a  
250 msec to 3 sec. Window  
Of Time**

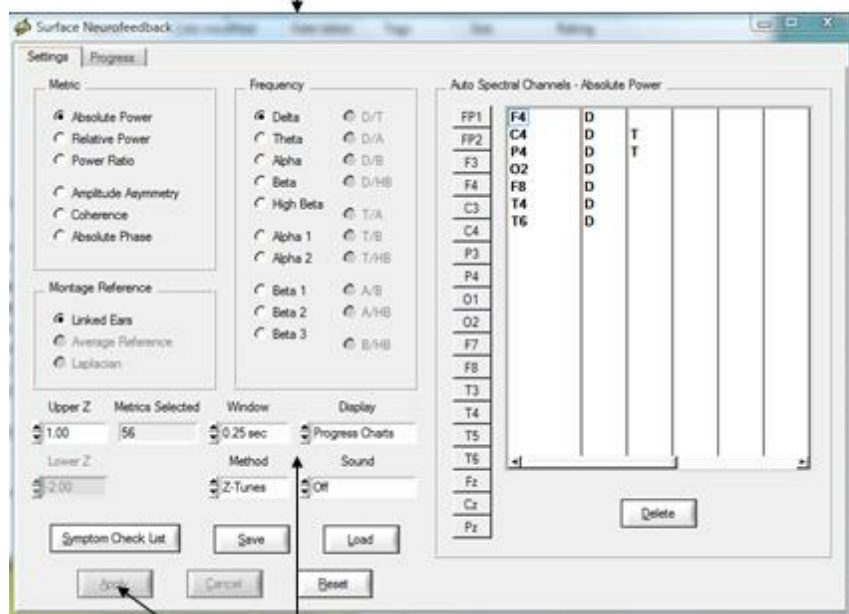




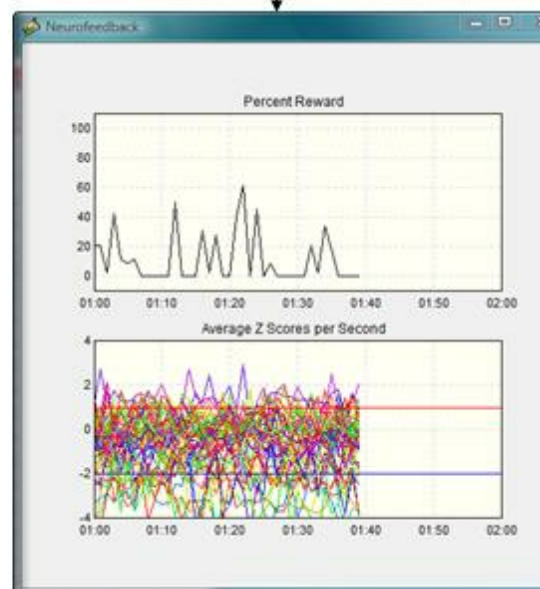


**Use the Progress Chart as a Feedback Display  
and Move the Display to the Client's Monitor**

**Neurofeedback Setup Panel**



**Select Progress Charts as Feedback to  
A Client and then Click Apply**

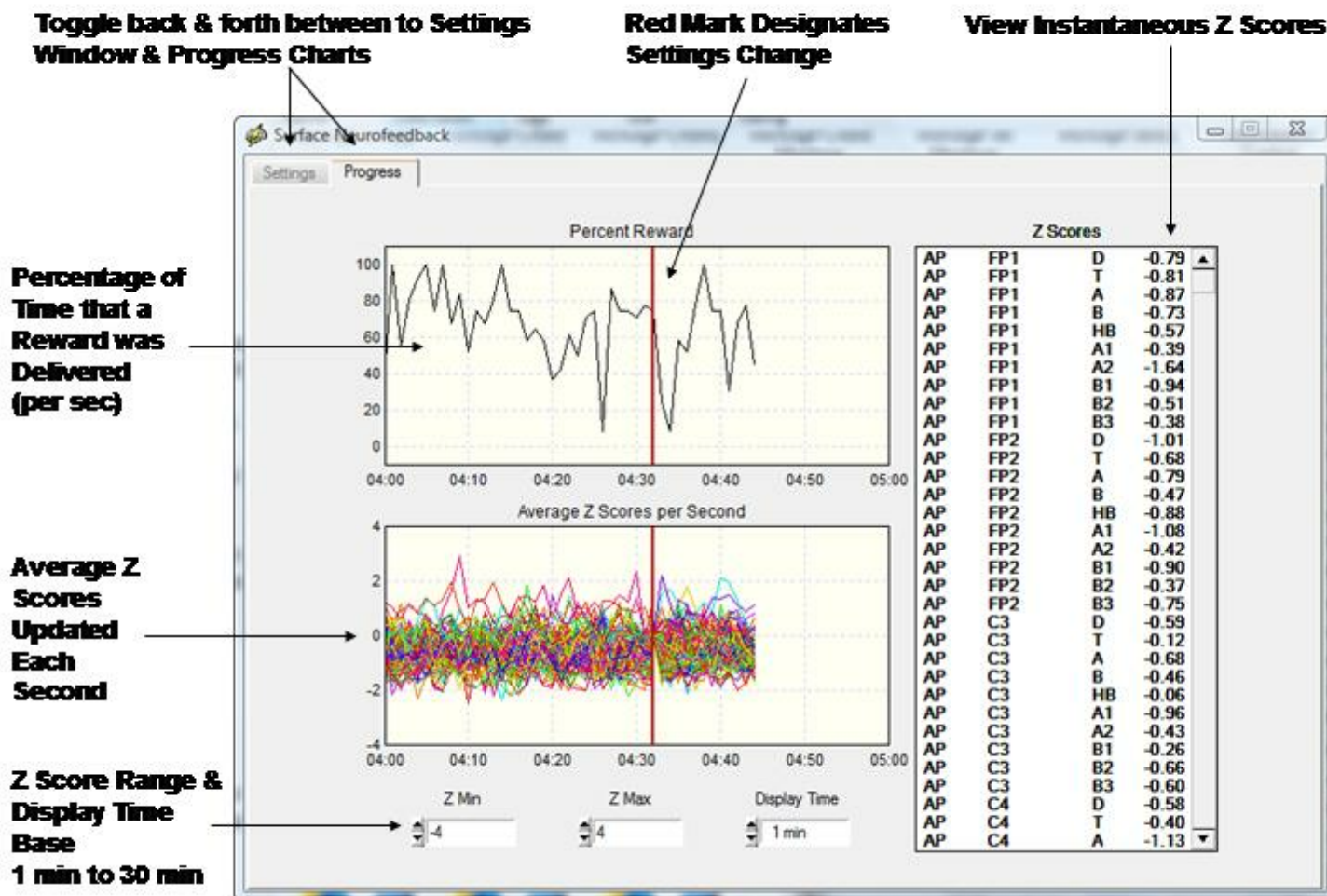


**Move to the  
Client's Monitor**

**View the progress of Neurofeedback by clicking OK in the Surface EEG Neurofeedback Panel**



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



Toggle between the Surface Neurofeedback Panel and the Progress Charts by clicking the Settings Tab or the Progress tab. If a setting is changed then in order for the new settings to be activated click Apply and then click the Progress tab and view the instantaneous Z Scores and % reward with the new settings. A red vertical line marks the point in time when the settings change occurred.

## Session Rounds Panel

Click Session Rounds tab in the protocol panel to activate the session rounds panel. The total training duration = number of rounds x round duration. For example, 8 rounds each at 5 minute duration = 40 minutes. Session duration = total training duration + inter-round delays. For example, 8 rounds each with 30 second delays between rounds = 43 minutes and 30 seconds for the session duration. Round restart method can be automatic or manual and all of the round settings can be changed. When the Apply button is clicked in the settings panel then





the Begin Session button will become active. To start the training session click Begin Session in either the session round panel or the protocol panel.

**Click Session Rounds**

**Number of Rounds x Round Duration = Training Duration**

**Session Duration = Training Duration + Inter-Round Delays**

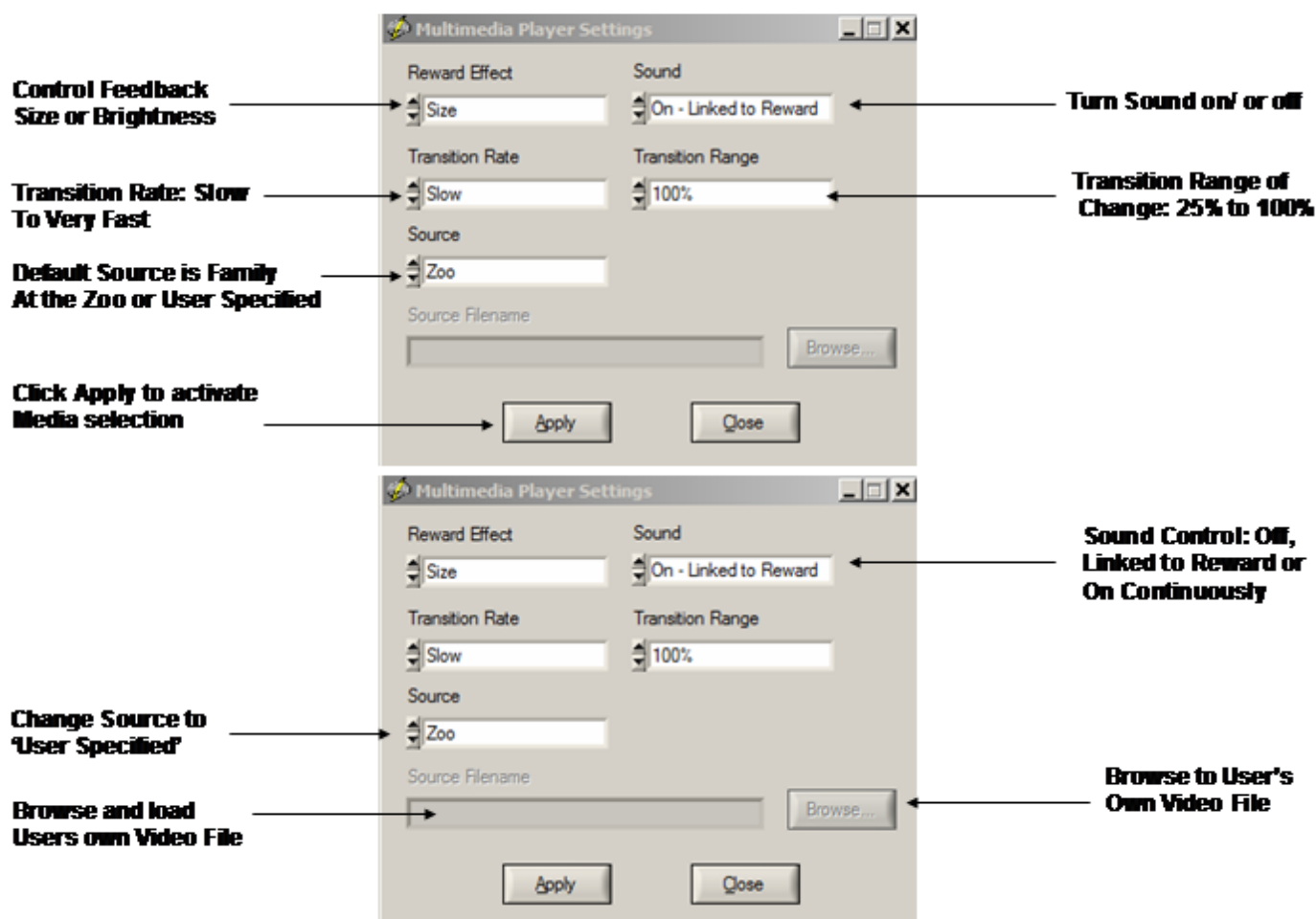
The screenshot shows the 'Surface Neurofeedback' window with three tabs: 'Protocol', 'Session Rounds', and 'Progress'. The 'Session Rounds' tab is active, showing a 'Session Setup' panel. Annotations with arrows point to various controls:

- Total Training Duration** points to 'Total Training Duration: 40:00'.
- Total Session Duration** points to 'Total Session Duration: 43:30'.
- Number of Rounds** points to a spinner control set to 8.
- Round Duration** points to a spinner control set to 5 minutes.
- Inter-Round Delay** points to a spinner control set to 30 seconds.
- Restart Method** points to a dropdown menu set to 'Automatic'.
- Round Counter** points to 'Current Round Number: 1' in the 'Session Progress' section, which also contains a 'Start Round' button.
- Begin, End & Close Session** points to the 'Begin Session', 'End Session', and 'Close' buttons at the bottom of the window.

Click the Display control to select different visual displays. The 1st is a green dot in the center of a head display panel that can be moved to a 2nd monitor. Other options include Brainmaster Multimedia and Deymed 3D displays that users must purchase from Brainmaster or Deymed before the display controls are visible inside of neuroguide. A free NeuroGuide multimedia player for videos can be selected. The neuroguide multimedia player control panel is shown below. The default video is a family trip to the zoo. If users want to use their own video then select User Specified in the Source control. Then browse to the location of the video and click apply to start the video. Select the feedback transition mode where brightness or size change when threshold is achieved. Turn sound off, or on linked to the reward or on continuously. Select the range of transition change where 100% is complete disappearance of the display to 25% of size reduction or brightness dimming, etc.



## Multimedia Control Panel Activated by Selecting Multimedia In the Protocol or Settings Panel under Visual Displays



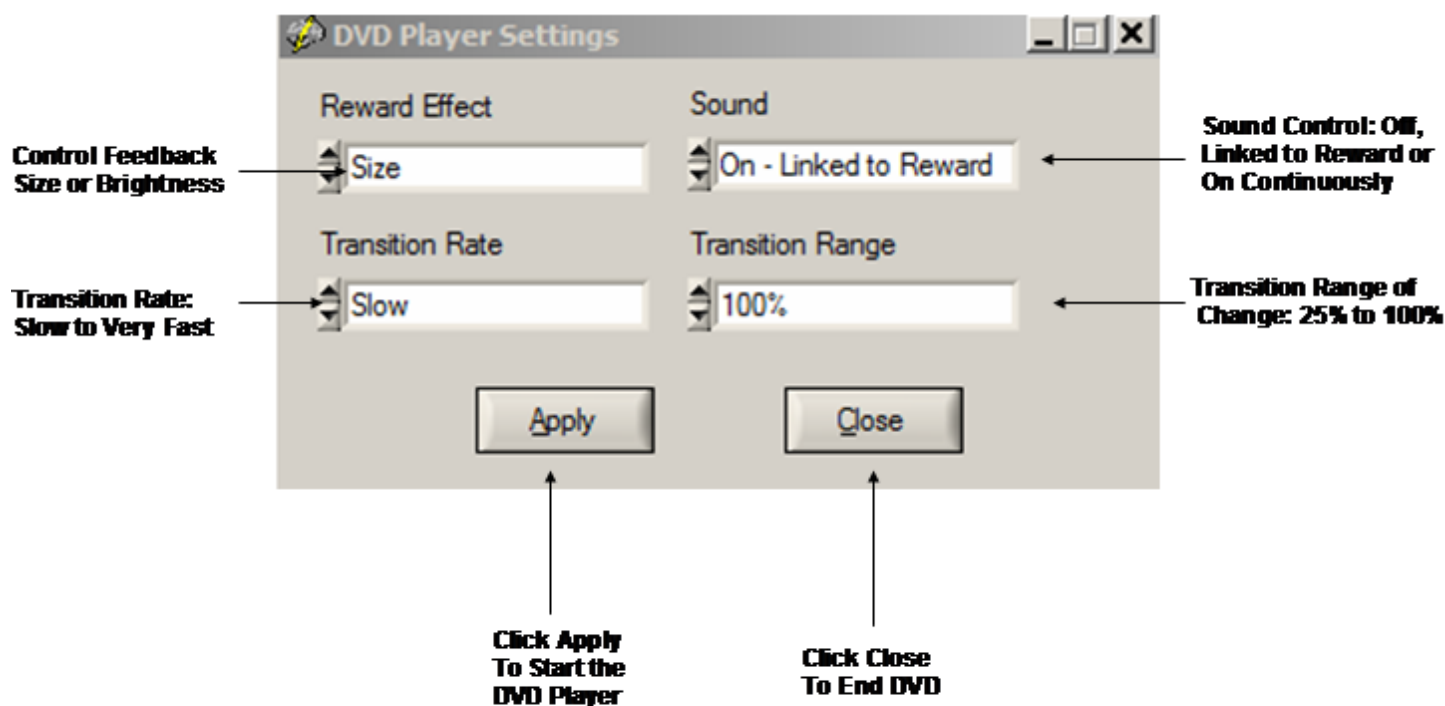
## DVD Player Controls and Activation

Click the Display control to select the NeuroGuide DVD Player. The NeuroGuide DVD player control panel is shown below. Insert a DVD into the

DVD/CD drive on the computer. Select the feedback transition mode where brightness or size change when threshold is achieved. Turn sound on continuously, linked to reward or off. Select the transition rate at which the DVD appears or disappears based on the reward. Control the transition range of change from only a small size change to a large size change based on a reward.

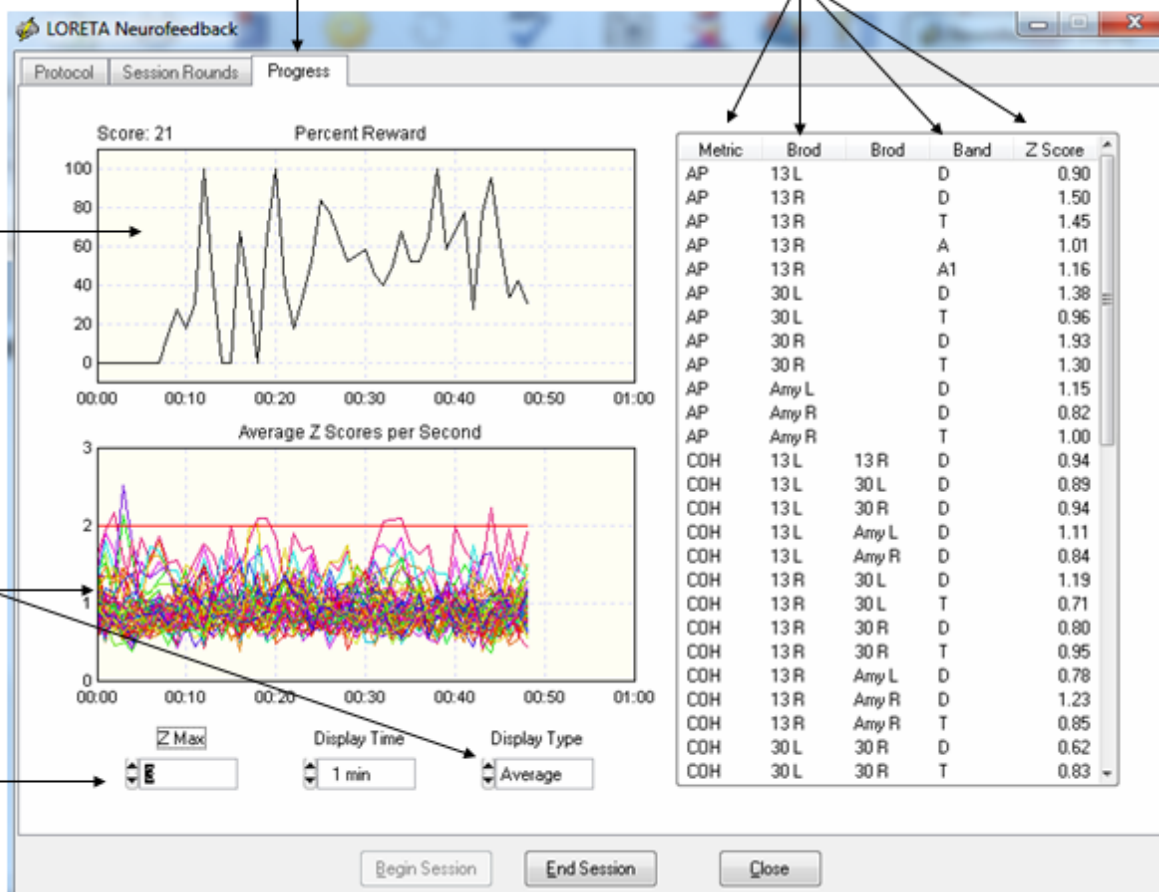


## **DVD Control Panel Activated by Selecting DVD Player in the Protocol or Settings Panel under Visual Displays**



## **Intra-Session Progress**

**During the Neurofeedback session, click the Progress Tab and view the Intra-Session Progress**

**Click the Intra-Session Progress Tab****View Brodmann Areas, Metrics & Z Scores in Real-Time****View the Percent Feedback History****View Average Z Scores or Min/Max Z Score History****Change the X & Y Scales**

## Inter-Session Progress Charts

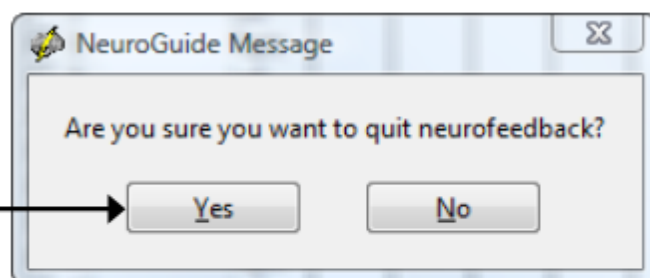
After each Neurofeedback session close the session and then save the session in the client's folder. The session files end in the extension \*.nfb and will be automatically selected and used to generate an Inter-Session Progress chart based on the chronological order of the sessions.

It is important that subject's sessions not be mixed with different clients and to save each session in the same subject's folder.

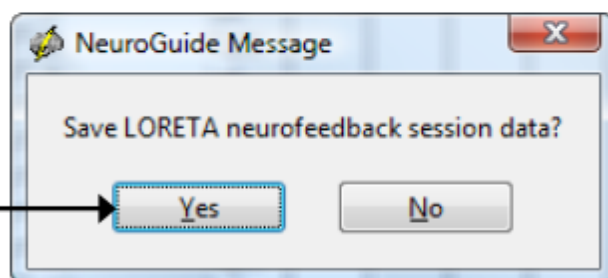


## To Create an Inter-Session Progress Chart...

**Close the  
NFB Session**



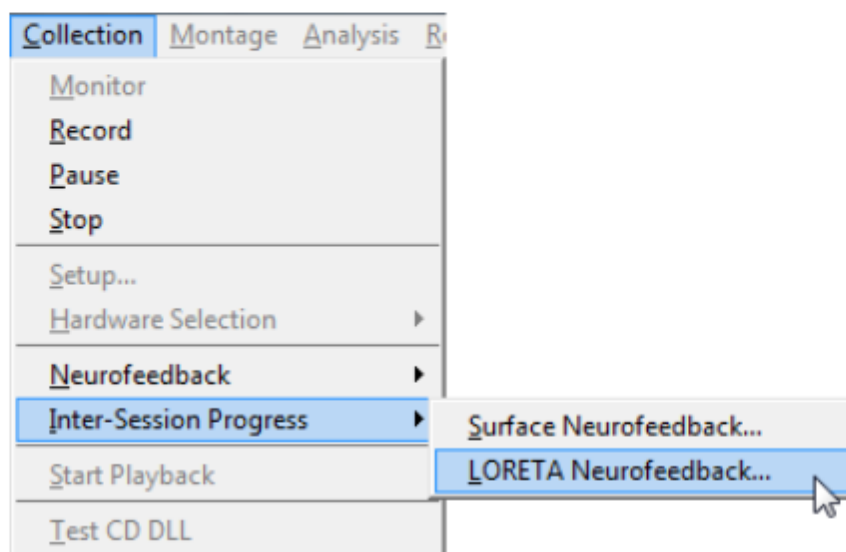
**Then Save the  
Session in the  
Subject's Folder**



**NeuroGuide orders the Sessions based on Date & Time**

## To View the Inter-Session Progress Charts...

**Click Collection > Inter-Session Progress > LORETA Neurofeedback**





LORETA Neurofeedback Inter-Session Progress

Plot Selections | Plotted Data

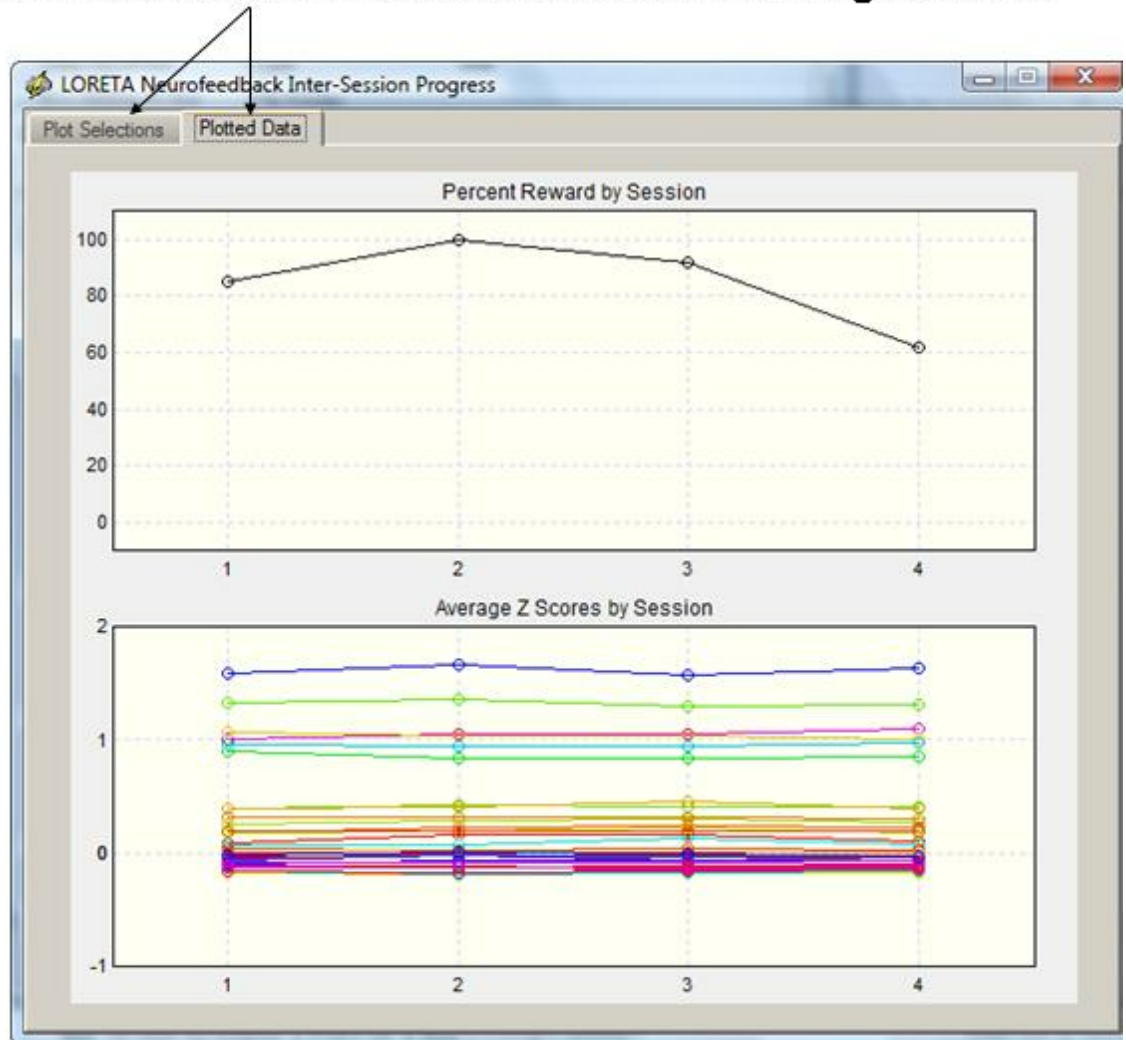
		D	T	A	B	HB	A1	A2	B1	B2	B3	Ave
Brodmann Area 7	Right	Yes	Yes	Yes	Yes		Yes		Yes			Yes
Brodmann Area 18	Right	Yes	Yes									Yes
Brodmann Area 19	Right	Yes	Yes	Yes			Yes					Yes
Brodmann Area 39	Right	Yes	Yes	Yes			Yes					Yes
Brodmann Area 40	Right	Yes	Yes	Yes	Yes		Yes		Yes			Yes
Ave		Yes	Yes	Yes	Yes		Yes		Yes			Yes

**Select or Deselect the Frequencies and Brodmann Areas to be Included in the Inter-Session Progress Charts**

Clear All Select All



**After Plot Selections then Click Plotted Data to View the Inter-Session Progress Charts**



## Phase Reset - Surface EEG

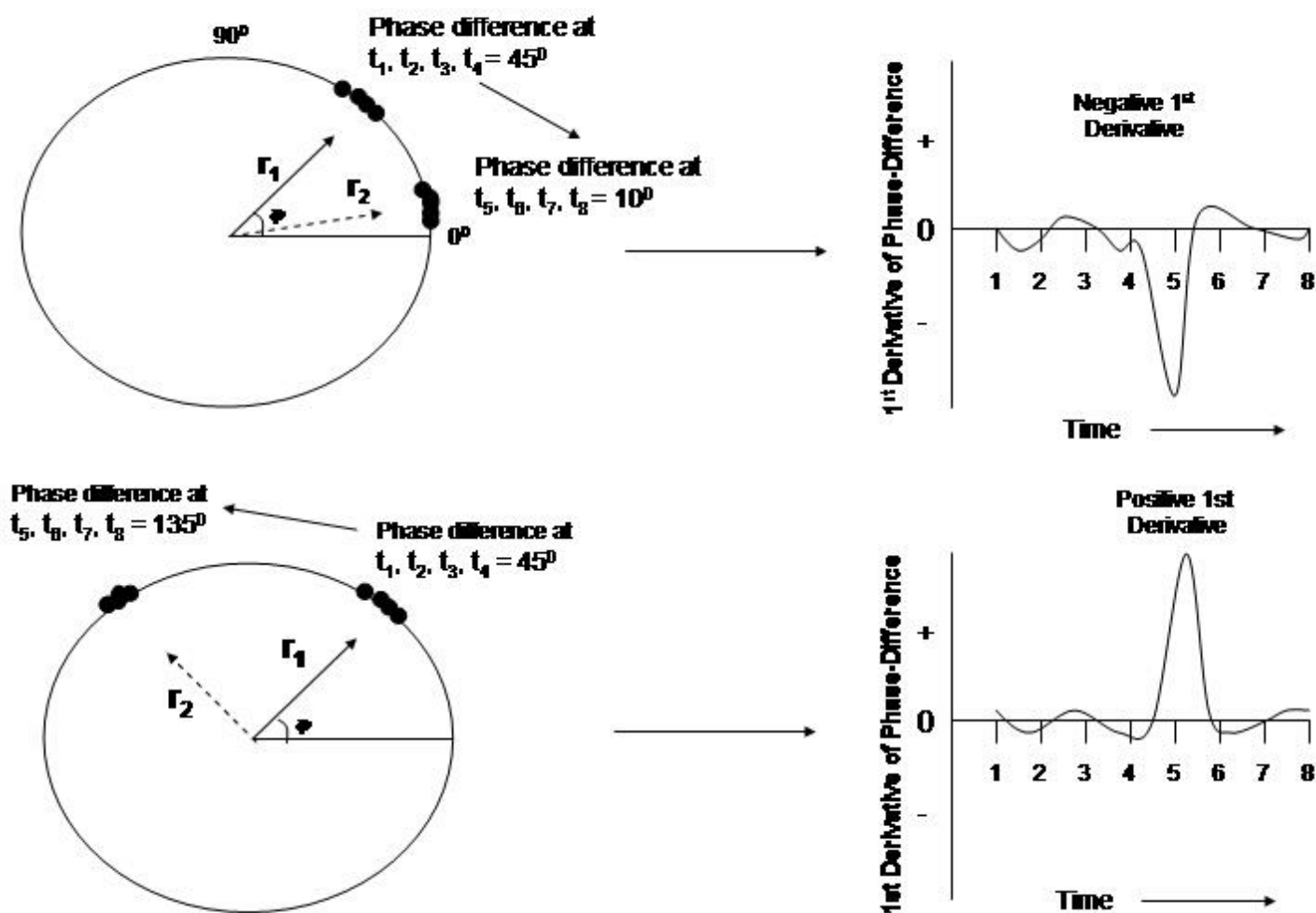
Click Report > Report Selections > Connectivity Suite > Phase Reset options. Phase reset is computed from the time series of instantaneous phase differences using Complex Demodulation and then straightening the phase differences and computing the absolute value of the first derivative of the straightened phase difference time series. When the first derivative exhibits a peak, then this is "Phase Reset". When the first derivative approximates zero, e.g.,  $< 5$  deg/cs, then this is "Phase Locking". That is, when there is little change in phase difference over time, then phase locking or phase synchrony is present. Below is an illustration of the definition of phase reset and phase locking. NeuroGuide uses peak detection algorithms to identify peaks in the 1st derivative of phase differences, the full width half maximum, the amplitude of the peak, the duration of the peak and the interval of time between





the offset of one phase reset event and the onset of the next phase reset event. Only edited selections of EEG are used in the phase reset analyses and there must be continuity between phase reset events in order for the phase locking interval to be computed. Further technical details of phase reset are explained at <http://www.appliedneuroscience.com/Articles.htm> and then download Article "How to compute EEG coherence with a hand calculator". Also, see Thatcher et al, (2007) "Self-organized criticality and the development of EEG phase reset. Human Brain Mapping (In Press).

### EEG Phase Reset as a Phase Transition in the Time Domain

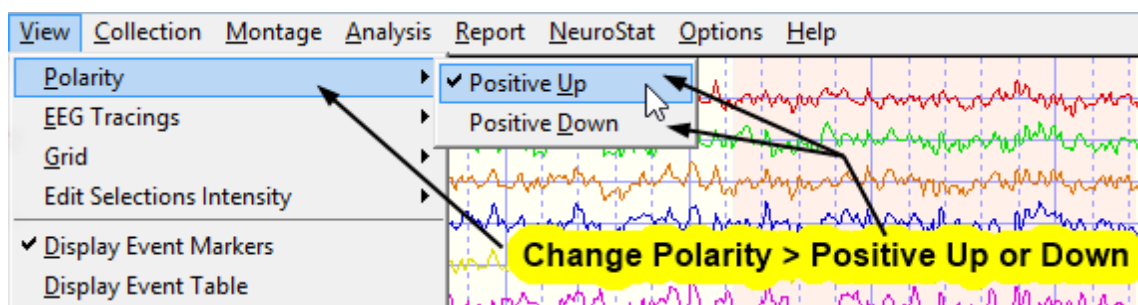


Left is the unit circle in which there is a clustering of phase angles and thus high coherence as measured by the length of the unit vector  $r$ . The vector  $r_1 = 45$  degrees occurs first in time and the vector  $r_2 = 10$  degrees and  $135$  degrees occurs later in time. The transition is between time point 4 and 5 where the 1st derivative is a maximum. The right displays are a time series of the approximated 1st derivative of the instantaneous phase differences for the time series  $t_1, t_2, t_3, t_4$  at mean phase angle =  $45$  degrees and  $t_5, t_6, t_7, t_8$  at mean phase angle =  $10$  degrees. Phase reset is defined as a significant negative or positive 1st derivative ( $y < 0$  or  $y > 0$ ). The 1st

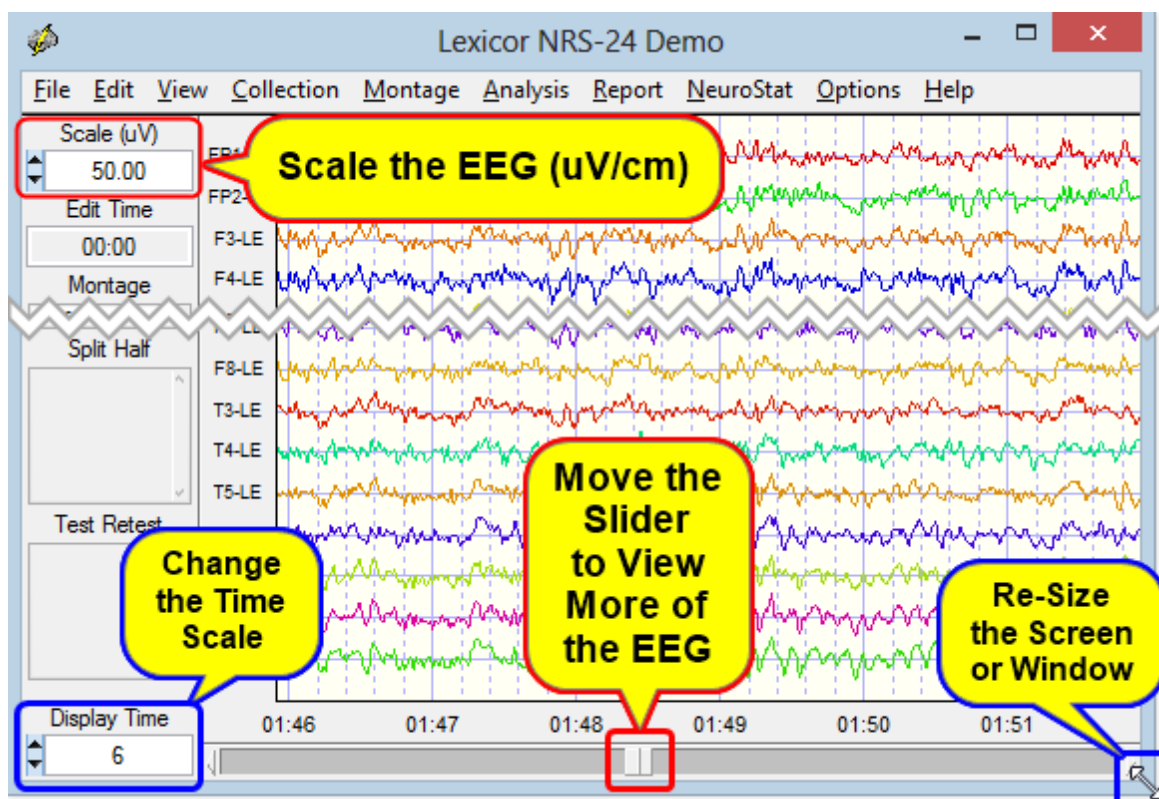


derivative near zero (e.g.,  $< 5$  degrees/cs) is when there is phase locking or phase stability and little change over time. The sign or direction of phase reset is arbitrary since two oscillating events are being brought into phase synchrony and represent a stable state as measured by EEG coherence independent of direction. The clustering of stable phase relationships over long periods of time is more common than are the phase transitions. The phase transitions are time markers of the thalamo-cortical-limbic-reticular circuits of the brain (John, 2005; Thatcher and John, 1977; Thatcher et al, 2007).

Click on View and change the Polarity or change the Grid Color or eliminate the Grid lines by changing the Intensity. The Default Screen Does Not Allow Access to Normative Databases. To Access the Normative Databases Double Click a Montage in the Montage Panel to the Left of the screen. Double Click Linked Ears in the Montage Window to reformat to Linked Ears... this will remove the Auxiliary and other Default Channels.



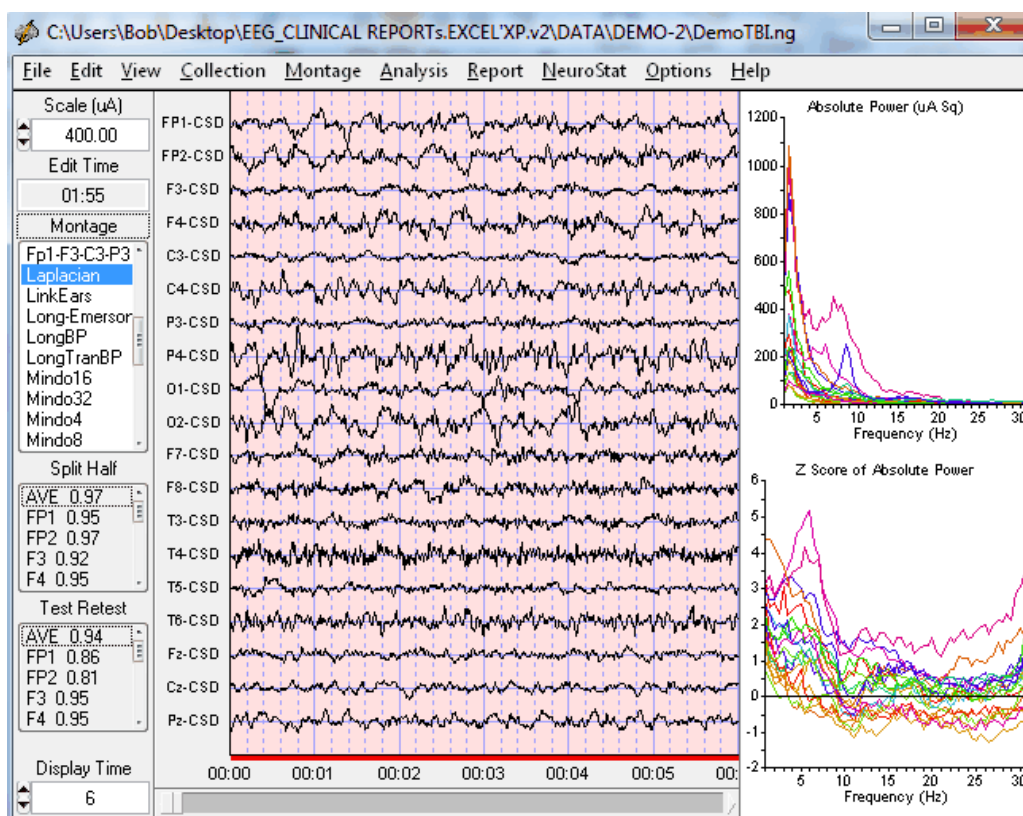
Scale the EEG tracings in uV/cm, change the Display Time Scale, Resize the Screen or Display Window and Move the Slider to View more of the EEG.



## Re-Montaging and the Use of the Linked Ears, Average Reference and Laplacian Norms

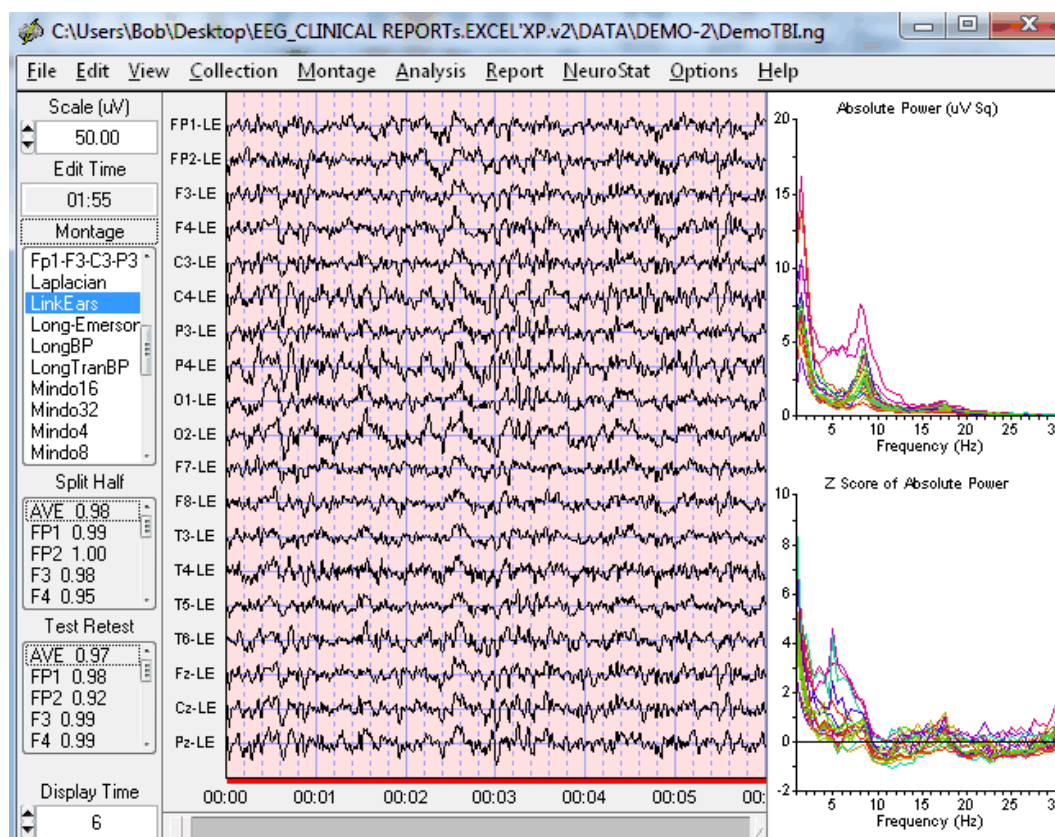
Double click on the Average Reference Montage or use the Tab & Arrow keys. The corresponding Z-Scores will be displayed in the lower right Z Score window. Scan the Z-Scores and compare to the Linked Ears montage.

Double click on the Laplacian Reference Montage or use the Tab & Arrow keys. The corresponding Z-Scores will be displayed in the lower right Z-Scores window. Hold the left mouse button and scan the Theta peak at 5 Hz to 6.5 Hz and make a written note of the Red Z-Scores and frequencies in the left margin of the EEG tracings.



Note that the scale is in microamperes because the Laplacian is an estimate of the current flowing at right angles through the skull (Nunez, 1981; 1994; Pasqual-Marqui et al, 1988).

Linked Ears Reference Montage Revisited - Double click on LINKEARS Montage & Re-Examine Theta and make notes as to which Locations show Red Z-Scores (i.e., > 1.96 SD). With linked ears reference the significant Z-Scores are more diffuse.



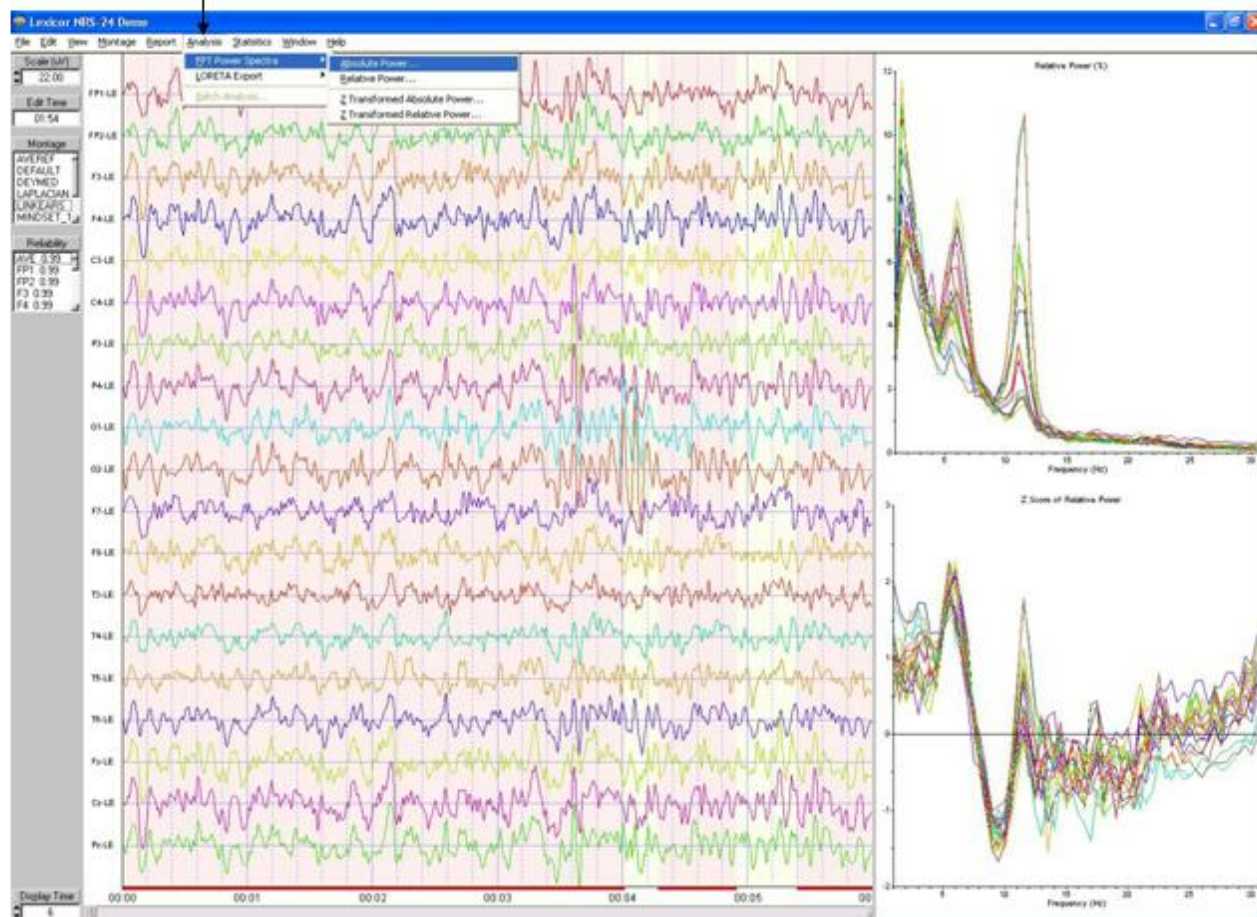
## Save Power Spectral Analyses in Tab Delimited Format

Click Analysis > FFT Power Spectra and then Absolute Power, Relative Power or Z Scores





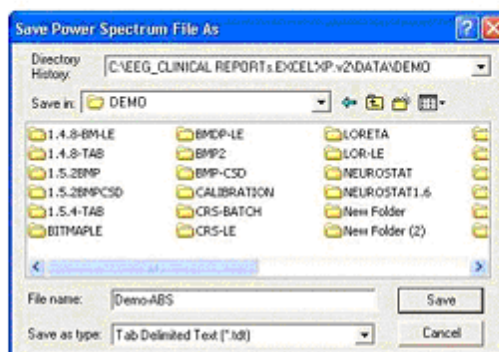
Click Analysis > FFT Power Spectra to Save 0.5 Hz Resolution FFT Results in Tab Delimited Format



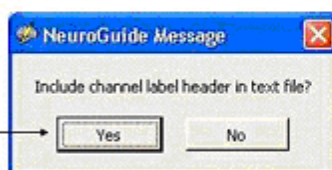
Navigate to a Folder and Name the File



**Navigate to Folder and Name the FFT File. Default extension is \*.tdt  
To designate that it is Tab Delimited**



Yes means that the  
Top row of the file will  
Be the channel labels

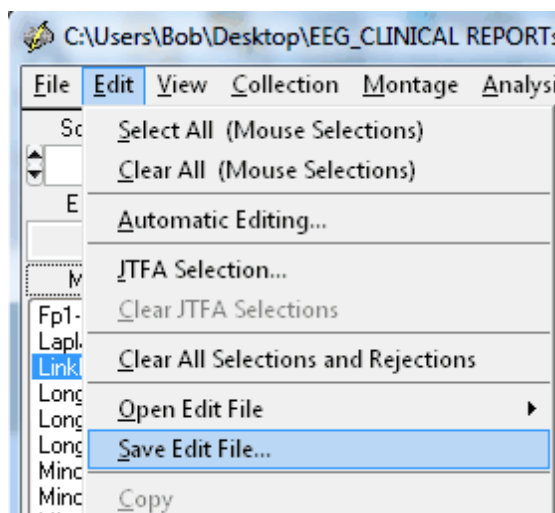


**Print EEG Tracings.** After making EEG selections then click **File > Print** to launch the windows print manager. Select properties and then "Landscape" and then click **OK** to print. NeuroGuide only prints the EEG selections and it prints "what you see is what you get" WYSIWYG, therefore, scale the volts or amperes and time display to your liking before printing.

## Save and Print EEG Selections

Save the final edit selections that will be used in the QEEG analyses by Clicking **Edit > Save Edit File...** If you want to only print a specific page, save the edits, then clear all selections and select the single page that you want to print.

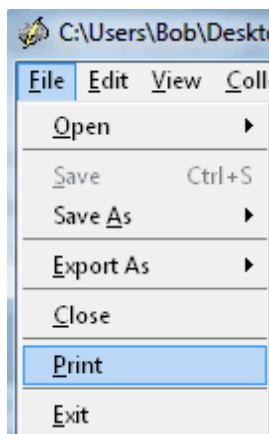




**Save in the patient/client's folder using the \*.edt extension**

**After importing a digital EEG file to open Edit Selections for that file Click Edit > Open Edit File > NeuroGuide and navigate to the location where the edits were saved. This only opens the Edit Selections for a given EEG data file and an EEG file must be imported first.**

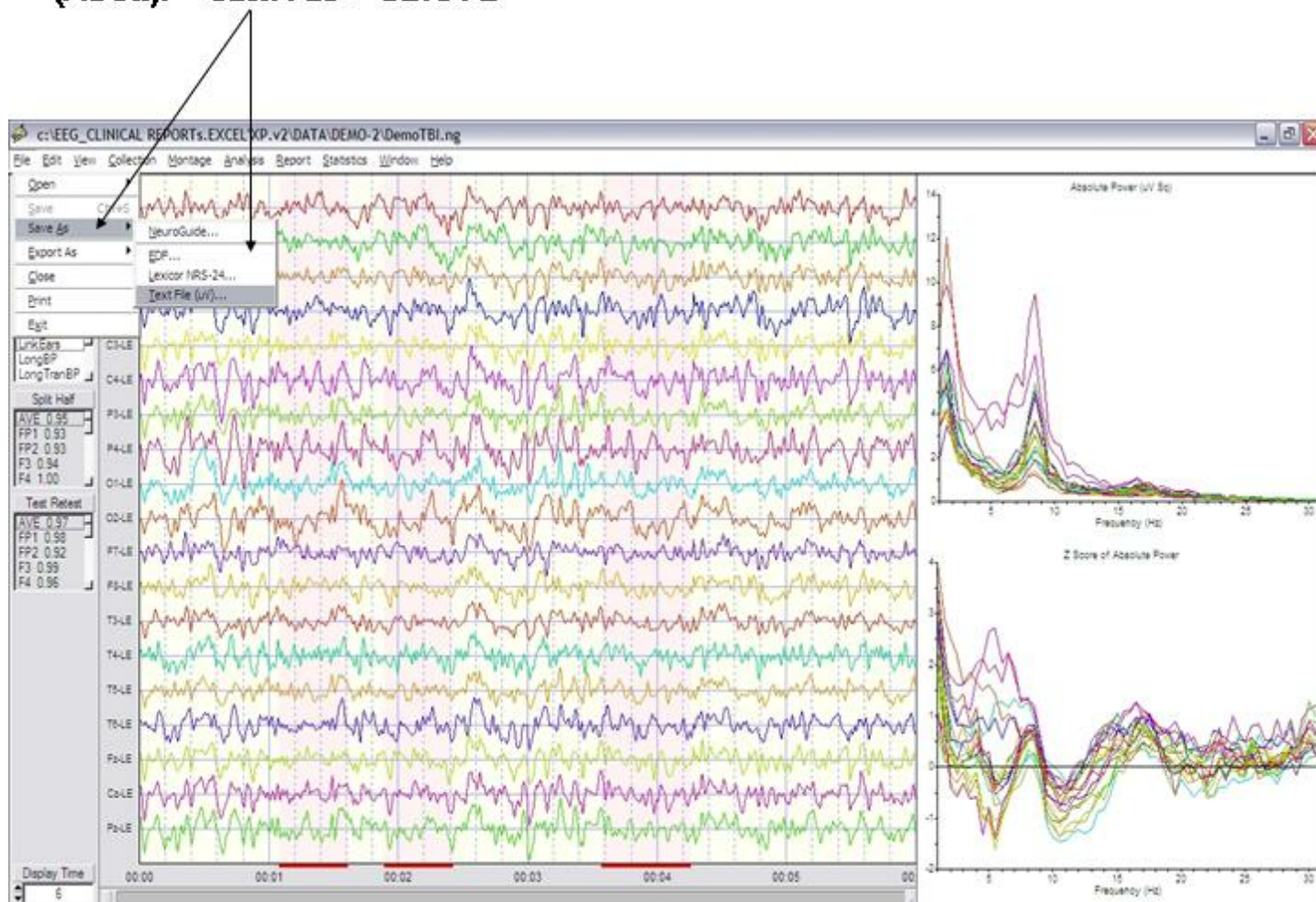
**Print or Export the Edited EEG in ASCII format by Highlighting Print or Export in the File Menu.**



**Save the Edited EEG Selections and patient information in NeuroGuide Format (\*.ng) . Save the EEG records without any edit selections in EDF format or Lexicor format or Text (ASCII) format.**



**Save Unedited EEG data in Different Formats: NeuroGuide, EDF, Lexicor and Text (ASCII). Click File > Save As**



## Selecting Report Content

Click Report > Report Selections to open the Report Dialog Box. Then Click the radial buttons to select the report content. To Save your selections click the Save button and then name and save your selections. To load previously saved selections click the Load Button at the bottom of the dialog box. To exit click OK or Cancel. Save your preferred selections as Default so that NeuroGuide will automatically load your preferred selections when you launch NeuroGuide.



Click the radial buttons in the Report Dialog Box to determine the report content. When completed, click OK and then Report > Generate Report.

To select only statistically significant Z Score connections for coherence, phase or amplitude asymmetry click Report > Report Selections > Connection Maps. The complete range of raw scores and Z Scores for connectivity measures is available in the connectivity Suite.

Click Report > Report Selections > Spectral Values in the dialog box and then select or de-select the FFT numerical spectral values to be included in the report. All numerical values can be saved by clicking Save > Tab Delimited Text file in the Output Windows, the window below controls a limited set of numerical values that are printed in the report itself.

Click: Report > Color Selections to Select the range of Z Scores and colors ranges in the Topographic Z Score maps.

In the color map settings dialog box select the Z Score range and color contrasts, then close the Color Map Settings window.



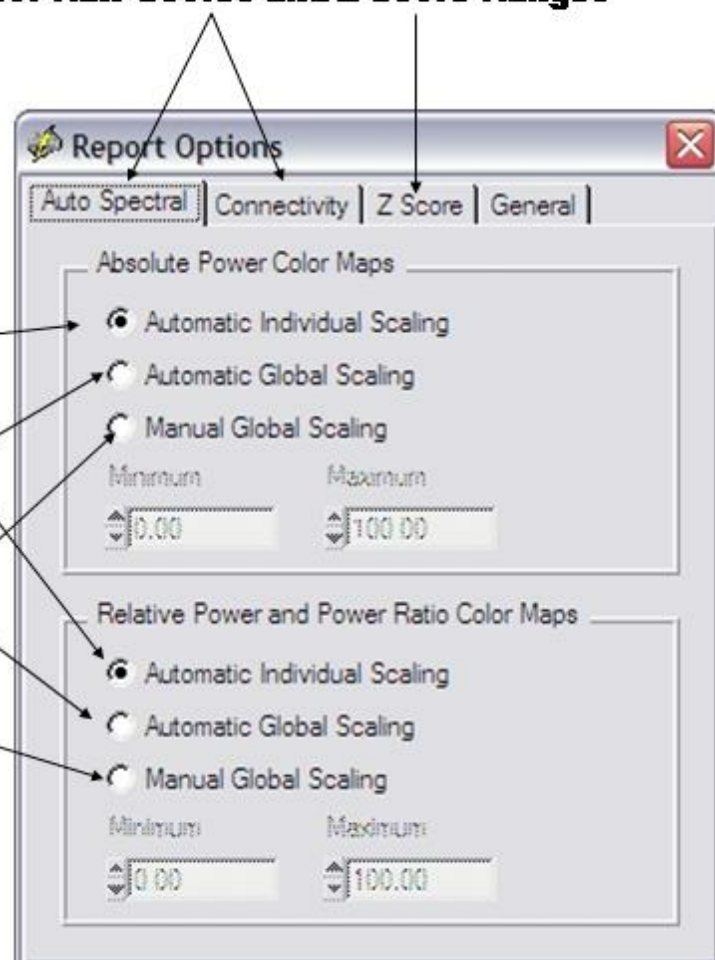
## Select Topographic Color Scales for Raw Scores and Z Score Ranges

Select Scaling of Absolute and Relative Topographic Maps

Individual Scaling for the Min-Max Values

Global Scaling for Min-Max of All Maps

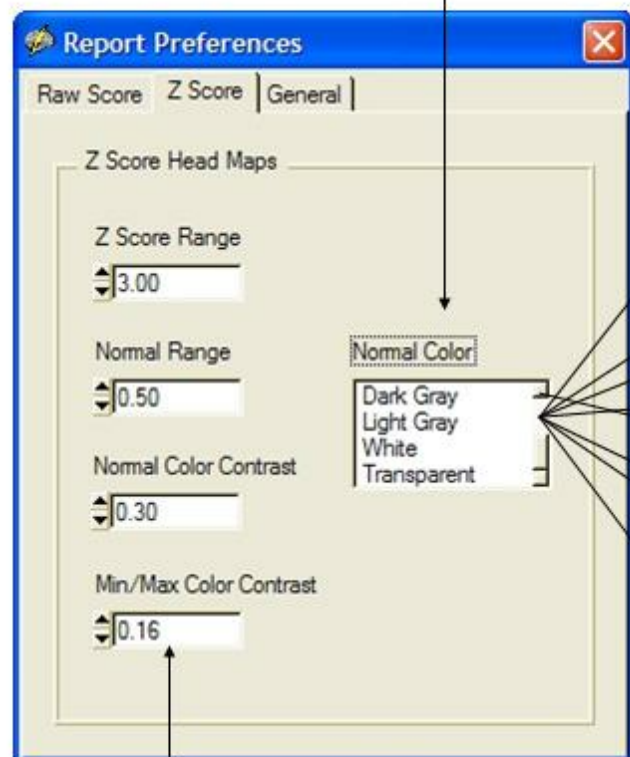
Manual Scaling for Min-Max of All Maps



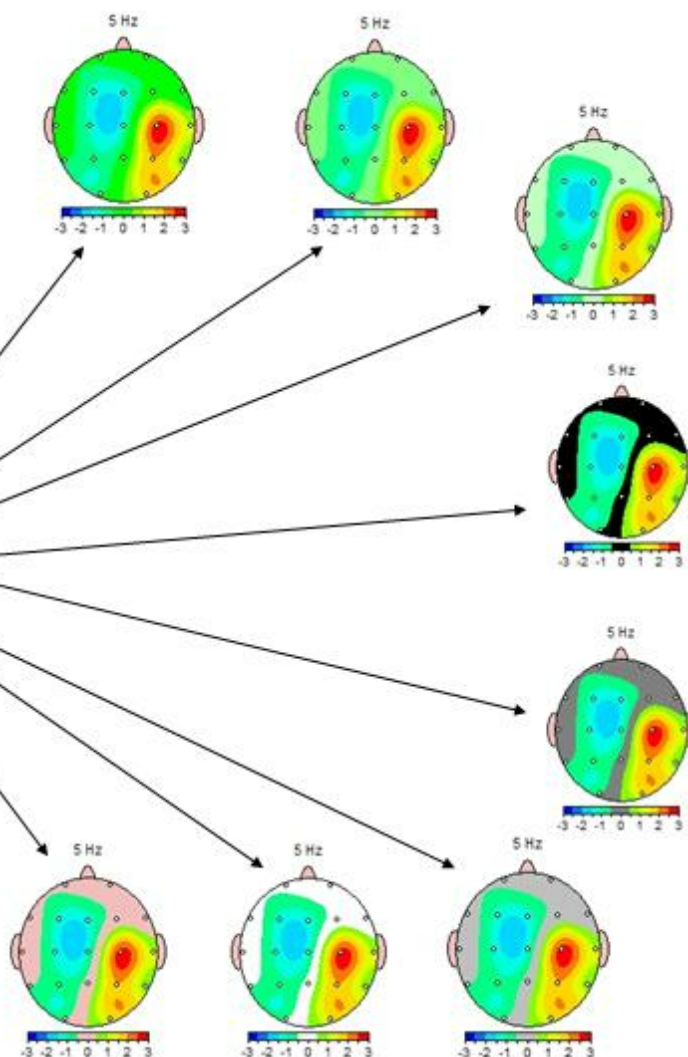
Click Z Score Tab to Scale the range of Normal Z Scores and to Change the Color Scheme



## Select Different Colors for the Normal Z Score Range



## Select Different Z Score Ranges and Boundaries



Save your report selections so that you can tailor the report to meet your needs and so that you can easily retrieve your selections in the future.

Load previously saved selections so as to quickly tailor the report to meet your needs.

After making your Selections (Final Items Checked and Unchecked) click OK in the Report Selections Dialog Box, then click Report > Generate Report to compute color maps and report content. Repeat with Different Montages and Conditions (Laplacian & Average Reference) for additional report output.

Click Report > Report Selections in the Menu. Uncheck and check FFT Connection maps that you want in your Report. The connectivity maps are limited to a smaller number of measures and the statistically significant pairs of leads only. This is in contrast to the Connectivity Suite which presents all 171 possible combinations and a full range of Z Scores for a wide range of connectivity measures.



**Click Report > Report Selections and Color Maps & Connectivity Maps**

**Report Selections**

☒ Subject Information  
☒ Technical Information  
☒ Summary

**Color Maps**

☒ Absolute Power  
☐ Relative Power  
☐ Power Ratio  
☐ Standard Bands  
☒ 1 Hz Bands

**Connection Maps**

☒ Amplitude Asymmetry  
☒ Coherence  
☒ Phase Lag

**Spectral Values**

☐ Absolute Power  
☐ Relative Power  
☐ Power Ratio  
☐ Peak Frequency  
☐ Amplitude Asymmetry  
☐ Coherence  
☐ Phase Lag

**Discriminant Functions**

☐ Learning Disability  
☒ Traumatic Brain Injury

**Predictive Functions**

☐ Brain Performance Index

**Burst Metrics**

☐ Number of Bursts  
☐ Burst Amplitude  
☐ Burst Duration  
☐ Burst Interval

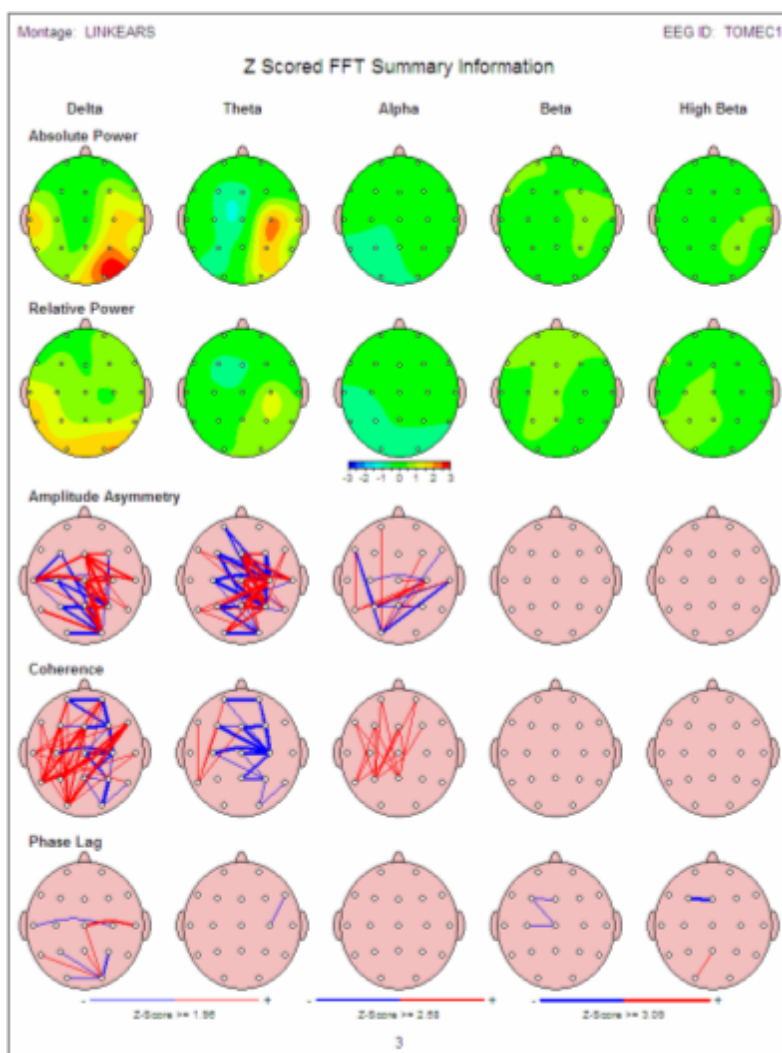
**Connectivity Suite**

☐ Amplitude Asymmetry  
☐ Coherence  
☐ Phase Lag  
☐ Cross Spectral Power  
☐ Instantaneous Connectivity  
☐ Lagged Connectivity  
☐ Correlation (Comodulation)  
**Phase Reset**  
☐ Phase Resets per Second  
☐ Phase Shift Amplitude  
☐ Phase Shift Duration  
☐ Phase Lock Duration  
☐ Rate of Phase Shift

☐ Raw Scores  
☒ Z Scores  
☒ Page Numbers

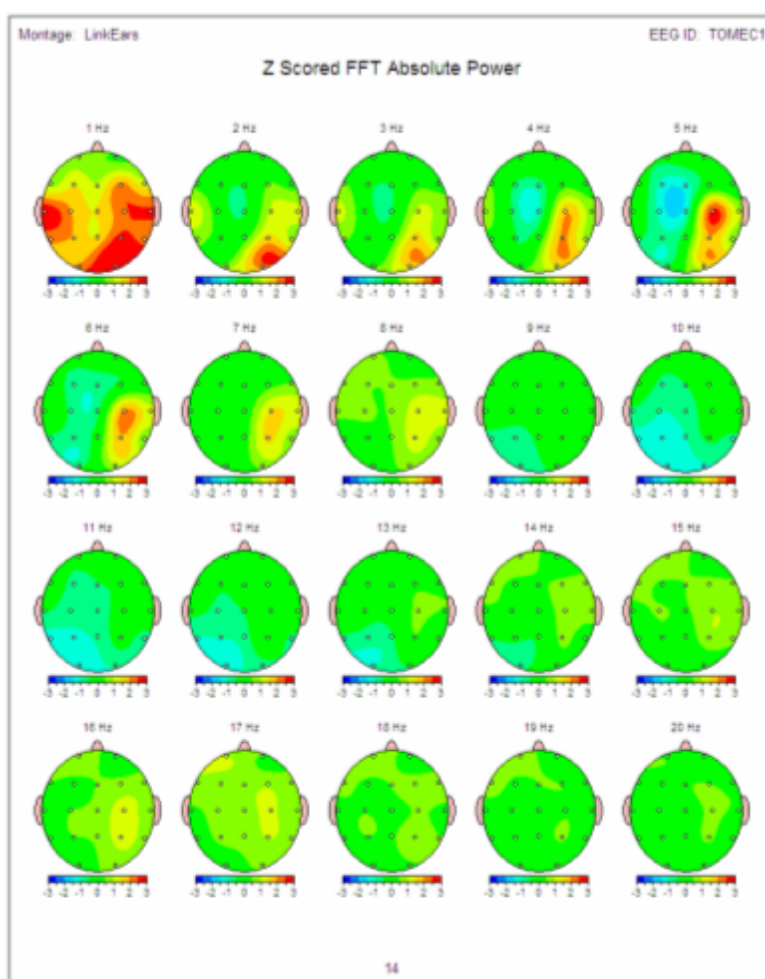
Load Save Default OK Cancel

First Page of Report is the Subject Information, then Technical Information and then a Summary Page. Below is an example of a summary page

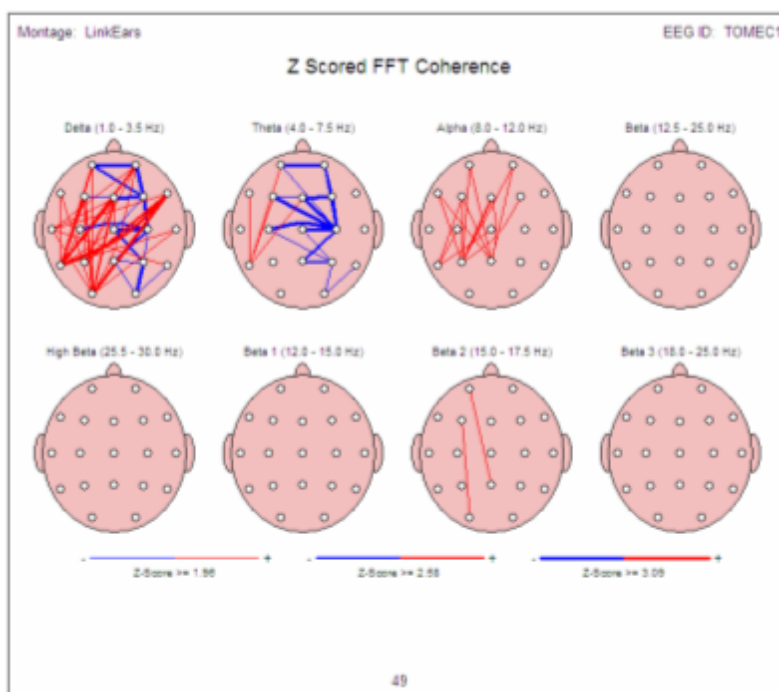


Example Page of the 1 Hz Z Absolute Power Z Score Maps





Example Page of the Coherence Z Scores



In the Analysis Output panel, click **Save > Bitmaps** to save the Results of the Color Maps in Bit Map Format or click **Save > Tab Delimited** to save the numerical values in ASCII Tab Delimited Format to be Export to Excel or Database Management or Statistics Programs. Create a Folder, then open the folder and name the bitmap files before saving them in the folder. Later navigate to the Folder to Import directly into Word, or Power Point or Print Shop Pro, etc.

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## Appendix A: Warning about Digital and Statistical Analyses of the EEG

**WARNING:** NeuroGuide does not diagnose and only provides displays of the digital EEG and statistical analyses of selected EEG segments. NeuroGuide requires competent human intervention for its many mathematical tools and NeuroGuide is only considered as an adjunct and/or as a supplement to other measures that may aid in evaluating the status of the EEG by a competent person. Clinical use of NeuroGuide requires a competent medical or clinical professional. NeuroGuide is a standalone software package that uses "look up" table functions to create Z Scores which are a reference based on published scientific selection criteria of samples of EEG (Thatcher et al. 1987; 1986; 1989; 2003) and the use of these tables is at the discretion of the competent professional. It is advised that reliability measures and validity tests using different montages and different selections of EEG be conducted as a routine procedure when using NeuroGuide. NeuroGuide was designed to allow for mouse click selections and testings of hypotheses and reliability and validity using digital analyses of the EEG. qEEG is not a substitute for EEG, but an addition to EEG. Some forms of clinically important information are better recognized by eye than by quantification, and the visual inspection of the waveform EEG data is a good way to monitor and control the level of consciousness as well as eye movement and muscle artifacts. A qEEG device will not substitute for lack of EEG training, qEEG is more demanding than classic EEG on both the clinician and technologist. Those performing and reading of qEEG studies must not only have basic EEG skills, but must also have a functional understanding of the numerical and statistical techniques used in qEEG, be specifically trained in qEEG analysis and be aware of the necessity for better control of artifact and subject state. qEEG should always be interpreted by a knowledgeable clinician in the light of all relevant information.

**CONTRA INDICATIONS:** EEG artifact can invalidate analyses and improper positioning of electrodes or significant deviations from accepted standards of electroencephalographic recording methodology can invalidate EEG recordings or erroneous storage of data and falsification of data, improper manipulation of data or unlawful uses of NeuroGuide including violations of copyright law and other improper uses of NeuroGuide are all contra indicated.



## **Appendix B: Computation of the Auto-spectral and Cross-spectral Densities, Coherence, Phase Delays and Amplitude Asymmetry of the Edited EEG Selections**

### **Use the Signal Generator to Calibrate the Digital Signal Processing**

**1 - Import of digital EEG data involves the following steps:**

- 1) Down-sample or up-sample to 128 Hz;**
- 2) Baseline the EEG by filtering at  $< 1$  Hz and  $> 40$  Hz (5th order Butterworth filters and creating values from zero time to negative time to allow the filter to start at time point = 0);**
- 3) After each edit selection baseline the spliced selections of EEG by filtering a second time at  $< 1$  Hz and  $> 40$  Hz.**

**2 - Amplifier equilibration is computed as the difference between the normative database amplifier characteristics in microvolts based on the frequency response of a calibrated sine wave from 1 to 40 Hz. The equilibration ratio for each EEG machine manufacturer is a coefficient in all of the subsequent spectral computations in the list of EEG machines in the File > Open window. The FFT (Fast Fourier Transform) parameters are: epoch = 2 seconds at a sample rate of 128 sample/sec = 256 digital time points and a frequency range from 0.5 to 40 Hz at a resolution of 0.5 Hz using a cosine taper window. Each 2 second FFT is 101 rows (frequencies 0 to 50 Hz) X 19 columns (electrode locations) = 1,919 element cross-spectral matrix for each subject. NeuroGuide uses the same equations as used by the Key Institute (see Key Institute equations 10 to 19 in the Key Institute Help Manual) and Bendat and Piersol, 1980; Otnes and Enochson, 1978 which are standard equations. The N in the Key Institute cross-spectrum equations 16 and 17 is the number of 2 second windows that are used in the computation of the average FFT which is the sum of the spectra from 2 second windows/N. The last whole integral of 256 points marks the end of window summation and averaging. The N sub T (Key Inst. equation 17) is the number of time frames per FFT window = 256 at 128 samples per second. A detailed documentation of the mathematical equations for the Fourier Transform and the Power Spectrum and Power Spectral Density is available at <http://www.appliedneuroscience.com/Brain%20Connectivity-A%20Tutorial.pdf>**

**3 - In order to minimize the effects of windowing in the FFT (Kaiser and Stermann, J. Neurotherapy, 4(3): 85-92, 2001) a EEG sliding average of the 256 point FFT cross-spectral matrix was computed for each normal subjects edited EEG by advancing in 64 point steps (75% overlap) and recomputing the FFT and continuing with the 64 point sliding window of 256 point FFT cross-spectrum for the entire edited EEG record. Each of the 101 frequencies for**



each 19 channels is log10 transformed to better approximate a normal distribution. The total number of 2 second windows is the number that is entered into the analysis of variance and t-tests and it is used to compute the degrees of freedom for a given statistical test.

4 - The FFT mean, variance, standard deviation, sum of squares, and squared sum of the real (cosine) and imaginary (sine) coefficients of the cross-spectral matrix is computed across the sliding average of edited EEG for all 19 leads for the total number of 101 frequencies and 1,919 log transformed elements for each subject at 0.5 Hz resolution. This creates the following eight basic spectral measurement sets and their derivatives

- 1) Cross-Spectral Power (square root of the sums of squares of the real and imaginary coefficients);
- 2) Auto-Spectral Power which is the diagonal of the cross-spectral matrix where the imaginary coefficient = 0 and power = sine square;
- 3) Amplitude asymmetry of auto-spectral power =  $(A-B)/(A+B) \times 200$  where A = EEG channel 1 and B = EEG channel 2;
- 4) Coherence = square of the cross-spectrum divided by the product of the two auto-spectra;
- 5) Phase = arctangent of the ratio of the real/imaginary components for frequencies from 0.5 to 50 Hz,;
- 6) Real coefficients;
- 7) Imaginary coefficients; and
- 8) Peak Frequency =  $\text{sum}(\text{freq.} \times \text{abs. power}(\text{freq}))/\text{sum abs. power}(\text{freq})$ , e.g.,  $(4.0 \times 2 + 4.5 \times 4 + 5.0 \times 2)/(2 + 4 + 2) = 4.5 \text{ Hz}$ .

(Bendat and Piersol "Engineering applications of correlation and spectral analysis", John Wiley & Sons, NY, 1980; Otnes and Enochson "Digital time series analysis", Wiley-Interscience, 1978; Press et al, "Numerical recipes in C".

5 - The frequency bands are slightly different for NG 1.0 to NG 2.3.8 and were changed on May 15, 2007 for NG 2.3.9 and later versions. The frequency bands for the various versions of NeuroGuide are shown below:



	NG v 1.0 - 2.3.8	NG v 2.3.9 and later
Delta	1.0 - 3.5 Hz	1.0 - 4.0 Hz
Theta	4.0 - 7.5 Hz	4.0 - 8.0 Hz
Alpha	8.0 - 12.0 Hz	8.0 - 12.0 Hz
Beta	12.5 - 25.0 Hz	12.0 - 25.0 Hz
Hi-Beta	25.5 - 30.0 Hz	25.0 - 30.0 Hz
Gamma	30.0 - 40.0 Hz	30.0 - 50.0 Hz
Alpha 1	NA	8.0 - 10.0 Hz
Alpha 2	NA	10.0 - 12.0 Hz
Beta 1	12.0 - 15.0 Hz	12.0 - 15.0 Hz
Beta 2	12.0 - 17.5 Hz	15.0 - 18.0 Hz
Beta 3	18.0 - 25.0 Hz	18.0 - 25.0 Hz
Gamma 1	NA	30.0 - 35.0 Hz*
Gamma 2	NA	35.0 - 40.0 Hz*
Gamma 3	NA	40.0 - 50.0 Hz*
* Coherence, Phase and Amplitude Asymmetry Sub-bands of Gamma		

The reason for the change in frequency band designation was to create uniformity between the FFT and the JTFA frequency analyses. The FFT spectrum is computed with 0.5 Hz resolution with the center frequency at 0.25 Hz within a given frequency 0.5 Hz band. The frequency bands in NeuroGuide do not have any gaps or overlaps, for example, frequency band 1.0 Hz to 2.0 Hz = 1.0 to 1.5 Hz + 1.5 Hz to 2.0 Hz. The adjacent frequency band, 2.0 to 3.0 = 2.0 to 2.5 Hz + 2.5 Hz to 3.0 Hz. The complex demodulation JTFA analyses use the same frequency bands as the FFT but without the sharp 0.5 Hz sub-bands as are used in the FFT.

6- Split-Half Reliability Coefficient is defined by the ratio of the variance of the even and odd seconds of the selected EEG record and referred to as the proportion of the obtained variance that is true variance. Test Re-Test reliability uses the same equations but is the ratio of the variance of the first half of the EEG selections vs the variance of the second half of the EEG selections (Ferguson, G.A., Statistical Analysis in Psychology and Education, McGraw-Hill, 1976. Test Re-Test reliability is especially useful for detecting state changes in vigilance during the course of the recording session.

7 - Time-Frequency means, standard deviations, sum of squares and squared sum of the real and imaginary coefficients are computed using complex demodulation. A 500 millisecond integration window and a five point recursive filter with a sixth order Butterworth band pass filter is used. The center frequencies and half bandwidths for absolute power, relative power,





amplitude asymmetry, coherence and phase differences are: Delta = 2.5 Hz, 1.5 Hz; theta = 6.0 Hz, 2 Hz; alpha = 10 Hz, 2.0 Hz; Beta = 8.5 Hz, 6.5 Hz; Hi-Beta = 27.5 Hz, 2.5 Hz; Beta-1 = 13.5 Hz, 1.5 Hz; Beta-2 = 16.5 Hz, 1.5 Hz; Beta-3 = 21.5 Hz, 3.5 Hz; Gamma = 35.0 Hz, 5.0 Hz; Alpha-1 = 9.0 Hz, 1.0 Hz and Alpha-2 = 11.0 Hz, 1.0 Hz. The center frequencies and band widths were selected in order to achieve high reliability and stability and to approximate accepted band widths used in EEG biofeedback. The computational details of complex demodulation are described in Otnes and Enochson "Digital time series analysis", Wiley-Interscience, 1978 and at: <http://www.appliedneuroscience.com/Brain%20Connectivity-A%20Tutorial.pdf>

8 - Z Scores are computed as  $\text{mean1} \text{ population mean} / \text{population st. dev.}$  where the population mean and standard deviation are computed across normal subjects for each age group and where mean1 = the average spectral value computed based on the users EEG selections for a given subject. There are 21 different age groupings from birth to 82 years of age. Go to Appendix-F to view the age groupings. Details as to selection criteria, artifact removal, reliability, cross-validation, fitting to a gaussian curve and other aspects of the norms are published in peer reviewed journals (see Thatcher et al, Science, 236: 1110-1113, 1987; Thatcher, J. Neurotherapy, 2(4): 8-39, 1998; Thatcher et al, J. Neurotherapy, 7 (No. 3/4): 87-122, 2003; Thatcher et al, Clinical EEG and Neuroscience, 36(2): 116-122, 2005). Z Scores of autospectral and cross-spectral power are based on 0.5 Hz frequency bins from 1 to 30 Hz (i.e., 61 total 0.5 Hz bins) and are displayed in the NeuroGuide edit screen when one selects the Dynamic FFT option (i.e., click View > Dynamic FFT > Absolute Power). Band Z Scores, e.g., 1 Hz bands, delta (1 to 4.0 Hz), theta (4 - 8 Hz), alpha (8 - 12 Hz), beta broad (12 - 25 Hz), beta 1 (12 - 15 Hz), beta 2 (15 - 18 Hz), beta 3 (18 - 25 Hz) and hi-beta (25 - 30 Hz) are the average of the 0.5 Hz Z Scores within a given band. Averaging of the Z Scores within a band provides for flexibility customizing bands as well as exact replication in the Dynamic FFT window which is a what you see is what you get WYSIWYG display that gives instant verification to the topographic maps and band Z Score values. Coherence, phase and amplitude asymmetry do not involve averaging of Z Scores within a band but rather the computation of the mean and standard deviation of band value using the cross-spectral FFT.

9 - Time-frequency Z Scores are computed using complex demodulation. The within subject variance as well as between subject variance is used to compute the database means and standard deviations. There is no averaging of Z Scores within a band, instead the absolute power within a band is determined by the center frequency and band width of the complex demodulation. The computational details of complex demodulation are described in Otnes and Enochson "Digital time series analysis", Wiley-Interscience, 1978 and at: <http://www.appliedneuroscience.com/Brain%20Connectivity-A%20Tutorial.pdf>



## Appendix C: Warning about Cross-Platform Data Transfers

**WARNING:** NeuroGuide uses a splicing method of appending edited selections of EEG (minimum segment length = 600 msec.) and then baselines using a Butterworth high pass filter at 1 Hz and a low pass filter at 55 Hz so as to minimize splicing artifact. When NeuroGuide exports the edited selections there is an approximation to baseline adjustment and possible splice artifact may occur when the edited data are imported into other software platforms. Amplifier matching will be violated if users, for example, collect EEG using a Deymed amplifier and then export in Lexicor format because NeuroGuide matches the amplifier characteristics of different EEG equipment manufactures and miss-labeling defeats the matching process.

Another warning about cross-platform comparisons are possible differences in FFT epoch lengths (NeuroGuide uses 2 second epoch lengths), windowing methods (NeuroGuide uses cosine taper windowing), successive vs. overlapping epochs (NeuroGuide uses 75% sliding epoch overlapping while other platforms do not use overlapping epochs, see Appendix B), etc. Within platform analyses using calibration sine waves are recommended and cross-platform comparisons are not recommended unless the exact same analytical procedures are used.

## Appendix D: Default LORETA Electrode Coordinates and T Matrix

ASCII Electrode Order and Spherical Coordinates for Use of the NeuroGuide Output Files with the Key Institutes LORETA Explorer. If the Lex-TalairachCoord.xyz file is not available then create this file by copying the values in the Table below and save as an ASCII file (tab delimited, free space or comma delimited). You will need this file in order to use the NeuroGuide output files with the LORETA Explorer. The user of course can always create their own electrode coordinate files and T matrices by using the Key Institutes Talairach Electrode Coordinate Maker 01.

19			
-3.28E+01	8.10E+01	-3.70E+00	Fp1
1.49E-09	9.02E+01	-4.63E+00	Fpz
-7.06E+01	3.16E+01	1.32E+00	F7
-5.09E+01	4.82E+01	5.04E+01	F3
1.49E-09	5.70E+01	7.11E+01	Fz
5.09E+01	4.82E+01	5.04E+01	F4
7.06E+01	3.16E+01	1.32E+00	F8
-8.25E+01	-1.95E+01	6.51E+00	T3
-6.11E+01	-1.31E+01	6.95E+01	C3
1.49E-09	-1.03E+01	9.65E+01	Cz
6.11E+01	-1.31E+01	6.95E+01	C4
8.25E+01	-1.95E+01	6.51E+00	T4



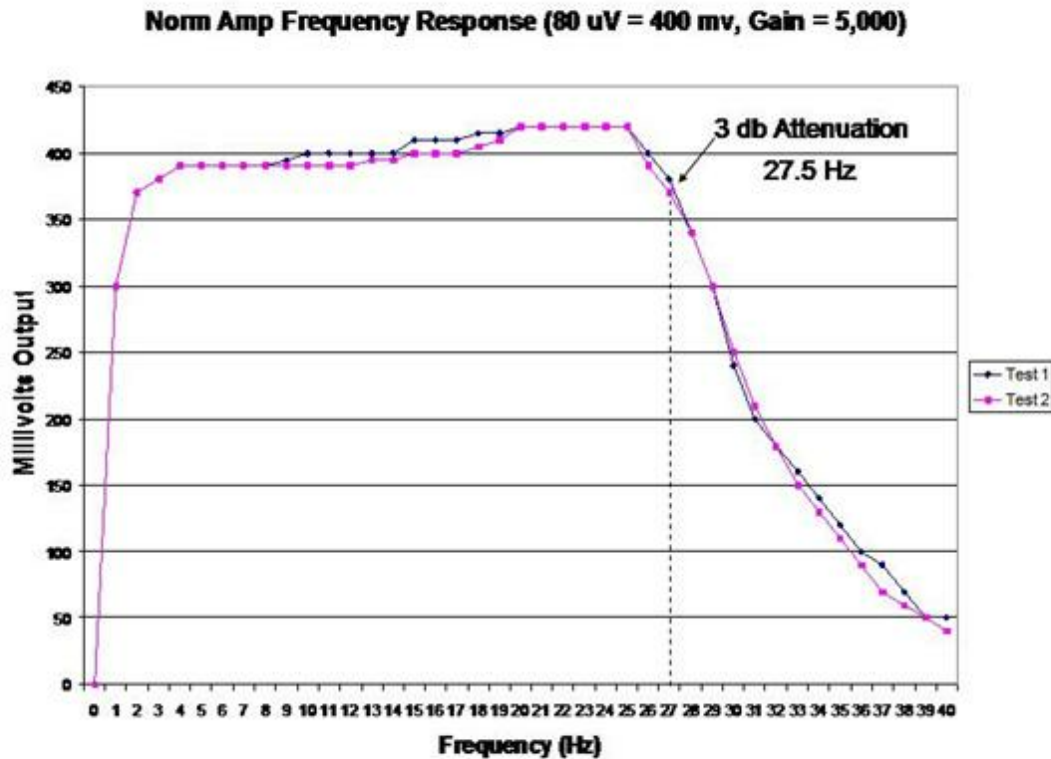
-7.34E+01	-7.25E+01	1.19E+01	T5
-5.14E+01	-7.75E+01	6.37E+01	P3
1.49E-09	-8.02E+01	8.37E+01	Pz
5.14E+01	-7.75E+01	6.37E+01	P4
7.34E+01	-7.25E+01	1.19E+01	T6
-3.17E+01	-1.16E+02	1.64E+01	O1
3.17E+01	-1.16E+02	1.64E+01	O2

## Appendix E: University of Maryland Amplifier Characteristics

Normative reference EEG was acquired using 20 identical amplifiers mounted in a rack at the Baltimore campus and another rack of 20 identical amplifiers at the Eastern Shore campus. Each of the amplifiers and A/D systems were calibrated before and after each subject's EEG and evoked potential acquisition.

- Gain = 104 v/v switchable to 105 v/v
- Gain Stability = 0.5%
- Common Mode Rejection = 100 db
- Bandwidth: 0.5 Hz to 27.5 Hz 3db point with notch filter at 60 Hz. Notch Q = 10, Notch rejection = 40 db, flatness less than 0.25 db.
- Input Impedance = 100 meg (differential or common mode).
- Noise Level = 0.5 uv p-p at 104 v/v & 1.5 uv p-p at 105 v/v.
- Nominal Output Level =  $\pm 0.5$ v at 104 v/v &  $\pm 5$ v at 105 v/v.
- Supply Voltage =  $\pm 15$ vdc.
- Supply Current = +15vdc: 37ma  $\pm 10\%$  & -15vdc: 37ma  $\pm 10\%$
- A to D conversion = 12 bit, sample and hold (Analog Devices).
- Sample Rate = 100 Hz.

Below is an example of the frequency response of the University of Maryland amplifiers

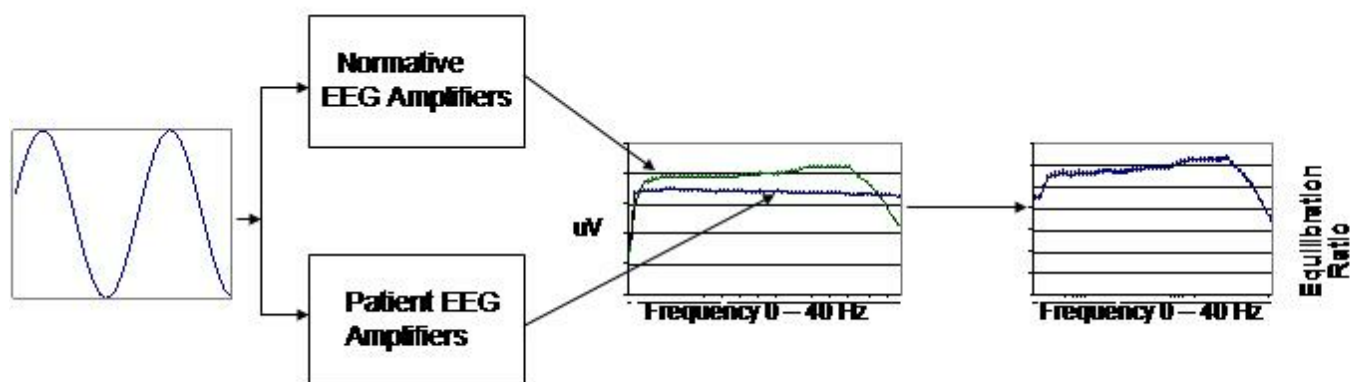


NeuroGuide uses calibrated sine waves injected into the input of different EEG machine amplifiers as well as the normative database amplifiers in order to equilibrate the frequency responses and thus match amplifier characteristics. The graph below is an illustration of the method of amplifier matching between 1 Hz and 30.5 Hz for the Deymed amplifier and the Univ. of Maryland amplifiers in which the equilibration ratio at each frequency is used to amplitude scale the FFT in order to match the frequency characteristics of amplifiers. Although 0 to 40 Hz is shown, matching is only between 1 Hz and 30.5 Hz as stated above.



## Normative Database Amplifier Matching – Microvolt Sine Waves 0 to 40 Hz

### Equilibration Ratios to Match Frequency Responses



## Appendix F: Normative Database

The NeuroGuide (NG) normative database in versions 1.0 to 2.4.6 included a total of 625 carefully screened individual subjects ranging in age from 2 months to 82 years. NG 2.5.1 involved the addition of 53 adult subjects ranging in age from 18.3 years to 72.6 years resulting in a normative database of 678 subjects. The inclusion/exclusion criteria, demographics, neuropsychological tests, Gaussian distribution tests and cross-validation tests are described in several peer reviewed publications (Thatcher et al, 1983; 1987; 2003).

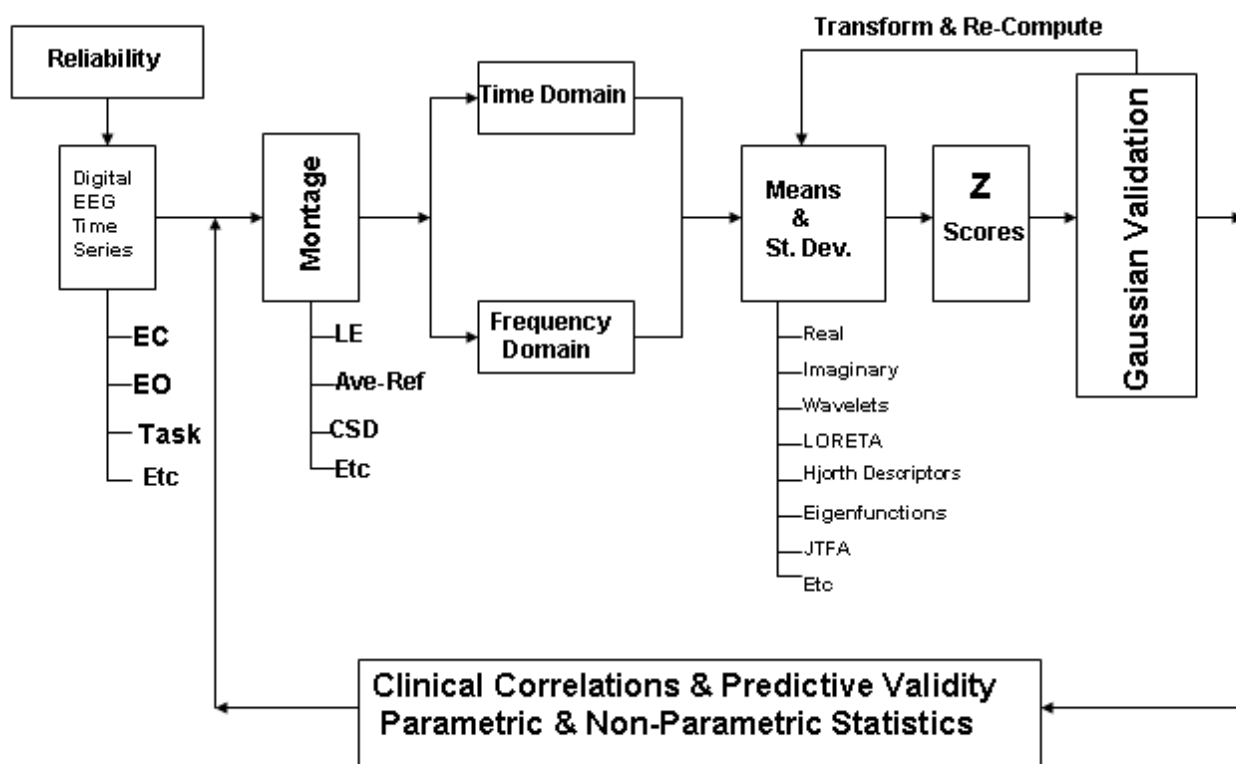
The age matching of norms in NeuroGuide version 1.0 to 2.3.8 involved stratification of age in five non-overlapping age groups as described in Thatcher et al, 2003. In order to increase the time resolution of age sliding averages were used for the stratification in NeuroGuide version 2.3.9. Two year means were computed using a sliding average with 6 month overlap of subjects. This produced a more stable and higher age resolution normative database and a total of 21 different age groups. The 21 age groups and age ranges and number of subjects



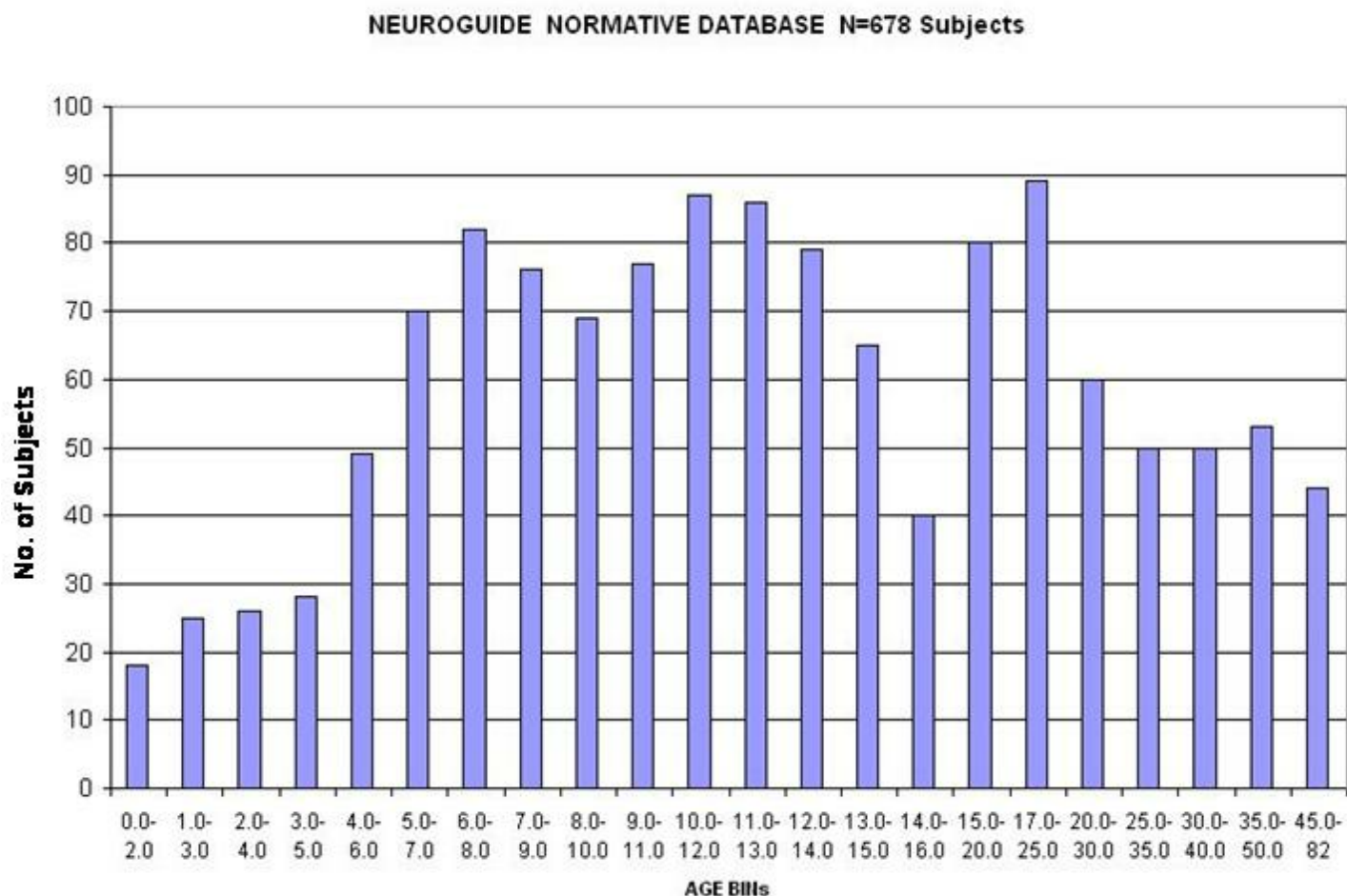
per age group is shown in the bar graph Appendix F figure 2 below.

NeuroGuide version 2.5.1 expanded the number of age groups to 22 with the addition of a finer adult age grouping between age 45 and 82. The 22 age groups and age ranges and number of subjects per age group is shown in the bar graph in Appendix F figure 3 below. NG 2.5.1 thus has a normative database of 678 subjects from 2 months of age to 82 years of age. The childhood norms from 2 months of age to 17.9 years of age are the same in NG 2.5.1 as they were in NG 2.3.9. Cross-validation and Gaussian tests were performed using the standard methods described in Thatcher et al (2003). Below is a diagram of the procedures used to test Gaussianity and cross-validation and clinical correlation (from Thatcher et al, 2003, figure 1):

## Normative Database Validation Steps



Below is a graph (Figure 2) that shows the 22 different age bins and the number of subjects per age bin in NG 2.5.1 and later releases of NeuroGuide:

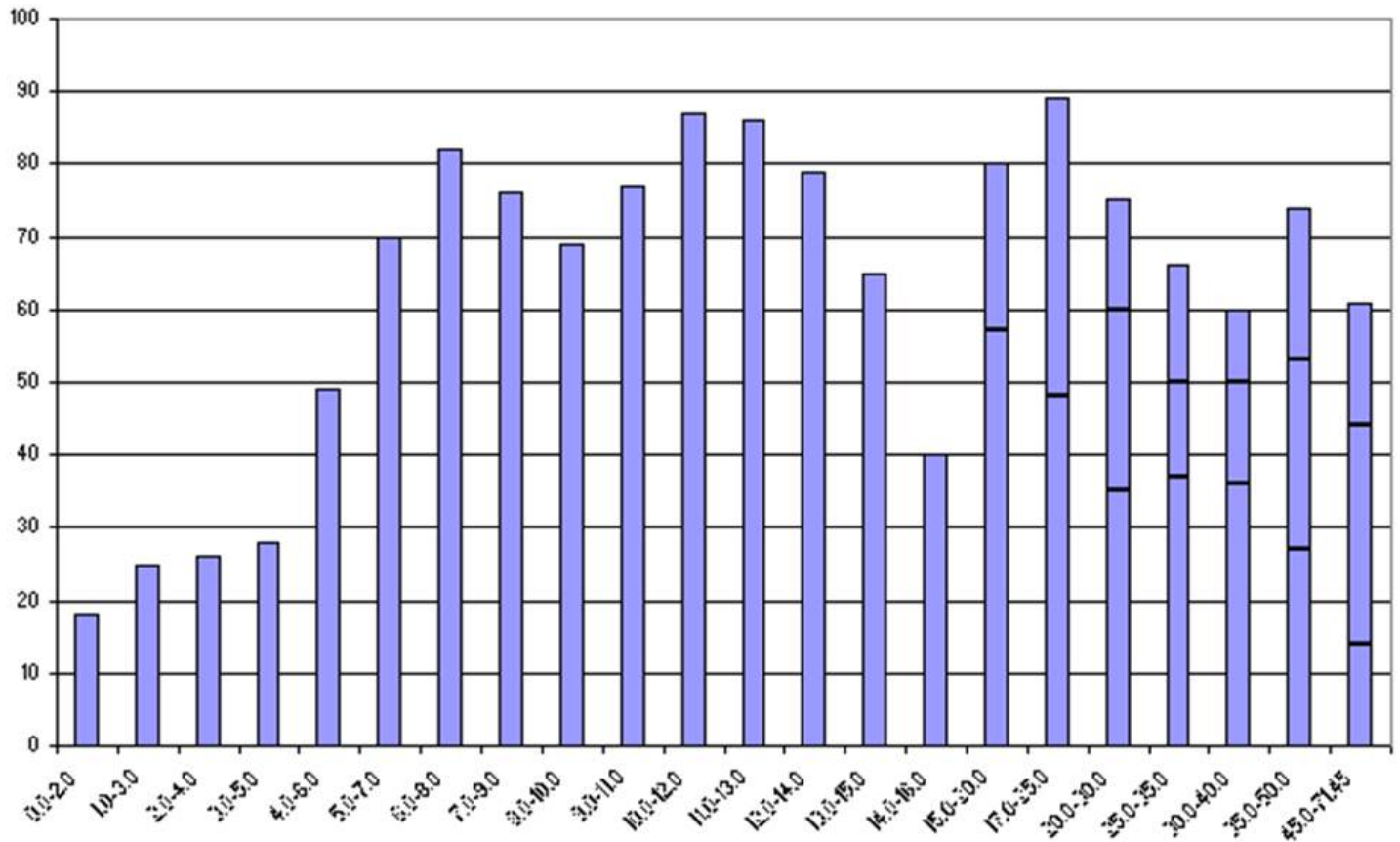


Graph of Normative Database Released with NG 2.6.8 (8/24/11). The blue color are the norms for NG 2.0 to 2.4.6, the magenta color are the added normative subjects in NG 2.5.1 to 2.6.7 and the yellow color are added 49 normative adult subjects in NG 2.6.8.





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

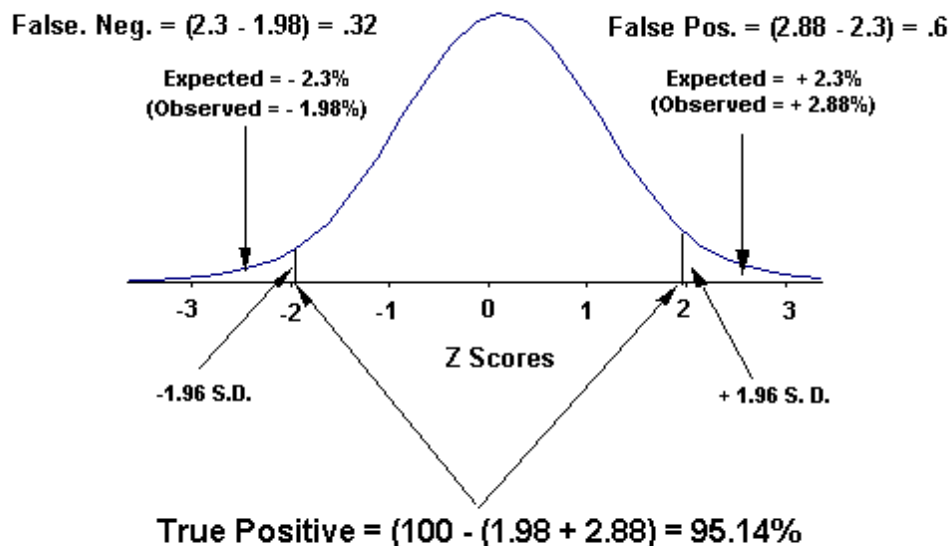


Cross-validation involved computing the sensitivity and classification accuracy of each normal subject in the normative database. An illustration of the computations are shown below and the complete details of the computation are provided in Thatcher et al, 2003.



## Sensitivity Based on Deviation from Gaussian

Cross-Validation Accuracy N = 625 Subjects



$$\text{Sensitivity} = \frac{TP}{TP + (FP + FN)} = \frac{95.14}{95.14 + 1.0} = 98.96\%$$

$$\text{Specificity} = \frac{TN}{TN + (FP + FN)} = \text{Undefined}$$

There are too many tables and charts to show all of the cross-validation results of the entire normative database which also includes Burst Metrics, Phase Reset and Cross-Spectra in the Connectivity Suite. Nonetheless, below are examples of the results of cross-validation for many of the normative database values. The method of cross-validation is described in Thatcher et al (2003) and is shown in the figure above.



Absolute Power								
	PERCENTAGES Based on the # of STDEVs						SENSITIVITY	
FREQ	< -1 SD	> 1 SD	< -2 SD	> 2 SD	< -3 SD	> 3 SD	2STDEVs	3STDEVs
Delta	17.55%	15.04%	2.86%	1.39%	0.25%	0.02%	95.64%	99.74%
Theta	17.15%	15.32%	2.17%	1.94%	0.16%	0.18%	95.64%	99.74%
Alpha	14.49%	14.95%	3.96%	1.10%	0.57%	0.08%	95.65%	99.75%
Beta	14.25%	14.68%	2.08%	2.23%	0.49%	0.36%	95.64%	99.75%
Hi-Beta	12.45%	14.06%	0.96%	3.38%	0.43%	0.67%	95.64%	99.75%
Beta1	14.64%	14.10%	2.40%	2.26%	0.49%	0.28%	95.64%	99.75%
Beta2	14.03%	14.20%	2.43%	2.27%	0.50%	0.38%	95.64%	99.75%
Beta3	13.78%	14.81%	1.47%	2.67%	0.36%	0.45%	95.64%	99.75%

Relative Power								
	PERCENTAGES Based on the # of STDEVs						SENSITIVITY	
FREQ	< -1 SD	> 1 SD	< -2 SD	> 2 SD	< -3 SD	> 3 SD	2STDEVs	3STDEVs
Delta	13.95%	13.30%	4.28%	0.37%	1.22%	0.00%	95.64%	99.75%
Theta	14.13%	13.65%	3.12%	1.88%	0.95%	0.10%	95.65%	99.75%
Alpha	15.83%	15.48%	3.05%	1.14%	0.55%	0.00%	95.64%	99.75%
Beta	15.53%	15.82%	1.74%	2.88%	0.24%	0.05%	95.64%	99.74%
Hi-Beta	12.53%	15.11%	0.81%	3.74%	0.19%	0.47%	95.64%	99.75%
Beta1	14.97%	15.85%	1.36%	2.92%	0.18%	0.32%	95.64%	99.75%
Beta2	14.86%	15.45%	1.80%	2.96%	0.29%	0.18%	95.64%	99.75%
Beta3	15.19%	15.13%	1.44%	3.41%	0.24%	0.27%	95.64%	99.75%

Relative Power Ratios								
	PERCENTAGES Based on the # of STDEVs						SENSITIVITY	
FREQ	< -1 SD	> 1 SD	< -2 SD	> 2 SD	< -3 SD	> 3 SD	2STDEVs	3STDEVs
D/T	14.78%	14.37%	3.43%	1.50%	0.43%	0.20%	95.65%	99.75%
D/A	15.16%	14.77%	2.90%	1.97%	0.18%	0.36%	95.64%	99.75%
D/B	15.69%	14.17%	3.44%	1.17%	0.41%	0.17%	95.64%	99.75%
D/HB	15.49%	11.97%	3.93%	0.63%	0.72%	0.28%	95.64%	99.75%
T/A	15.90%	14.50%	2.62%	1.89%	0.30%	0.19%	95.64%	99.75%
T/B	15.21%	14.86%	2.77%	2.21%	0.36%	0.16%	95.65%	99.75%
T/HB	15.06%	13.33%	3.12%	1.23%	0.47%	0.28%	95.64%	99.75%
A/B	16.07%	15.86%	2.93%	1.31%	0.26%	0.05%	95.64%	99.74%
A/HB	15.33%	14.15%	3.54%	0.84%	0.36%	0.18%	95.64%	99.75%
B/HB	14.59%	12.96%	1.90%	1.50%	0.14%	0.23%	95.63%	99.74%
ALL	15.42%	14.23%	3.14%	1.49%	0.39%	0.21%	95.64%	99.75%

Peak Frequency								
	PERCENTAGES Based on the # of STDEVs						SENSITIVITY	
FREQ	< -1 SD	> 1 SD	< -2 SD	> 2 SD	< -3 SD	> 3 SD	2STDEVs	3STDEVs
Delta	15.30%	14.87%	1.92%	2.43%	0.16%	0.41%	95.64%	99.75%
Theta	14.10%	15.86%	1.58%	3.44%	0.20%	0.44%	95.65%	99.75%
Alpha	15.92%	15.89%	0.85%	3.37%	0.03%	0.37%	95.64%	99.74%
Beta	13.99%	14.89%	1.47%	3.48%	0.20%	0.56%	95.65%	99.75%
Hi-Beta	11.89%	14.53%	1.45%	3.13%	0.24%	0.61%	95.64%	99.75%
Beta1	12.85%	13.08%	3.59%	1.27%	1.36%	0.09%	95.64%	99.76%
Beta2	14.91%	14.94%	2.51%	2.36%	0.34%	0.23%	95.64%	99.75%
Beta3	14.88%	14.50%	1.85%	2.61%	0.27%	0.28%	95.64%	99.75%
ALL	14.23%	14.82%	1.90%	2.76%	0.35%	0.37%	95.64%	99.75%



Amplitude Asymmetry			Cross-Spectral Power			Phase Reset per Second			Burst per Second		
SENSITIVITY			SENSITIVITY			SENSITIVITY			SENSITIVITY		
FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs
Delta	95.64%	99.75%	Delta	95.65%	99.75%	Delta	95.64%	99.75%	Delta	95.64%	99.75%
Theta	95.64%	99.75%	Theta	95.64%	99.75%	Theta	95.64%	99.75%	Theta	95.64%	99.75%
Alpha	95.64%	99.75%	Alpha	95.64%	99.75%	Alpha	95.64%	99.74%	Alpha	95.64%	99.75%
Beta	95.65%	99.75%	Beta	95.64%	99.75%	Beta	95.63%	99.75%	Beta	95.63%	99.75%
Hi-Beta	95.65%	99.75%	Hi-Beta	95.65%	99.75%	Hi-Beta	95.64%	99.75%	Hi-Beta	95.64%	99.75%
Beta1	95.64%	99.75%	Beta1	95.64%	99.75%	Beta1	95.66%	99.75%	Beta1	95.64%	99.75%
Beta2	95.64%	99.75%	Beta2	95.64%	99.75%	Beta2	95.64%	99.75%	Beta2	95.64%	99.75%
Beta3	95.65%	99.75%	Beta3	95.64%	99.75%	Beta3	95.64%	99.75%	Beta3	95.64%	99.75%
ALL	95.64%	99.75%	ALL	95.64%	99.75%	ALL	95.64%	99.75%	ALL	95.64%	99.75%

Coherence		IN PHASE		Phase Reset Ampl. Means		Burst Amplitude Means					
SENSITIVITY		SENSITIVITY		SENSITIVITY		SENSITIVITY					
FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs
Delta	95.64%	99.75%	Delta	95.64%	99.75%	Delta	95.64%	99.75%	Delta	95.63%	99.74%
Theta	95.64%	99.75%	Theta	95.64%	99.75%	Theta	95.64%	99.75%	Theta	95.63%	99.75%
Alpha	95.64%	99.75%	Alpha	95.64%	99.75%	Alpha	95.64%	99.75%	Alpha	95.64%	99.75%
Beta	95.64%	99.75%	Beta	95.64%	99.75%	Beta	95.64%	99.75%	Beta	95.64%	99.75%
Hi-Beta	95.64%	99.75%	Hi-Beta	95.65%	99.75%	Hi-Beta	95.64%	99.75%	Hi-Beta	95.64%	99.76%
Beta1	95.64%	99.75%	Beta1	95.64%	99.75%	Beta1	95.65%	99.77%	Beta1	95.64%	99.75%
Beta2	95.64%	99.75%	Beta2	95.64%	99.75%	Beta2	95.64%	99.75%	Beta2	95.64%	99.75%
Beta3	95.64%	99.75%	Beta3	95.64%	99.75%	Beta3	95.64%	99.75%	Beta3	95.64%	99.75%
ALL	95.64%	99.75%	ALL	95.64%	99.75%	ALL	95.64%	99.75%	ALL	95.64%	99.75%

Absolute Phase		OUT OF PHASE		Phase Reset Duration Means		Burst Duration Means					
SENSITIVITY		SENSITIVITY		SENSITIVITY		SENSITIVITY					
FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs
Delta	95.64%	99.75%	Delta	95.64%	99.75%	Delta	95.64%	99.75%	Delta	95.64%	99.75%
Theta	95.64%	99.75%	Theta	95.64%	99.75%	Theta	95.64%	99.75%	Theta	95.64%	99.75%
Alpha	95.64%	99.75%	Alpha	95.64%	99.75%	Alpha	95.64%	99.75%	Alpha	95.64%	99.75%
Beta	95.64%	99.75%	Beta	95.64%	99.75%	Beta	95.63%	99.75%	Beta	95.62%	99.74%
Hi-Beta	95.65%	99.75%	Hi-Beta	95.65%	99.75%	Hi-Beta	95.64%	99.75%	Hi-Beta	95.64%	99.75%
Beta1	95.64%	99.75%	Beta1	95.64%	99.75%	Beta1	95.66%	99.75%	Beta1	95.64%	99.75%
Beta2	95.64%	99.75%	Beta2	95.64%	99.75%	Beta2	95.64%	99.75%	Beta2	95.64%	99.75%
Beta3	95.64%	99.75%	Beta3	95.64%	99.75%	Beta3	95.64%	99.75%	Beta3	95.64%	99.75%
ALL	95.64%	99.75%	ALL	95.64%	99.75%	ALL	95.64%	99.75%	ALL	95.64%	99.75%

Comodulation		Rate of Phase Shift Means		Phase Locking Interval Mns		Inter-Burst Interval Means					
SENSITIVITY		SENSITIVITY		SENSITIVITY		SENSITIVITY					
FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs	FREQ	2STDDEVs	3STDDEVs
Delta	95.64%	99.75%	Delta	95.64%	99.75%	Delta	95.65%	99.75%	Delta	95.64%	99.75%
Theta	95.64%	99.74%	Theta	95.64%	99.75%	Theta	95.64%	99.75%	Theta	95.64%	99.75%
Alpha	95.64%	99.74%	Alpha	95.64%	99.75%	Alpha	95.64%	99.76%	Alpha	95.64%	99.75%
Beta	95.64%	99.75%	Beta	95.63%	99.75%	Beta	95.62%	99.75%	Beta	95.63%	99.75%
Hi-Beta	95.64%	99.75%	Hi-Beta	95.64%	99.75%	Hi-Beta	95.64%	99.75%	Hi-Beta	95.64%	99.75%
Beta1	95.64%	99.74%	Beta1	95.65%	99.75%	Beta1	95.63%	99.75%	Beta1	95.64%	99.75%
Beta2	95.64%	99.74%	Beta2	95.64%	99.75%	Beta2	95.64%	99.75%	Beta2	95.64%	99.74%
Beta3	95.64%	99.75%	Beta3	95.64%	99.75%	Beta3	95.64%	99.75%	Beta3	95.64%	99.75%
ALL	95.64%	99.75%	ALL	95.64%	99.75%	ALL	95.64%	99.75%	ALL	95.64%	99.75%

## Appendix G: Low Resolution Electromagnetic Tomography (LORETA) Normative Reference Database: Birth to 82 years

### 1.0- Introduction





There are many potential uses of a normative EEG database among the most important being a statistical guess as to the error rate or to the probability of finding a particular subjects EEG measure within a reference normal population. Most other uses of a reference EEG database also involve statistics and the same statistics that all of modern clinical medicine relies upon. For example, null hypothesis testing, measures of reliability, sensitivity, power, predictive validity, content validity, etc. all depend on specific assumptions and statistical procedures.

Low Resolution Electromagnetic Tomography (LORETA) (Pascual-Marqui et al, *Int. J. Psychophysiol.*, 18: 49-65, 1994; Pascual-Marqui, *Internat. Journal of Bioelectromagnetism* 1: 75-86, 1999) is a distributed inverse model of 2,394 gray matter pixels to estimate the current sources in 3-dimensions that give rise to the surface EEG. The use of a normative LORETA database depends upon the statistical distribution of the 3-dimensional sources. The statistical stability of a normative database is directly related to the extent that the distribution of sources in a large population of normal individuals approximates a Gaussian distribution. This appendix demonstrates how the use of the FFT cross-spectrum of 2,394 sources from a large population of normal subjects provides a reasonable approximation to Gaussian and how leave-one-out cross-validation statistics demonstrate sensitivities > 95% accurate in the statistical estimation of values based on the NeuroGuide normative database. Expertise in the use of the Key Institute LORETA Viewer is necessary and validation of the maximum Z Scores by the surface EEG in frequency and scalp location are important. The user of the NeuroGuide LORETA normative database is encouraged to read the Key Institute documentation and always validate the LORETA solutions based on the surface EEG.

## 1.1 Key Institute and Applied Neuroscience, Inc. LORETA Normative EEG Database comparative validation

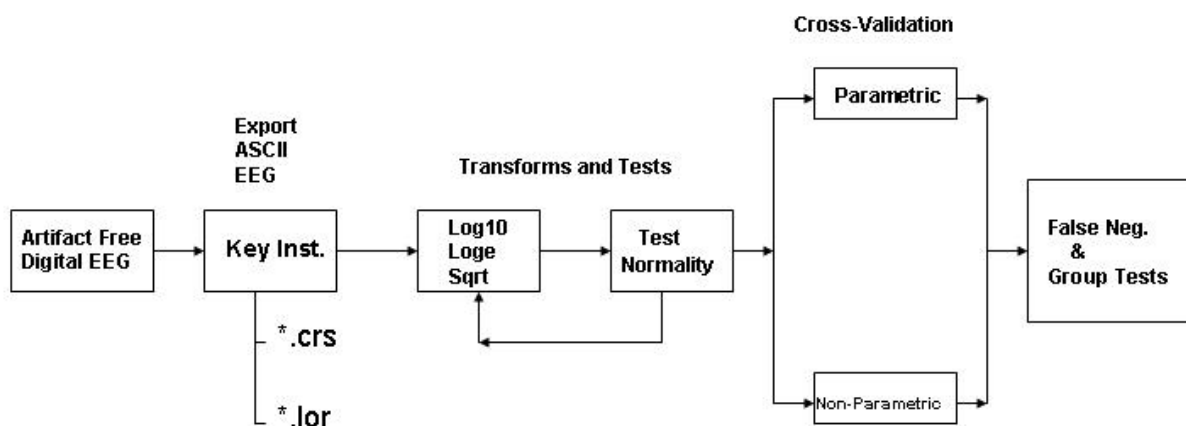
Four different normative reference databases were computed: eyes open and eyes closed for linked ears and for average reference montages. Five sequential age groupings of 625 normal subjects (Thatcher et al, *J. Neurotherapy*, 7(3/4): 87-121, 2003) were selected to cover the age range from 2 months to 82 years. The age groupings were: 1- Two months to 5.99 years; 2- 6.0 years to 9.99 years; 3- 10 to 13 years; 4- 13 to 16 years and 16 to 82 years. The details of the selection/exclusion criteria, clinical validation using neuropsychological tests and other aspects of normative reference database creation are described in Thatcher et al (*J. Neurotherapy*, 7(3/4): 87-121, 2003).

To make sure that the calculations of the 2,394 LORETA currents were correct, two different procedures were compared: 1- the Key Institute computation of currents followed by leave-one-out cross-validation and, 2- NeuroGuide computation of currents followed by cross-validation. Figure 1 is an illustration of a step by step procedure by which the ASCII digital time series was exported to the Key Institute and then the Key Institute software was used to compute \*.crs files that were transformed into \*.LOR files from which means and standard



deviations of the 2,394 gray matter pixels were computed. In order to approximate Gaussian distributions, skewness and kurtosis were calculated and then the individual subject values were transformed by log10 and skewness and kurtosis were re-calculated. Other transforms such as square root and loge were used but these transforms were not as effective in reducing skewness and kurtosis. The left side of the figure is the edited and artifact clean and reliable Digital EEG Time Series which may be re-referenced or re-Montaged to average reference, which is then analyzed using the Key Institute software.

## LORETA Normative Database Cross-Validation Tests



**Fig. 1** Illustration of cross-validation procedures using the Key Institute software to compute the cross-spectrum and means and standard deviations of the 2,394 LORETA currents. Leave-one-out cross-validation procedures were followed and parametric and non-parametric sensitivities were compared.

The second method which yielded essentially the same results as obtained using the Key Institute software involved computing the cross-spectrum in NeuroGuide and then multiplying the diagonal of the cross-spectral matrix (19 columns) by the Key Institute T matrix of 2,394 x, y & z rows for each frequency (1 to 30 Hz), then computing J or the current source density as the square root of the sum of the squares for each frequency and each of the 2,394 pixels (same



procedure as described by the Key Institute manual for the computation of \*.crs files). Figure 2 illustrates the cross-validation procedures using the NeuroGuide software and the Key Institute T matrix.

## LORETA Normative Database Cross-Validation Tests Using the NeuroGuide Cross-Spectral Software

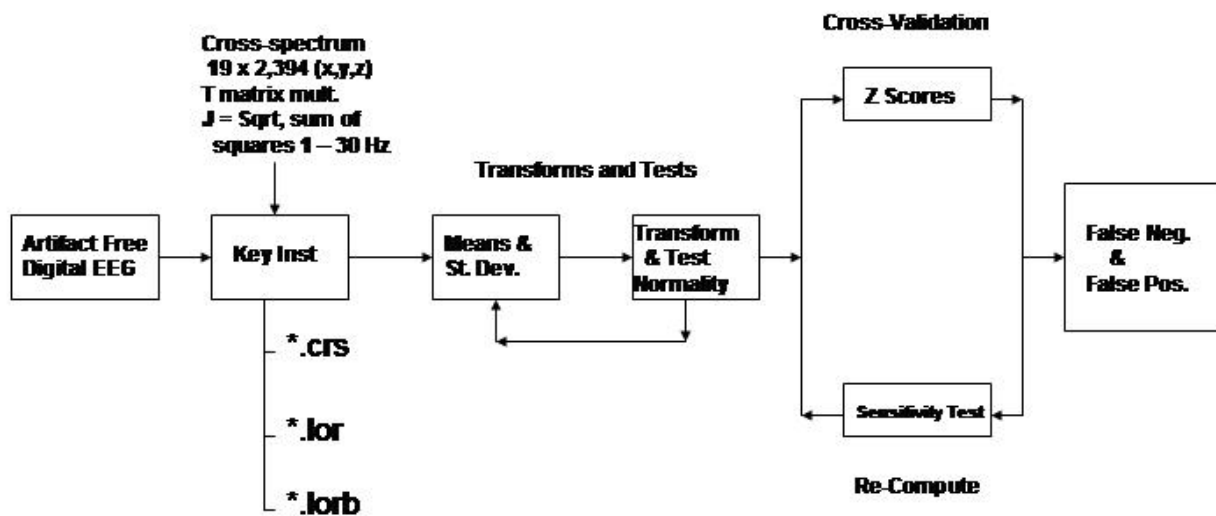


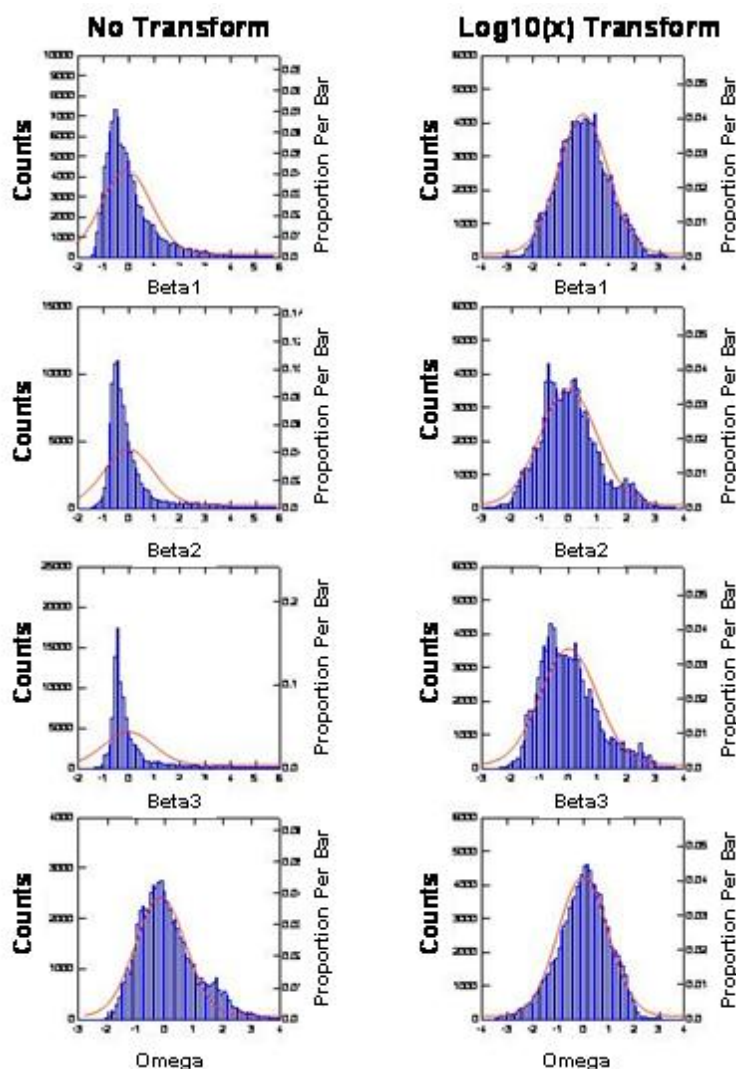
Fig. 2 - Illustration of cross-validation procedures using the NeuroGuide software to compute the cross-spectrum and means and standard deviations of the 2,394 LORETA currents. Approximations to Gaussian were achieved and statistical sensitivities of the Z Scores were computed.

## 2.0 Results

### 2.1 Gaussian Distributions and Affects of Log transforms

Figure 3 shows examples of the pre and post log<sub>10</sub> distribution of LORETA Z Scores in the adult subjects for different frequency bands.





**Fig. 3 - Distribution of the 2,394 LORETA currents in the delta (0.5 3 Hz), theta (3 7 Hz) and alpha (8 13 Hz) without transforms (left) and with log10 transform (right). The log transform adequately approximated a normal Bell Shaped distribution.**

The ideal Gaussian and the average cross-validation values of the database by which estimates of statistical sensitivity can be derived were published in Thatcher et al, J. Neurotherapy, 7: 121, 2003. True positives (TP) = the percentage of Z Scores that lay within the tails of the Gaussian distribution, False negatives (FN) = the percentage of Z Scores that fall outside of the tails of the Gaussian distribution. The error rates or the statistical sensitivity of a QEEG normative database are directly related to the deviation from a Gaussian distribution. These facts provide a mathematical method of estimating the statistical sensitivity of a normative EEG database in terms of the deviation from Gaussian for the NeuroGuide normative database of surface EEG values as well as for the 2,394 gray matter pixel LORETA norms.


**TABLE I - LORETA CROSS-VALIDATION: Log10 Transform\_n=106**

Frequency	SKEWNESS	KURTOSIS	1 STANDARD DEVIATIONS		2 STANDARD DEVIATIONS		3 STANDARD DEVIATIONS		SEN 2SD	SEN 3SD
			z < -1 SD	z > 1 SD	z < -2 SD	z > 2 SD	z < -3 SD	z > 3 SD		
FREQ 1	0.08	0.84	13.76%	14.60%	2.22%	2.52%	0.51%	0.45%	95.64%	99.75%
FREQ 2	0.19	0.39	14.47%	15.20%	1.79%	2.44%	0.21%	0.46%	95.64%	99.75%
FREQ 3	0.24	0.14	15.79%	15.62%	1.66%	2.54%	0.03%	0.35%	95.64%	99.74%
FREQ 4	0.29	0.16	15.73%	15.83%	1.21%	2.63%	0.02%	0.42%	95.64%	99.74%
FREQ 5	0.27	0.17	15.79%	15.13%	1.44%	2.85%	0.00%	0.41%	95.64%	99.74%
FREQ 6	0.33	0.32	15.39%	14.77%	1.62%	3.11%	0.01%	0.54%	95.64%	99.75%
FREQ 7	0.33	0.30	15.25%	15.44%	1.79%	2.99%	0.00%	0.50%	95.64%	99.75%
FREQ 8	0.38	0.47	15.90%	14.69%	1.72%	3.19%	0.00%	0.44%	95.65%	99.75%
FREQ 9	0.21	0.29	15.66%	15.22%	2.20%	2.88%	0.00%	0.32%	95.65%	99.74%
FREQ 10	0.17	0.23	14.52%	16.43%	2.18%	2.38%	0.00%	0.30%	95.64%	99.74%
FREQ 11	0.64	1.51	12.62%	15.23%	1.65%	3.21%	0.00%	0.87%	95.64%	99.75%
FREQ 12	0.29	0.80	13.91%	15.06%	1.88%	3.17%	0.23%	0.44%	95.65%	99.75%
FREQ 13	0.22	0.82	13.97%	15.20%	1.83%	2.93%	0.44%	0.45%	95.64%	99.75%
FREQ 14	0.25	0.82	14.08%	14.75%	1.79%	3.05%	0.34%	0.46%	95.64%	99.75%
FREQ 15	0.20	0.78	13.97%	15.10%	2.03%	2.86%	0.41%	0.46%	95.65%	99.75%
FREQ 16	0.21	0.82	14.05%	14.93%	2.02%	2.88%	0.37%	0.43%	95.65%	99.75%
FREQ 17	0.27	0.97	14.02%	14.41%	1.84%	2.92%	0.31%	0.61%	95.64%	99.75%
FREQ 18	0.27	0.94	13.85%	13.86%	1.75%	3.56%	0.38%	0.52%	95.65%	99.75%
FREQ 19	0.30	0.90	13.20%	14.21%	1.79%	3.54%	0.31%	0.54%	95.65%	99.75%
FREQ 20	0.27	0.75	13.26%	15.16%	1.74%	3.26%	0.43%	0.33%	95.65%	99.75%
FREQ 21	0.34	0.73	13.38%	15.47%	1.71%	3.14%	0.19%	0.54%	95.64%	99.75%
FREQ 22	0.33	0.73	13.93%	14.90%	1.62%	3.33%	0.24%	0.57%	95.65%	99.75%
FREQ 23	0.25	0.68	13.34%	15.09%	1.98%	3.34%	0.31%	0.52%	95.65%	99.75%
FREQ 24	0.30	0.75	13.71%	14.62%	1.81%	3.40%	0.34%	0.59%	95.65%	99.75%
FREQ 25	0.43	0.93	13.11%	14.77%	1.78%	3.39%	0.08%	0.77%	95.65%	99.75%
FREQ 26	0.42	0.94	12.78%	14.70%	1.74%	3.32%	0.14%	0.80%	95.65%	99.75%
FREQ 27	0.47	1.04	12.29%	14.51%	1.76%	3.30%	0.15%	0.83%	95.65%	99.75%
OVERALL	0.29	0.68	14.14%	15.00%	1.80%	3.04%	0.20%	0.51%	95.64%	99.75%

**Fig. 4 - Statistical sensitivities based for the eyes closed condition in a group of adult subjects for linked ears and average reference.**



## LORETA zCROSS-VALIDATION\_EC(A)\_zLOG10(x)

<b>LE</b>										
<b>SUMMARY</b>	<b>SKEW</b>	<b>KURT</b>	<b>&lt; -1 SD</b>	<b>&gt; 1 SD</b>	<b>&lt; -2 SD</b>	<b>&gt; 2 SD</b>	<b>&lt; -3 SD</b>	<b>&gt; 3 SD</b>	<b>SEN 2SD</b>	<b>SEN 3SD</b>
DELTA	0.03	-0.46	17.37%	16.84%	1.45%	1.59%	0.03%	0.00%	95.63%	99.74%
THETA	-0.06	-0.08	15.93%	15.77%	2.30%	1.70%	0.12%	0.08%	95.64%	99.74%
ALPHA	-0.37	0.71	13.26%	15.55%	3.12%	1.40%	0.80%	0.00%	95.64%	99.75%
BETA1	0.15	-0.12	15.68%	16.24%	1.23%	2.50%	0.03%	0.14%	95.63%	99.74%
BETA2	0.48	0.35	13.74%	14.50%	0.82%	4.57%	0.00%	0.16%	95.65%	99.74%
BETA3	0.73	0.40	13.77%	14.90%	0.23%	4.89%	0.00%	0.15%	95.65%	99.74%
OMEGA	-0.35	0.21	15.31%	15.48%	3.12%	0.83%	0.34%	0.00%	95.64%	99.74%
<b>AVE</b>										
<b>SUMMARY</b>	<b>SKEW</b>	<b>KURT</b>	<b>&lt; -1 SD</b>	<b>&gt; 1 SD</b>	<b>&lt; -2 SD</b>	<b>&gt; 2 SD</b>	<b>&lt; -3 SD</b>	<b>&gt; 3 SD</b>	<b>SEN 2SD</b>	<b>SEN 3SD</b>
DELTA	-0.09	-0.46	18.56%	16.19%	1.77%	1.26%	0.06%	0.00%	95.63%	99.74%
THETA	-0.26	0.19	15.86%	14.92%	3.21%	1.58%	0.16%	0.01%	95.64%	99.74%
ALPHA	-0.62	1.34	12.31%	14.78%	3.74%	1.12%	1.09%	0.00%	95.64%	99.75%
BETA1	-0.07	-0.06	15.25%	16.10%	2.38%	1.71%	0.10%	0.00%	95.64%	99.74%
BETA2	0.25	0.32	13.94%	14.36%	1.74%	3.65%	0.00%	0.10%	95.65%	99.74%
BETA3	0.54	0.23	15.76%	15.12%	0.50%	4.37%	0.00%	0.09%	95.64%	99.74%
OMEGA	-0.64	0.65	14.98%	14.24%	4.37%	0.60%	0.56%	0.00%	95.65%	99.75%

Fig. 5 - Statistical sensitivities for the eyes open condition in a group of adult subjects for linked ears and average reference.

## LORETA zCROSS-VALIDATION\_EO(B)\_zLOG10(x)

<b>LE</b>										
<b>SUMMARY</b>	<b>SKEW</b>	<b>KURT</b>	<b>&lt; -1 SD</b>	<b>&gt; 1 SD</b>	<b>&lt; -2 SD</b>	<b>&gt; 2 SD</b>	<b>&lt; -3 SD</b>	<b>&gt; 3 SD</b>	<b>SEN 2SD</b>	<b>SEN 3SD</b>
DELTA	-0.27	0.26	15.15%	14.55%	3.19%	1.38%	0.00%	0.00%	95.64%	99.74%
THETA	0.11	-0.05	16.00%	16.44%	1.45%	2.03%	0.00%	0.07%	95.63%	99.74%
ALPHA	0.38	-0.24	15.56%	18.30%	0.25%	2.24%	0.00%	0.16%	95.62%	99.74%
BETA1	0.37	-0.03	16.04%	16.76%	0.64%	3.18%	0.00%	0.00%	95.64%	99.74%
BETA2	0.36	0.79	13.73%	13.35%	1.88%	4.20%	0.00%	0.24%	95.66%	99.74%
BETA3	0.90	0.99	11.87%	14.57%	0.08%	5.26%	0.00%	0.31%	95.65%	99.74%
OMEGA	0.11	-0.36	16.15%	17.34%	1.15%	1.59%	0.00%	0.00%	95.63%	99.74%
<b>AVE</b>										
<b>SUMMARY</b>	<b>SKEW</b>	<b>KURT</b>	<b>&lt; -1 SD</b>	<b>&gt; 1 SD</b>	<b>&lt; -2 SD</b>	<b>&gt; 2 SD</b>	<b>&lt; -3 SD</b>	<b>&gt; 3 SD</b>	<b>SEN 2SD</b>	<b>SEN 3SD</b>
DELTA	-0.43	0.60	14.20%	13.61%	3.81%	1.36%	0.06%	0.00%	95.65%	99.74%
THETA	-0.02	0.16	14.87%	15.92%	2.60%	1.99%	0.00%	0.06%	95.64%	99.74%
ALPHA	0.49	0.00	15.50%	17.76%	0.18%	2.70%	0.00%	0.35%	95.63%	99.74%
BETA1	0.38	0.07	15.90%	16.75%	0.68%	3.42%	0.00%	0.00%	95.64%	99.74%
BETA2	0.37	0.71	14.23%	13.50%	1.33%	3.91%	0.00%	0.31%	95.65%	99.74%
BETA3	0.89	0.96	12.29%	14.83%	0.08%	5.05%	0.00%	0.46%	95.65%	99.75%
OMEGA	-0.12	0.18	14.83%	16.81%	2.53%	1.53%	0.09%	0.00%	95.64%	99.74%



## Appendix H: LORETA Source Correlations

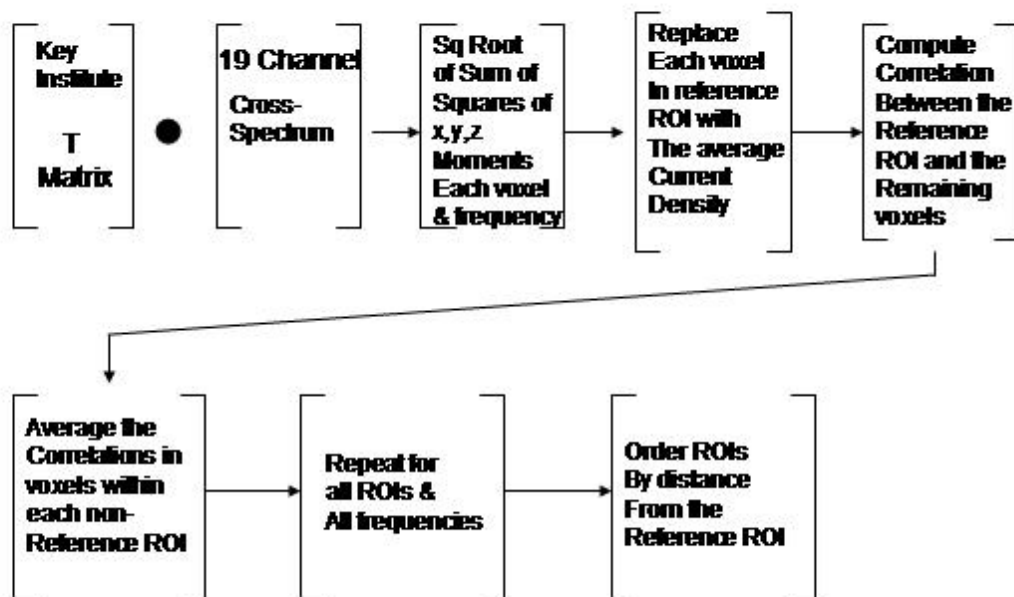
NeuroGuide uses the standard Key Institute Tab Delimited File of Brodmann Areas and Anatomical Names to identify each of the 2,394 gray matter voxels that are associated with one of 66 different Regions of Interest (ROIs with 33 from the left hemisphere and 33 from the right hemisphere) or with one of 94 Brodmann areas (ROIs with 47 from the left hemisphere and 47 from the right hemisphere). The current source values are computed for all 2,394 gray matter gray matter voxels using the Key Institute cross-spectral equations for each successive 256 points or each two second epoch of EEG. For a 2 second epoch the square root of the sum of squares of the x, y & z values or the resultant current value is computed for each of the 2,394 pixels and a .lor file is produced for each 2 second epoch. The current density values ( $A/m^2$ ) of voxels within a selected ROI are averaged and each voxel in the selected ROI is replaced with the average value for that ROI. Then a Pearson Product correlation coefficient is computed for the covariance of current density over successive two second epochs between all combinations of ROIs for each frequency from 1 Hz to 40 Hz. The correlation values range from -1 to +1 and the statistical significance level is determined by the number of degrees of freedom which is the number of 2 second epochs minus 1. For example, 60 seconds of EEG = 30 two second epochs or  $30 - 1 = 29$  degrees of freedom and for  $r = 0.562$  then  $P < .001$ . The ROI correlation with itself = 1, and for purposes of using the LORETA Viewer the ROI correlation to itself is set to zero and thus a selected ROI is white in the Key Institute viewer.

### Source Correlation Flow Chart





## Source Correlation Flow Chart



Source Correlation Norms were computed by averaging gray matter voxels and combining anatomical regions so that the number of voxels is sufficient to achieve a reasonable approximation to a gaussian distribution. The total number of ROIs in the source correlation norms = 46 and they are shown in the table below. The anatomical names are contained in the Z Score ROI control panel. The match of the numbers 1, 2 & 3 in the "Regions of Interest" column include the average ROIs to select 46 ROIs from the larger universe of 66 ROIs. For example, within the Frontal Lobule the extra-nuclear gyrus and the inferior frontal gyrus were averaged as represented by 1 and the medial frontal gyrus and subcallosal gyrus were averaged as represented by 2, etc. The numbers 1, 2 & 3 order the averaging within Lobules and not between Lobules.



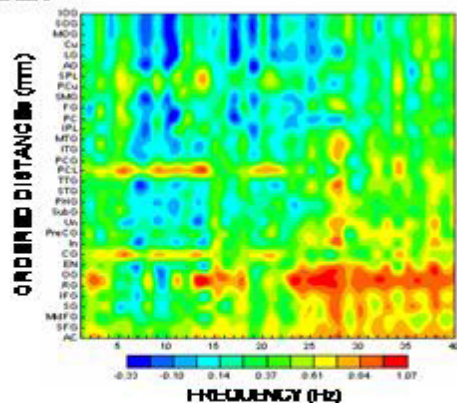
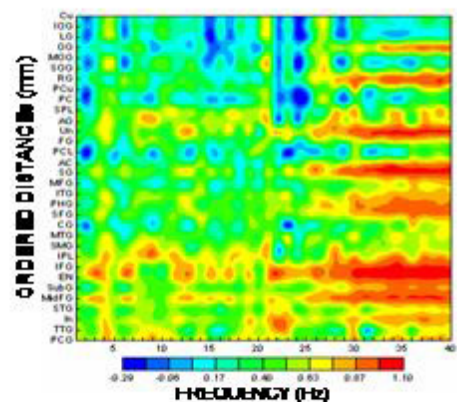
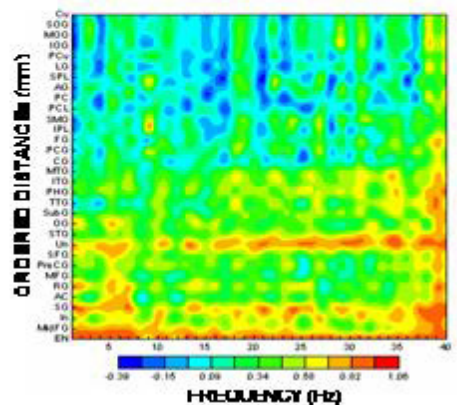
Superior Frontal Gyrus					
	Region	(mm)		Region	(mm)
MFG	Medial Frontal Gyrus	17.63	PCL	Paracentral Lobule	76.40
MidFG	Middle Frontal Gyrus	20.82	PHG	Parahippocampal Gyrus	76.13
AC	Anterior Cingulate	26.24	IPL	Inferior Parietal Lobule	88.27
IFG	Inferior Frontal Gyrus	40.21	MTG	Middle Temporal Gyrus	87.54
EN	Extra-Nuclear	48.66	ITG	Inferior Temporal Gyrus	89.62
PreCG	Precentral Gyrus	52.96	SMG	Supramarginal Gyrus	95.80
SG	Subcallosal Gyrus	51.08	PC	Posterior Cingulate	96.81
CG	Cingulate Gyrus	53.33	FG	Fusiform Gyrus	96.36
OG	Orbital Gyrus	51.68	SPL	Superior Parietal Lobule	102.72
RG	Rectal Gyrus	52.77	PCu	Precuneus	104.04
In	Insula	55.48	AG	Angular Gyrus	108.61
SubGyr	Sub-Gyr	70.97	LG	Lingual Gyrus	115.04
TTG	Transverse Temporal Gyrus	70.06	Cu	Cuneus	119.81
PCG	Postcentral Gyrus	72.97	SOG	Superior Occipital Gyrus	122.93
STG	Superior Temporal Gyrus	71.42	MOG	Middle Occipital Gyrus	122.70
Un	Uncus	72.51	IOG	Inferior Occipital Gyrus	127.90
Middle Occipital Gyrus					
	Region	(mm)		Region	(mm)
IOG	Inferior Occipital Gyrus	13.96	STG	Superior Temporal Gyrus	63.46
SOG	Superior Occipital Gyrus	20.47	TTG	Transverse Temporal Gyrus	67.00
AG	Angular Gyrus	29.91	In	Insula	72.50
LG	Lingual Gyrus	30.03	PCL	Paracentral Lobule	74.46
Cu	Cuneus	31.64	CG	Cingulate Gyrus	80.05
PC	Posterior Cingulate	38.38	PreCG	Precentral Gyrus	81.57
SMG	Supramarginal Gyrus	43.02	Un	Uncus	83.70
FG	Fusiform Gyrus	44.56	EN	Extra-Nuclear	91.62
PCu	Precuneus	45.84	SG	Subcallosal Gyrus	93.98
MTG	Middle Temporal Gyrus	48.94	IFG	Inferior Frontal Gyrus	103.83
IPL	Inferior Parietal Lobule	50.95	MidFG	Middle Frontal Gyrus	111.36
SPL	Superior Parietal Lobule	52.28	AC	Anterior Cingulate	114.05
SubG	Sub-Gyr	58.55	MFG	Medial Frontal Gyrus	116.70
PHG	Parahippocampal Gyrus	59.42	RG	Rectal Gyrus	119.03
ITG	Inferior Temporal Gyrus	60.37	SFG	Superior Frontal Gyrus	122.70
PCG	Postcentral Gyrus	63.26	OG	Orbital Gyrus	133.22

Below are examples of the cross-validation tests of the LORETA source correlation normative database and the relationship between 'U' shaped fibers and LORETA spatio-temporal correlations.

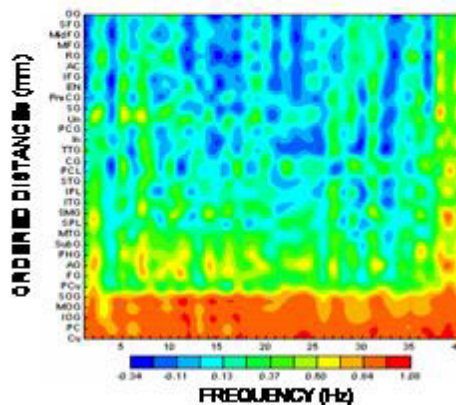
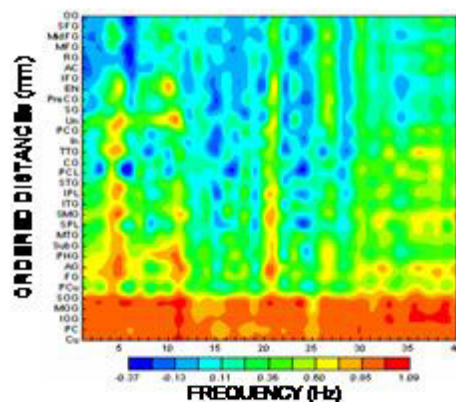
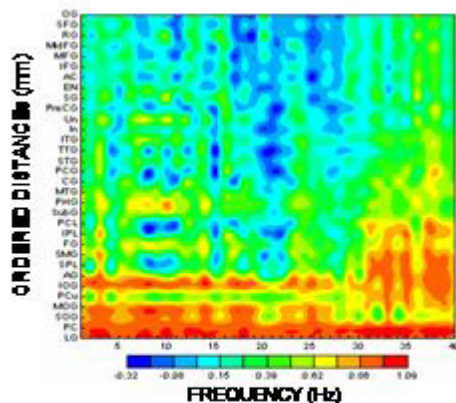


## Subjects:

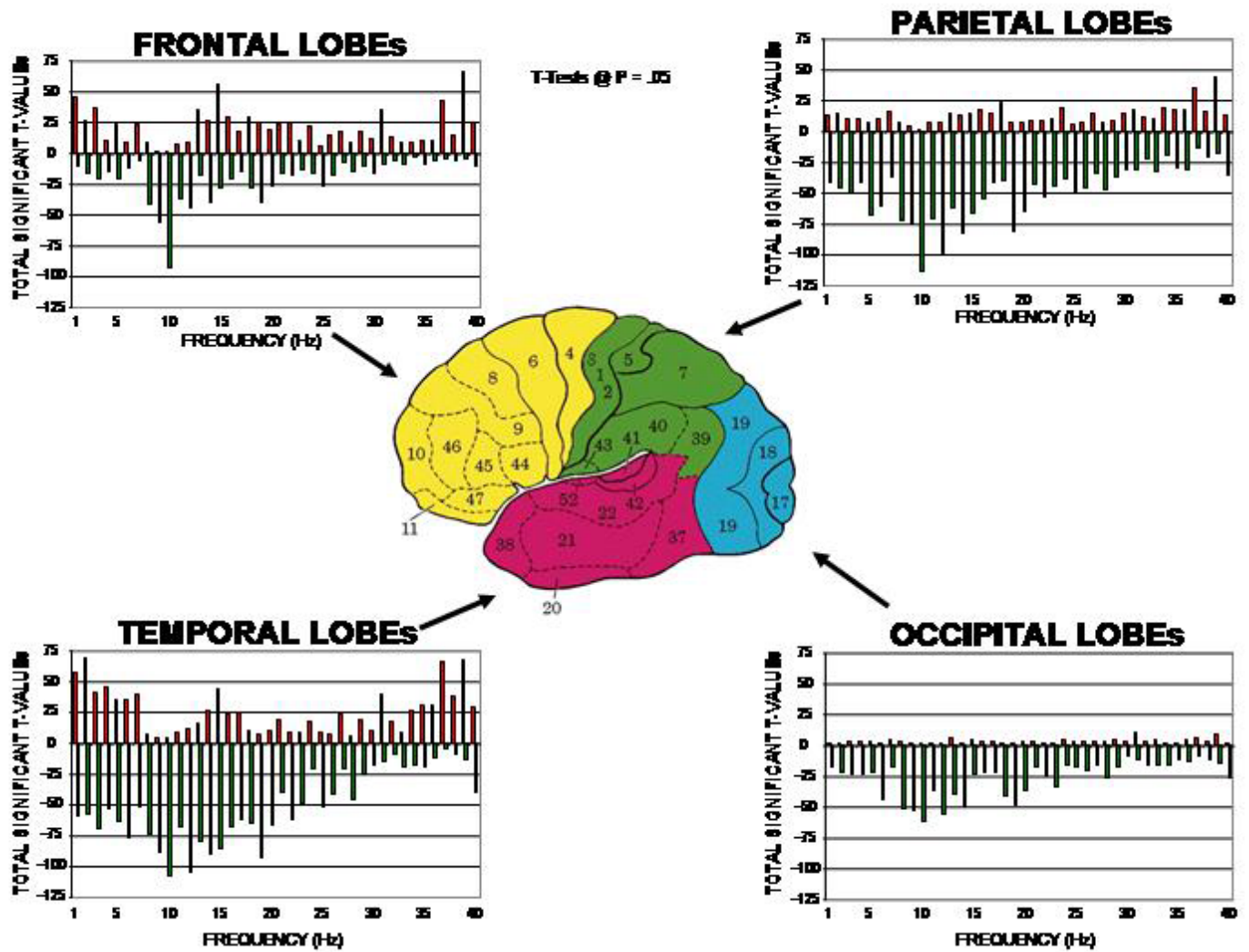
### Left Frontal

**1.****2.****3.**

### Left Occipital











landmarks established by von Brodmann in 1909 and referred to as Brodmann areas. The time series of current source vectors in the x, y & z directions were computed at the center voxel of each of forty seven left hemisphere and 47 right hemisphere Brodmann Areas. In addition to the x, y & z time series from each voxel the resultant vector was computed as the square root of the sum of the squares for the x, y and z source moments.

The Hilbert transform of the LORETA time series was computed using complex demodulation to compute instantaneous coherence and phase-differences between each pair of the Brodmann area time series (Granger and Hatanaka, 1964; Thatcher et al, 2008; Bloomfield, 2000). All combinations of 47 pairs of the LORETA Brodmann area time series were used to compute "instantaneous" coherence and phase differences from the left hemisphere and the homologous 47 Brodmann areas from the right hemisphere. Homologous combinations were also computed but not diagonal combinations. LORETA coherence and phase differences were computed for each of 10 frequency bands (Delta = 1.0-4.0 Hz; theta = 4.0-8.0 Hz; alpha1 = 8-10 Hz; Alpha-2 = 10-12 Hz; Beta1 = 12-15 Hz; Beta2 = 15-18 Hz; Beta3 = 18-25 Hz; Hi-Beta = 25-30 Hz).

## **Appendix J: A Few of the Normative Database Publications, Replications and Validations (see the National Library of Medicine database for more citations)**

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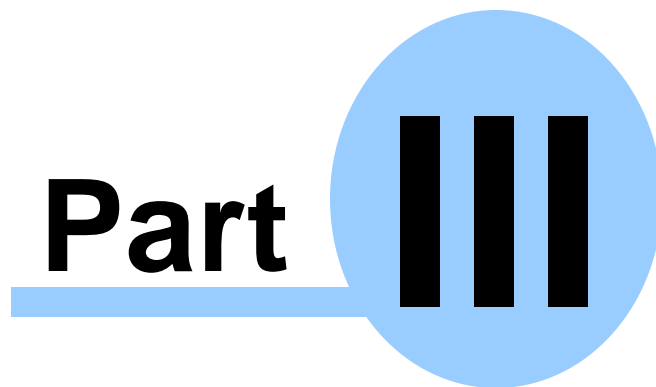
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# NeuroStat

## Manual and Tutorial

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(All EEG Selections and/or Sine Wave Segments are for Illustrative Purposes Only)



# NeuroStat Manual & Tutorial

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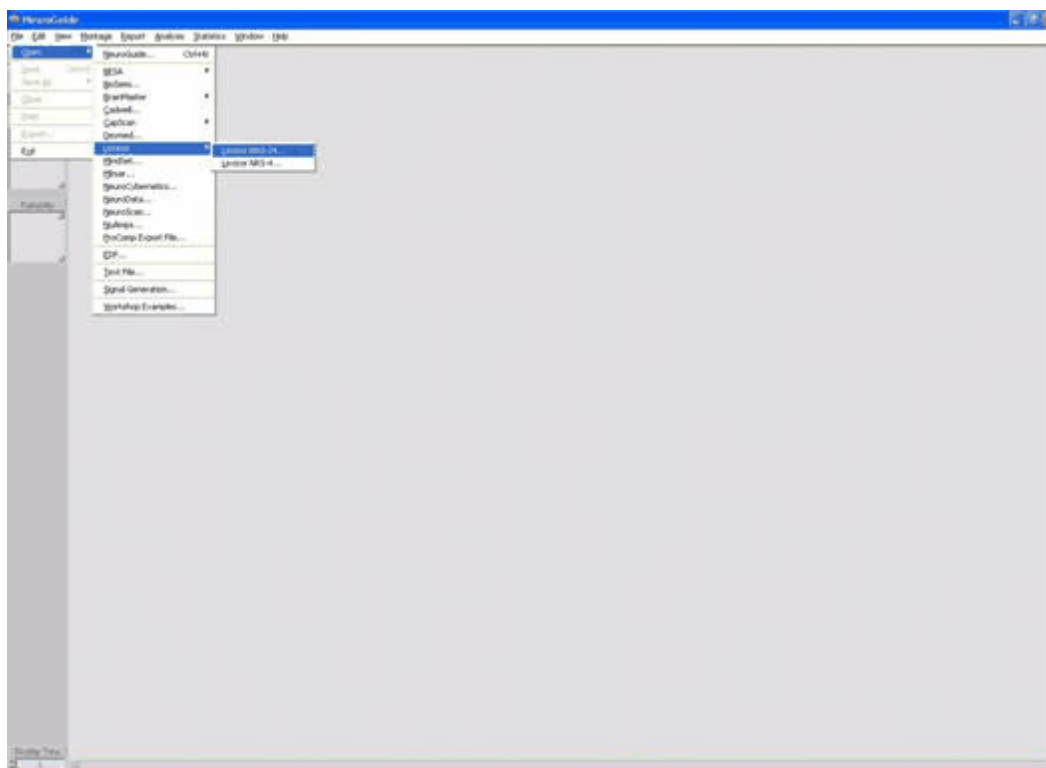
## Introduction:

**NeuroStat is a program that provides statistical comparisons and descriptive statistics of EEG samples saved as Individual NeuroGuide Analysis Files or \*.NGA files. NeuroStat also provides individual and group parametric statistical tests using the Key Institute LORETA program. Individual comparison options are independent t-tests, paired t-tests and ANOVA as well as absolute and percent differences. Individual statistics are used for pre vs post treatment comparisons or differences between eyes closed and eyes open, etc.**

**Group comparative statistics may require the use of [NeuroBatch](#)<sup>266</sup> to produce a NeuroGuide Group Analysis File or \*.NGG file of the surface EEG Group paired t-tests do not require the use of NeuroBatch and LORETA statistical analyses do not require the use of NeuroBatch. Descriptive Group statistics include Means and Standard Deviations and independent t-tests between Groups (does not assume equal variance or sample sizes). Group statistics are used to compare different groups of subjects such as 100 ADD children to 100 normal children, etc. Use [NeuroBatch](#)<sup>266</sup> to create the \*.NGG files before using NeuroStat.**

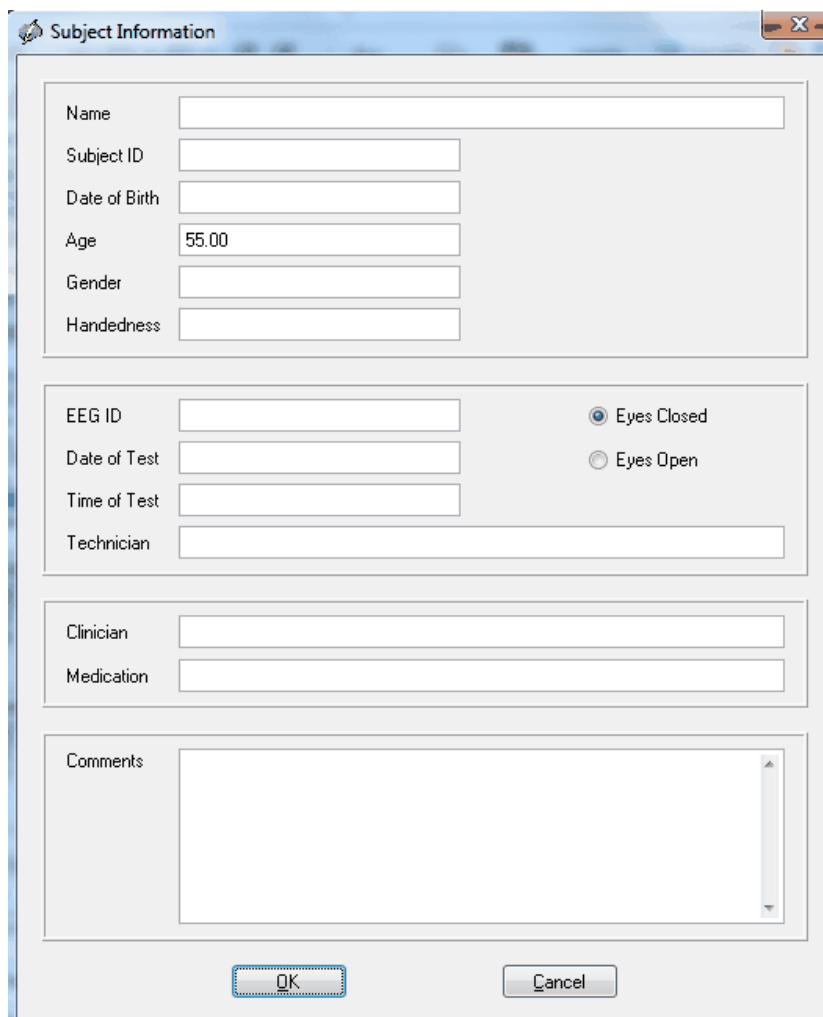
**Step 1      In Demo Mode Hold the Left Mouse Button and Click File > Open > Lexicor NRS24.**

**Click File > Open > Lexicor > Lexicor NRS-24**





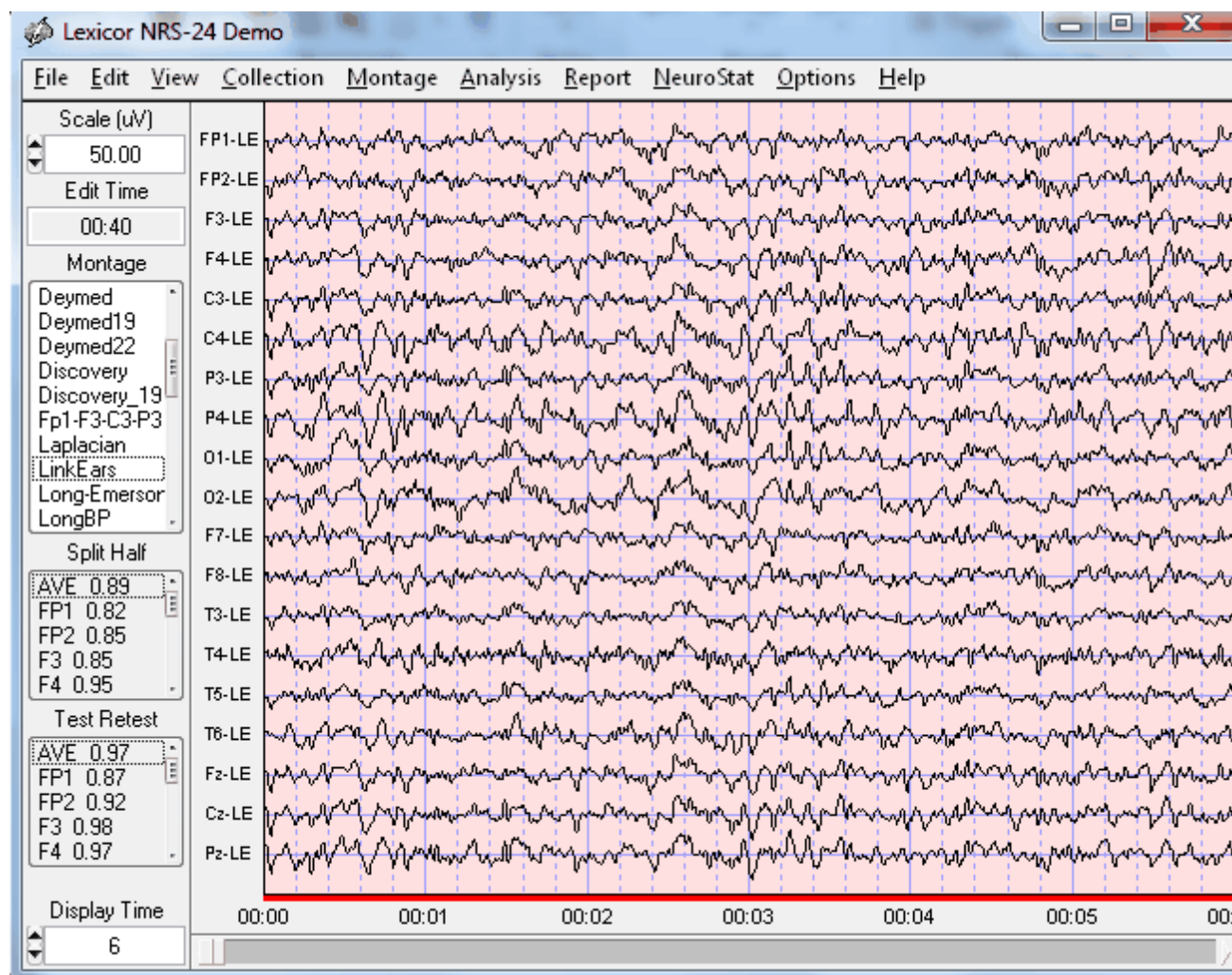
Enter identifying subject information, especially age and eye condition and then Click OK.



The "Subject Information" dialog box contains the following fields and controls:

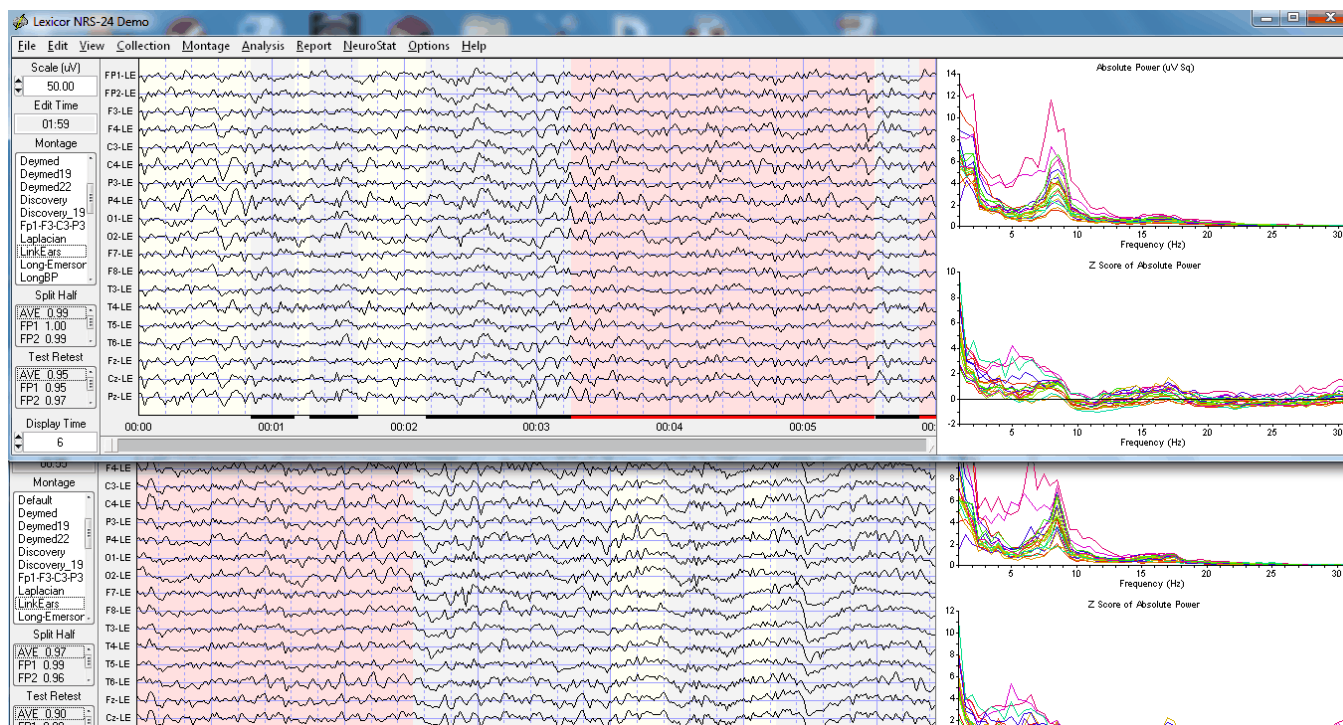
- Name: Text input field
- Subject ID: Text input field
- Date of Birth: Text input field
- Age: Text input field with "55.00" entered
- Gender: Text input field
- Handedness: Text input field
- EEG ID: Text input field
- Date of Test: Text input field
- Time of Test: Text input field
- Technician: Text input field
- Eyes Closed: Radio button (selected)
- Eyes Open: Radio button
- Clinician: Text input field
- Medication: Text input field
- Comments: Text area
- OK: Button
- Cancel: Button

Depress the left mouse button and select the 1st 40 seconds for demonstration purposes. Open a 2nd NeuroGuide demo and import the Lexicor file and same subject information and select the last 40 seconds for demonstration purposes.



## Step 2 Simultaneously View Two NeuroGuides to Compare Pre vs Post Treatment Effects

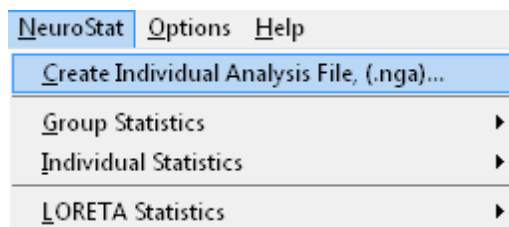
Repeat Step #1 and position the 2nd NeuroGuide near the bottom of the computer screen and the 1st NeuroGuide near the top of the computer screen. Re-size the two NeuroGuides so that one can view both at the same time.



This procedure is valuable because a single mouse click can toggle between two different EEG records and guide the creation of the NeuroGuide Analysis files. Lets assume that the top NeuroGuide is a Pre-Treatment EEG and the bottom is a Post-Treatment EEG. In order to achieve differences it is a good idea to select different segments of the demo EEG file for comparison.

### Step 3 Create NeuroGuide Analysis File. (For Demonstration Purposes Only)

Create an NeuroGuide Analysis File (\*.NGA) by clicking NeuroStat > \*.NGA that are of interest for comparison purposes.



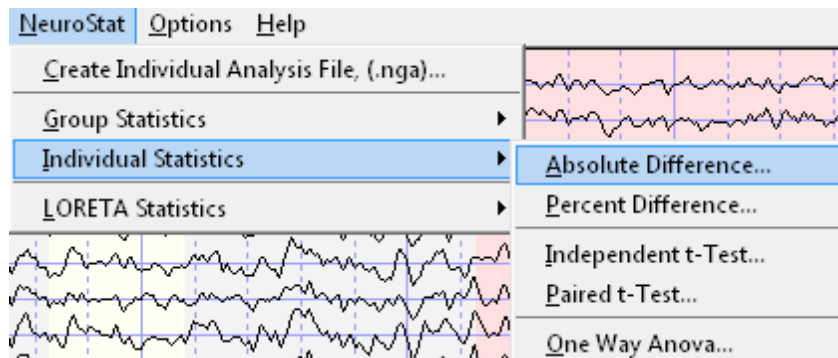
Save the .nga file in the patient's folder and label it Pre-Treatment.nga. Repeat this step for the lower or 2nd NeuroGuide and save it as Post-Treatment.nga. Toggle Between the Top and Bottom Window and Repeat Step # 2 to create different NeuroGuide Analysis Files \*.NGA and then select a individual comparative test or compute Pair t-Tests.



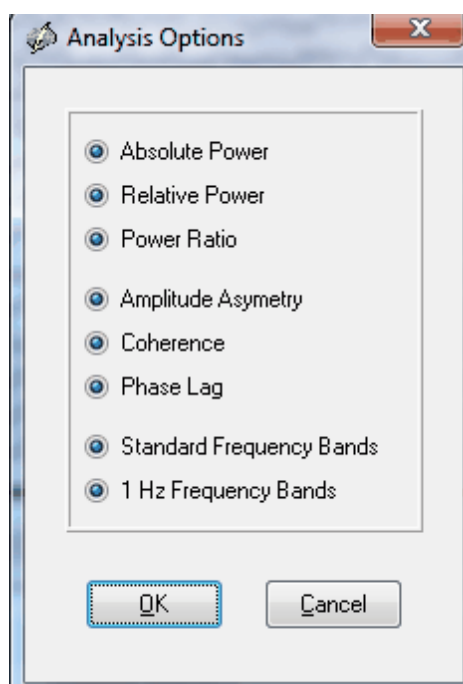


## Compute Individual Statistics and Select Variables

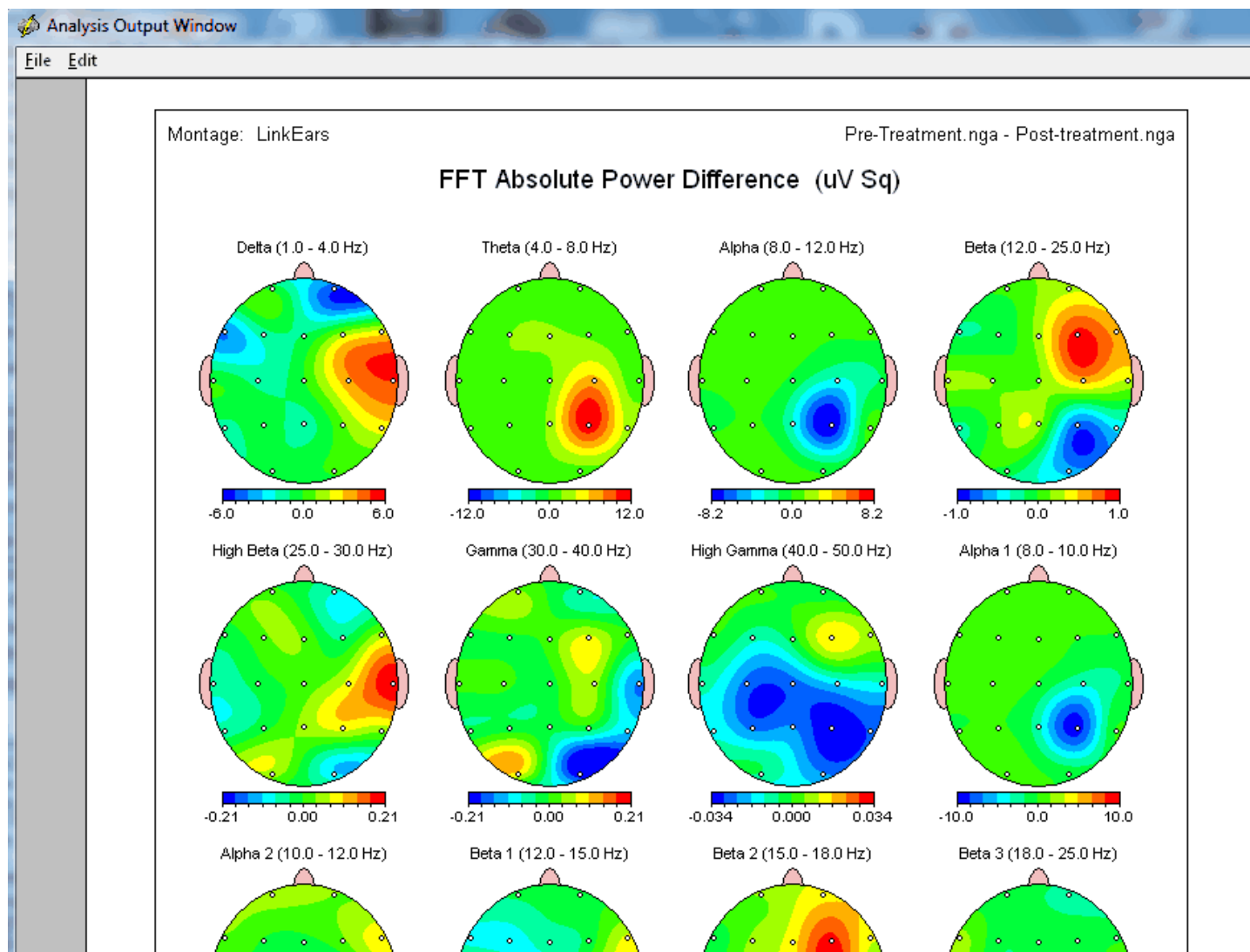
In the main NeuroGuide menu, Click **NeuroStat > Individual Statistics > Absolute Difference**.



Here is the list of metrics to include in the statistical analyses. Click **OK**



In the "Open NeuroGuide Individual Analysis File 1", Navigate to where you saved the Pre-Treatment.nga file and double click on it. Then double click on the Post-Treatment file when the "Open NeuroGuide Individual Analysis File 2".

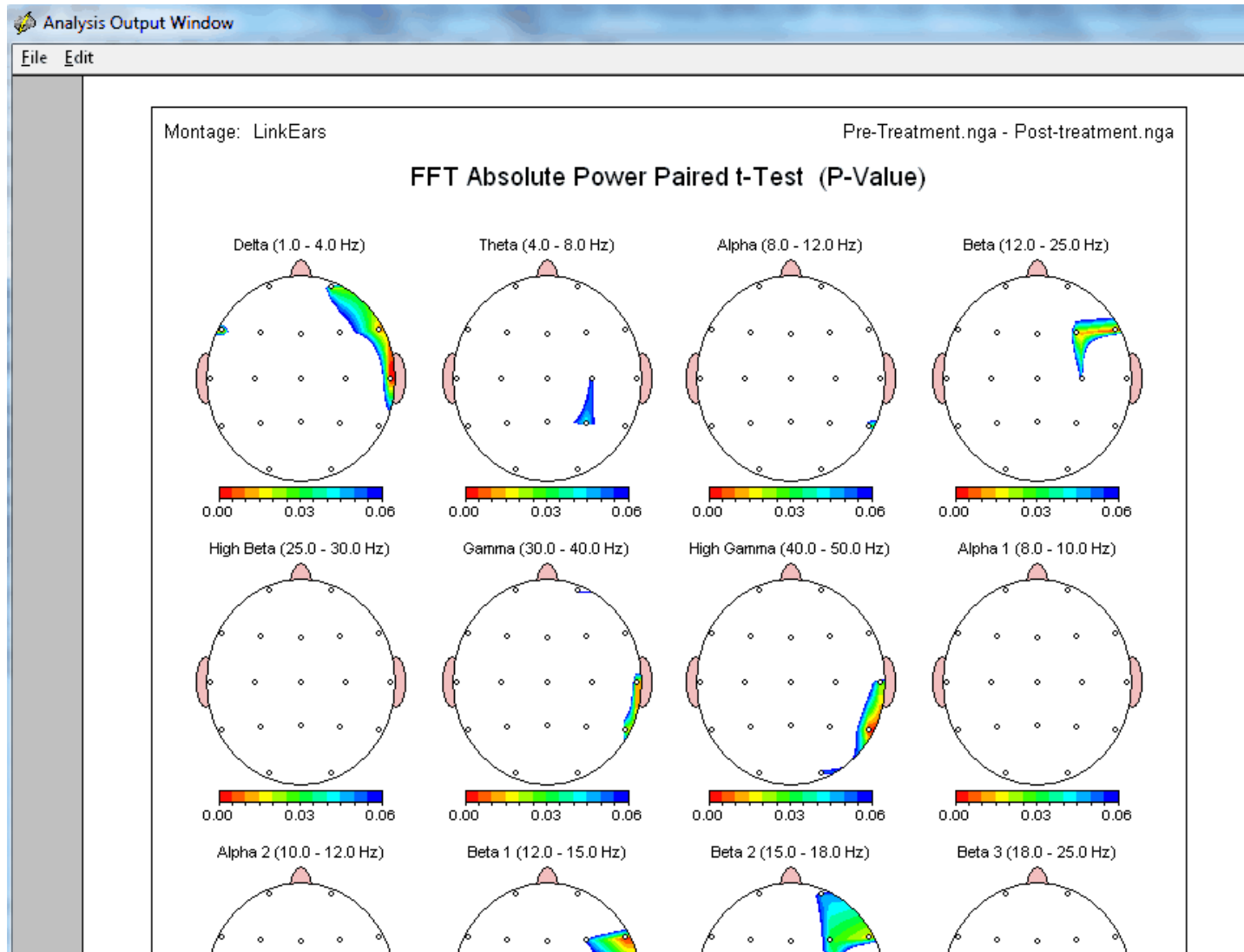


Interpretation of Absolute Differences is based on the order of the file names in the upper right corner of the Analysis Output Window. For example, if Pre-Treatment is larger than Post-Treatment the color = **Red**. If Post is larger than Pre then the color = **Blue**. That is, if  $A > B$  then the color is **Red**. If  $B > A$  then the color is **Blue**.

Click File > Save > Bitmap and then navigate to the patient's folder and create a sub-folder and label it NeuroStat Bitmap Abs. diff. Open the folder name the file abs and click **OK** to save all of the bitmaps. To save the tab delimited raw values click File > Save > Tab Delimited Text.

Repeat this exercise but select Percent Difference. It is a good idea to 1st compute either Absolute Difference or Percent Difference before computing individual statistics because one needs to know the direction of significant differences.

Compute Paired t-Tests or Independent t-Tests or ANOVA depending on what you want to do. Here is an example of a Paired t-Test.



The P values range from 0.0001 to 0.06 in the display. The color scale shows the magnitude of the P values where White is > 0.06. Click Save > Tab Delimited Text to save the raw P values and then open the tab delimited file using Microsoft Excel or Word to see the exact P values. Repeat this test for independent t-tests and ANOVA.

Adjust the Scales of the Color Topographic Maps by clicking Report > Color Map Settings. In the Report Options panel select Automatic Individual Scaling where the minimum and maximum range is set for each individual map or Automatic Global Scaling where the min and max are computed for all maps or Manual Scaling in which the user sets the min and max.



**Scale within individual Maps**

**Scale Maps Globally**

**Scale Maps Manually**

**Report Options**

Raw Score | Z Score | General

Absolute Power Color Maps

☒ Automatic Individual Scaling

☐ Automatic Global Scaling

☐ Manual Global Scaling

Minimum: 0.00 Maximum: 100.00

Relative Power and Power Ratio Color Maps

☒ Automatic Individual Scaling

☐ Automatic Global Scaling

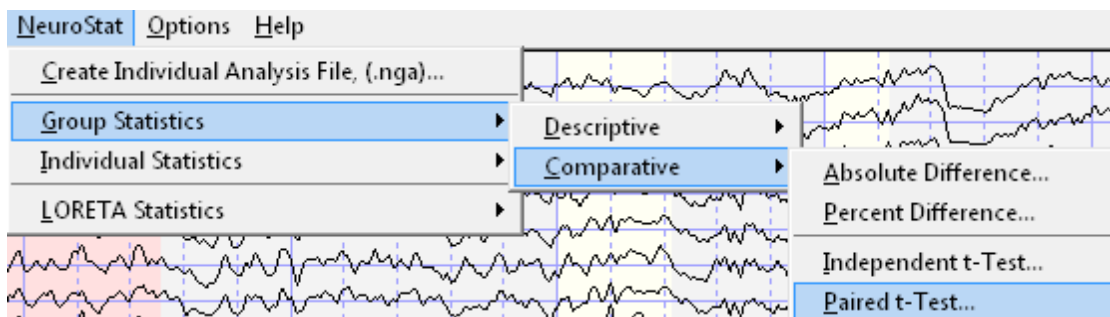
☐ Manual Global Scaling

Minimum: 0.00 Maximum: 100.00

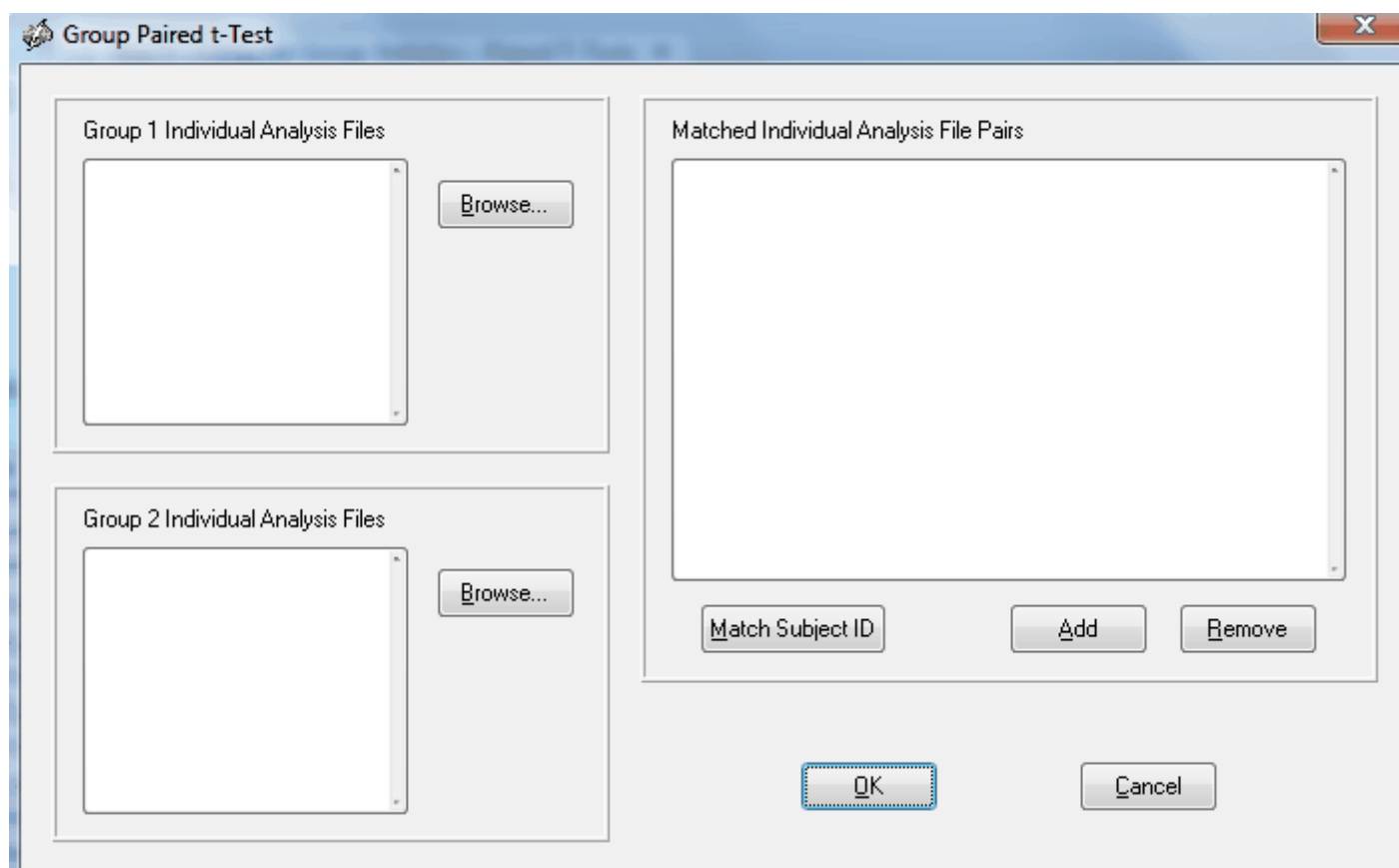
There are two categories of group statistics. One is Group Paired t-Tests and the 2nd is Independent Group statistics. Group Paired t-Tests can use the individual statistic \*.nga files described by Step #3. The 2nd method does not use \*.nga files and instead one must create \*.ngg files based on the individual .nga files.

## Group Paired t-Tests

Create the Individual Analysis Files for each subject that comprises each group. Save the \*.nga files for group one in one folder and for group two in a 2nd folder. Then click NeuroStat > Group Statistics > Comparative > Paired t-Test



In the Group Paired t-Test panel click the top Browse button and then navigate to the folder when you saved the \*.nga files for group one. Then click the bottom Browse button and navigate to the folder where you saved the \*.nga files for group two. Click the Match Subject ID button to order the subject ID for the two groups because Paired t-Tests require that the same subject be test two times and subject ids must be aligned correctly. Then click the ADD button to add the matched subjects to the list of Matched Individual Analysis File Pairs. Click the Remove button if you want to remove a subject or pair. Once all the subjects are matched then click OK to start the statistical analyses.



## Step 6 Compute Group Statistics After Creating NeuroGuide Group Analysis Files (\*.NGG) using NeuroBatch



Click **Analysis > NeuroBatch** and read the **NeuroBatch** manual which gives the step by step procedure to create **Group Analysis Files \*.NGG**. **NGG** files are the input to the **Group Statistics** component of **NeuroStat** where **NeuroBatch** is used to create the group means and standard deviation values, etc. which are then utilized in **NeuroStat**.

**NeuroStat** imports the **\*.NGG** files created by **NeuroBatch** and then computes the group statistics and color topographic displays and tab delimited outputs. **NeuroBatch** is required for **NeuroStat** group statistics only. Individual comparative statistics such as **Pre-Treatment vs. Post-Treatment** comparisons and **Paired t-Tests** do not require **NeuroBatch**.

**NeuroGuide Batch Analysis**

**Input File Parameters**

Input File Format  
NeuroGuide  
University of Maryland (\*.raw)  
Cadwell Easy EEG

Input Directory  
Browse...

Input File Extension

**Montage Parameters**

☐ Additional Montage Information Required

Montage  
ABM X24  
ANT 21  
AveRef

**Age Parameters**

☐ Additional Age Information Required

Age Database Text File Name  
Browse...

**Output Parameters**

Output Process  
Generate Subject Reports  
Create Individual Analysis Files  
Create Group Analysis File  
Options...

**Edit Parameters**

☐ Additional Edit Information Required  
☐ Select All EEG Time Points  
☐ Automatic Editing

Edit File Format  
NeuroGuide  
QND  
Spectrum 32 Index File

Edit Directory  
Browse...

Edit File Extension

**Eyes Condition Parameters**

☐ Additional Eyes Condition Information Required  
☒ Eyes Closed  
☐ Eyes Open

**Batch Analysis Monitor**

Run Close

Click **Statistics > Group Statistics > Descriptive > Mean or Standard Deviation** and then navigate to where you saved the **\*.ngg** file using **NeuroStat** to view these statistics. The **NeuroStat** options are the same for the **Individual Analysis Comparative Statistics**. See **Step #4**



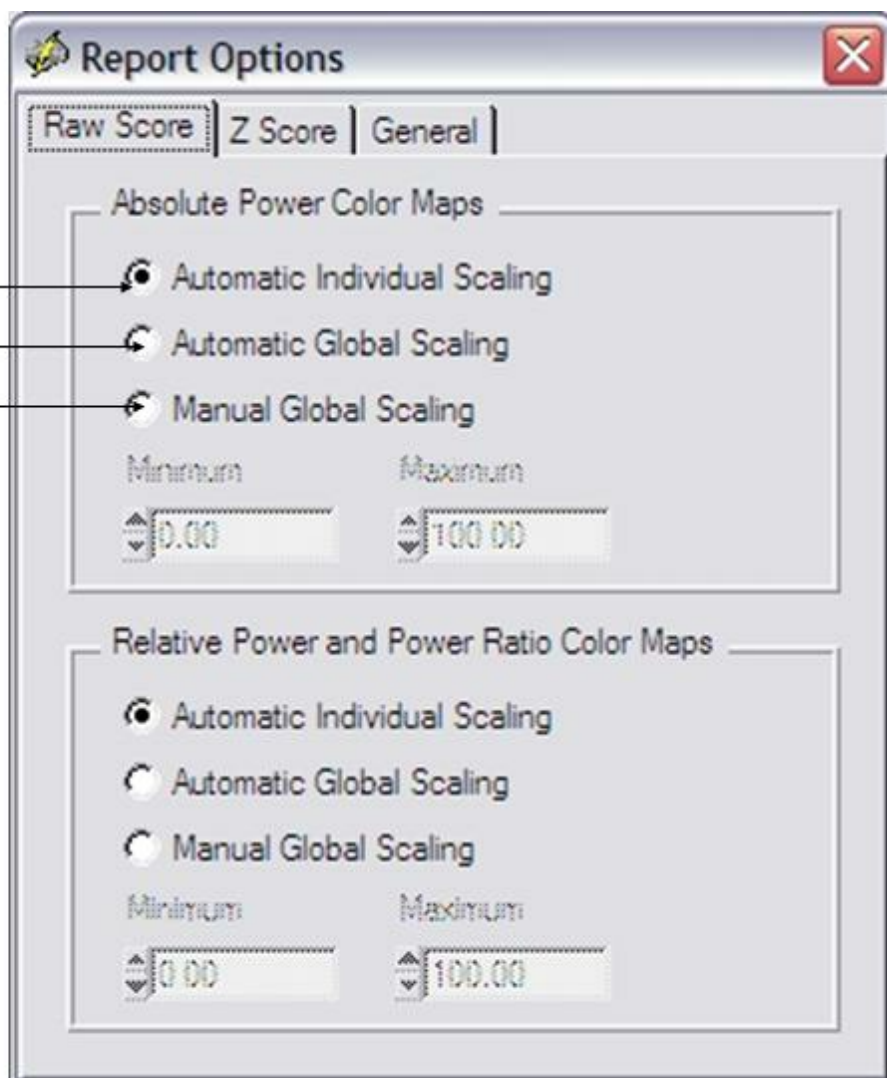


Adjust the Scales of the Color Topographic Maps by clicking Report > Color Map Settings. In the Report Options panel select Automatic Individual Scaling where the minimum and maximum range is set for each individual map or Automatic Global Scaling where the min and max are computed for all maps or Manual Scaling in which the user sets the min and max.

**Scale within individual Maps**

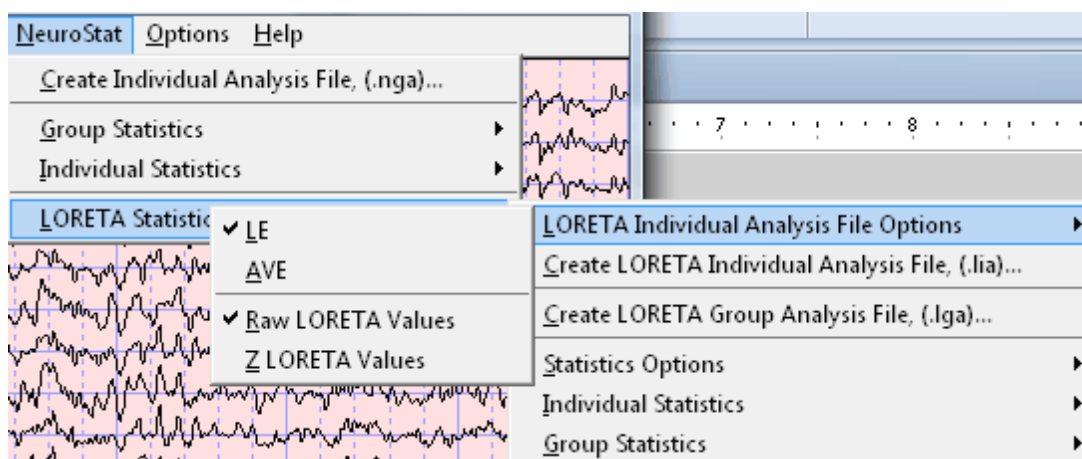
**Scale Maps Globally**

**Scale Maps Manually**

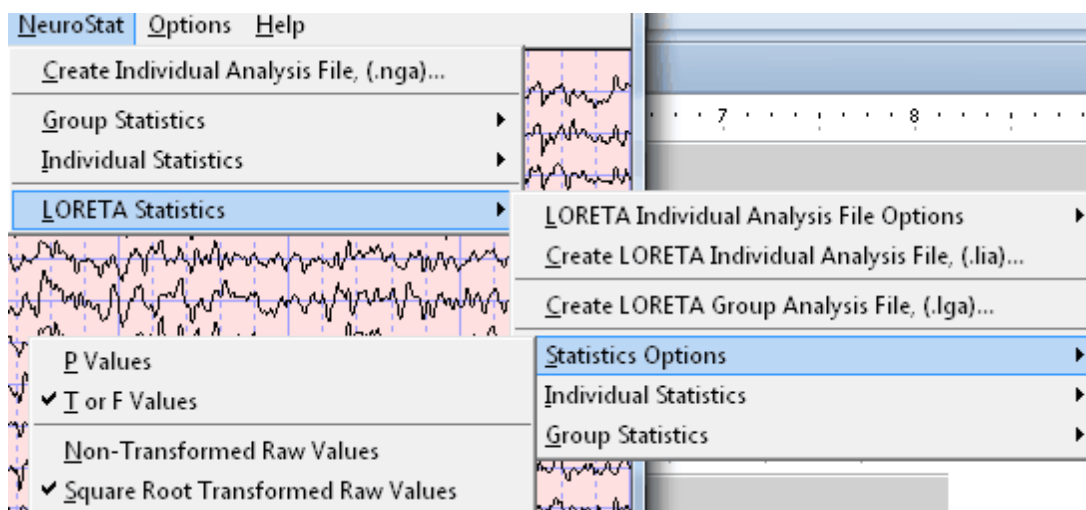


## Step 7 3-Dimensional LORETA: Individual Statistics

Follow Steps #1 and #2 and open two NeuroGuides and position them on the top and bottom of the display screen. Click Statistics > LORETA Statistics > Individual Analysis File Options and select LE and Raw LORETA Values. Either raw or Z Scores can be used in LORETA statistics. Then click NeuroStat > Create LORETA Individual Analysis File (.lia) and save the .lia file in the subject's folder as Pre-Treatment.lia. Do the same for the 2nd LORETA and save the .lia file as Post-Treatment.lia



Click NeuroStat > LORETA Statistics > Statistics Options and make sure that T or F values are selected. This is because the LORETA viewer does is not capable of display differences between small P values. The T or F values are larger and easier to see in the LORETA viewer. To determine statistical significance of T or F values consult a standard statistical text book with tables of T or F values and then calculate the degrees of freedom to determine the level of statistical significance. Two second epochs are used in the FFT and therefore the degrees of freedom are the total number of two seconds epochs minus 2. For example, two 40 second samples of data =  $(20 + 20) - 2 = 38$  df.



Click NeuroStat > LORETA Statistics > Individual Statistics > Comparative > Percent Difference. Double click the Pre-Treatment.lia in the Open LORETA Individual Analysis File 1 window. Then Double click Post-Treatment.lia in the Open LORETA Individual Analysis File 2 window.

A Save LORETA Statistics window will open so that one can save the results of the analysis in an ASCII \*.lor format for purposes of importing into Excel or for use with the Key Institute software, etc. For purposes of this tutorial click Cancel to proceed to the computation of the statistic.



After the Key Institute software is launched, click **ScaleWin** on the Key Institute menu bar and position the color scale window in the lower left corner of the screen. Then advance through the frequencies by clicking the Time Frame right arrow to examine the percent differences between the 0 to 30 seconds of EEG versus the period from 10 seconds to 40 seconds of the EEG. Note that the maximum percent difference varies from about 30% at 1 Hz to about 9 % at 9 Hz.

Now click **Statistics > LORETA Statistics > Individual Statistics > Comparative > Paired t-Test**. Double click the **Pre-Treatment.ila** in the **Open LORETA Individual Analysis File 1** window. Do the same for the **Post-Treatment.ila** in the **Open LORETA Individual Analysis File 2** window. Click cancel when the **Save LORETA Statistics** window opens.

After the Key Institute software is launched, click **ScaleWin** on the Key Institute menu bar and position the color scale window in the lower left corner of the screen. Move the **Change Linearity** wiper to the extreme right position or 100. For the moment keep the **Change Max** wiper in the default middle position so that the maximal probability values will be displayed. To evaluate statistical significance move the change max wiper to 1.0 and check the **Fix Maximum** box. Move the mouse over the regions of interest and read the t or F values in the window at the bottom right of the viewer. Advance through the frequencies by clicking the Time Frame right arrow. Use a standard statistics table to determine the level of statistical significance based on the degrees of freedom. Repeat these steps by selecting a different statistic, such as **Independent t-Tests** or **ANOVA**. Also, evaluate the descriptive statistic option by clicking **Statistics > LORETA Statistics > Individual Statistics > Descriptive** to evaluate single \*.ila files.

### 3-Dimensional LORETA: Group Statistics

Launch **NeuroGuide** and open the **Demo Lexicor NRS-24** file. Select the first 0 to 30 seconds and then click **Statistics > LORETA Statistics > Create LORETA Individual Analysis File (\*.ila)**. Name the file as **Beginning1.ila** and then save.

Click **Edit > Clear Selections** and then depress the left mouse button and select EEG starting at 10 seconds and continuous to 40 seconds. Then click **Statistics > LORETA Statistics > Create LORETA Individual Analysis File (\*.ila)**. Name the file as **Beginning2.ila** and then save.

Click **Edit > Clear All Selections** and then click the **End Key**. Position the mouse on the last EEG values and depress the left mouse button and select EEG starting at 3.48 seconds and move the mouse to the right and stop at 3:18 seconds. Then click **Statistics > LORETA Statistics > Create LORETA Individual Analysis File (\*.ila)**. Name the file as **End1.ila** and then save.



Click **Statistics > LORETA Statistics > Create LORETA Group Analysis File (\*.lga)**. In the LORETA Group Analysis File Creation window Click **browse** to browse to the folder where the individual analysis files were saved (i.e., the \*.lia files) and click **Done**.

In the LORETA Group Analysis File Creation window click the file **Beginning1.lia** and click **Add**. Then click the file **Beginning2.lia** and click **Add**. Then Click **O.K.** In the **Save LORETA Group Analysis Output File As** name the Group file **Beginning.lga**.

Now let us create the second group file. Click **Statistics > LORETA Statistics > Create LORETA Group Analysis File (\*.lga)**. In the LORETA Group Analysis File Creation window Click **browse** to browse to the folder where the individual analysis files were saved (i.e., the \*.lia files) and click **Done**.

In the LORETA Group Analysis File Creation window click the file **End1.lia** and click **Add**. Then click the file **End2.lia** and click **Add**. Then Click **O.K.** In the **Save LORETA Group Analysis Output File As** name the Group file **End.lga**.

Click **Statistics > LORETA Statistics > Statistics Options** in order to select **P values** or **T values** as well as the non-transformed raw values (squared source current vectors (square root of the sum of squares of the x, y & z moments) or the square root transformed raw values which will return source current values in units of amperes/meter squared.

Click **Statistics > LORETA Statistics > Group Statistics > Comparative > Paired t-test**. Select by double clicking the file **Beginning.lga**, then double click on the file **End.lga**. A **Save LORETA Statistics** window will open so that one can save the results of the analysis in an ASCII \*.lor format for purposes of importing into Excel or for use with the Key Institute software, etc. For purposes of this tutorial click **Cancel** to proceed to the computation of the statistic.

After the Key Institute software is launched, click **ScaleWin** on the Key Institute menu bar and position the color scale window in the lower left corner of the screen. Move the **Change Linearity** wiper to the extreme right position or 100. For the moment keep the **Change Max** wiper in the default middle position so that the maximal probability values will be displayed. To evaluate statistical significance move the change max wiper to 1.0 and check the **Fix Maximum** box. Move the mouse over the regions of interest and read the t or F values in the window at the bottom right of the viewer. Use a standard statistics table to determine the level of statistical significance based on the degrees of freedom. Advance through the frequencies by clicking the **Time Frame**. Repeat these steps by selecting a different statistic, such as independent t-tests. Also, evaluate the descriptive statistic option by clicking **Statistics > LORETA Statistics > Group Statistics > Descriptive** to evaluate single \*.lga files.



## Appendix A: Computation of the Auto-spectral and Cross-spectral Densities of the Edited EEG Selections

1. The FFT parameters are: epoch = 2 seconds at a sample rate of 128 sample/sec = 256 digital time points and a frequency range from 0.5 to 40 Hz at a resolution of 0.5 Hz using a cosine taper window to minimize leakage. Each 2 second FFT is 81 rows (frequencies 0 to 40 Hz) X 19 columns (electrode locations) = 1,539 element cross-spectral matrix for each subject.
2. In order to minimize the effects of windowing in the FFT (Kaiser and Stermann, J. Neurotherapy, 4(3): 85-92, 2001) a EEG sliding average of the 256 point FFT cross-spectral matrix was computed for each normal subjects edited EEG by advancing in 64 point steps (75% overlap) and recomputing the FFT and continuing with the 64 point sliding window of 256 point FFT cross-spectrum for the entire edited EEG record. Each of the 81 frequencies for each 19 channels is  $\log_{10}$  transformed to better approximate a normal distribution. The total number of 2 second windows is the number that is entered into the analysis of variance and t-tests and it is used to compute the degrees of freedom for a given statistical test.
3. A mean, variance, standard deviation, sum of squares, and squared sum of the real (cosine) and imaginary (sine) coefficients of the cross-spectral matrix is computed across the sliding average of edited EEG for all 19 leads for the total number of 81 and 1,539 log transformed elements for each subject. This creates the following six basic spectral measurement sets and their derivatives 1- Cross-Spectral Power (square root of the sums of squares of the real and imaginary coefficients); 2- Auto-Spectral Power which is the diagonal of the cross-spectral matrix where the imaginary coefficient = 0 and power = sine square; 3- Coherence = square of the cross-spectrum divided by the product of the two auto-spectra; 4- Phase = arctangent of the ratio of the real/imaginary components for frequencies from 0.5 to 40 Hz;; 5- Real coefficients; 6 Imaginary coefficients.
4. The results of the computations are stored in the NeuroGuide Analysis File, designated as \*.NGA. These results are used in the comparative statistical analyses when one selects and opens the .NGA files in the menu operation of Statistics>Comparative Statistics. Calibration of NeuroStat is by computing the statistics contained in the NRS-24 demo sample of EEG from an unidentified traumatic brain injured patient.
5. The results of the LORETA computations from a single selection of EEG are stored in a LORETA individual analysis file \*.LIA. The .lia file contains all of the cross-spectral values for each 2 second epoch so that the means and standard deviations, higher statistical moments and sum of squares, etc. can be computed for each gray matter pixel in the Montreal Neurological normative MRI. Details of the computation of the T matrix



and the J currents as the square root of the sum of the squares (x, y & z) is described in Appendix F in the NeuroGuide manual. The mathematics for the LORETA statistics are identical to the surface EEG statistics except there is a larger number of individual comparisons (2,393) in comparison to the surface 19 channel situation.

6. This issue of multiple comparisons when using LORETA is best handled by the statistics of "Planned Comparisons" or where one first creates hypotheses as to frequencies and Brodmann Areas before launching LORETA. For example, if the surface EEG at F3 is > 2 standard deviations deviant from normal at 4 Hz, then the hypothesis prior to launching LORETA is significant deviations from normal in left Brodmann Areas 8 & 9 at 4 Hz. Bonferroni corrections (i.e., alpha/n) are blind exploratory adjustments and result in large Type II errors. Hypothesis testing is preferred over multiple comparison adjustments.

## Appendix B: Equations and Statistics

1. Absolute Differences: Mean test 1 Mean Test 2 for 19 channels and 81 frequencies or in the case of LORETA for 2,394 gray matter pixels from 1 to 30 Hz in 1 Hz increments (by averaging 0.5 Hz bands).
2. Percent Differences:

$$\frac{\bar{X}_{test1} - \bar{X}_{Test2}}{\bar{X}_{test1} + \bar{X}_{Test2}} \times 100$$

where X bar = mean

3. Independent t test (Assuming Population Variance Not Equal) (from Winer, R.J., *Statistical Principles in Experimental Design*, McGraw-Hill, New York, 1962, p. 42 43):

$$t = \frac{(\bar{X}_1 - \bar{X}_2) - (u_1 - u_2)}{\sqrt{(s_1^2/n_1) + (s_2^2/n_2)}}$$

, To test the hypothesis that  $u_1 - u_2 = 0$  against a two-tailed alternative hypothesis  $P < .025$ .

4. Paired t-test (from Winer, R.J., *Statistical Principles in Experimental Design*, McGraw-Hill, New York, 1962, p. 44 46):

$$t = \frac{\bar{d} - (u_1 - u_2)}{\sqrt{s_d^2/n}}$$

where the mean differences between test 1 and test 2 and the variance of the differences and n = number of FFT windows in test 1 + test 2.





5. One Way Analysis of Variance (from Hayes, W.J. *Statistics for the Social Sciences*, Holt, Rinehart and Winston, Inc., New York, 1973, p. 473-475):

$$\text{Sum of squares total (SS total)} = \frac{\bar{X}_{test1} - \bar{X}_{Test2}}{\bar{X}_{test1} + \bar{X}_{Test2}} \times 100$$

$$\text{Sum of squares within (SS within)} = \frac{(\bar{X}_1 - \bar{X}_2) - (u_1 - u_2)}{\sqrt{(s_1^2/n_1) + (s_2^2/n_2)}}$$

$$\text{Sum of squares between (SS between)} = \frac{\bar{d} - (u_1 - u_2)}{\sqrt{s_d^2/n}}$$

Where M = mean and j = number of groups to be compared, i.e., j = 2 and i = number of FFT windows in both test 1 and test 2. Degrees of freedom = J - 1 and i - 2 and F = Mean square between groups/mean square within groups. Probability is computed using the F based on 1 and i - 2 degrees of freedom.

6. Repeated Measures Analysis of Variance (from Hayes, W.J. *Statistics for the Social Sciences*, Holt, Rinehart and Winston, Inc., New York, 1973, p. 571-573):

$$\text{Sum of squares between (SS between)} = \sum_j \sum_i (y_{ij} - M)^2$$

$$\text{Sum of squares within (SS within)} = \sum_j \sum_i (y_{ij} - M_j)^2$$

$$\text{Sum of squares between treatments} = \sum_j \sum_i (y_{ij} - M_i)^2$$

SS residual SS within SS between treatments. J = number of groups (2) and n = number of FFT windows in both test 1 and test 2. The degrees of freedom are 1 and n - 2.

7. Covariance, Correlation and R<sup>2</sup> (from Winer, R.J., *Statistical Principles in Experimental Design*, McGraw-Hill, New York, 1962, p. 44-52):



$$L_1 = n \sum X_1^2 - (\sum X_1)^2 \quad \text{and} \quad L_2 = n \sum X_2^2 - (\sum X_2)^2$$

$$L_{12} = n \sum X_1 X_2 - (\sum X_1)(\sum X_2) = \text{Covariance}$$

$$r_{12} = \frac{L_{12}}{\sqrt{L_1 L_2}} = \text{Correlation}$$

$$r_{12}^2 = R^2$$

= R<sup>2</sup> or the percent variance shared by test 1 and test 2

# NeuroBatch

## Manual and Tutorial

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# Part IV

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(All EEG Selections and/or Sine Wave Segments are for Illustrative Purposes Only)



## NeuroBatch Manual & Tutorial

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## INTRODUCTION

NeuroBatch is a program that provides for automatic processing of large numbers of edited EEG files in batch mode. Color topographic maps and tab delimited output is provided for each edited EEG file as well as NeuroGuide Analysis files that can be imported into NeuroStat for the purposes of individual and group statistics. NeuroStat is an independent software program which does not rely upon NeuroBatch except for the creation of Group Analysis Files (\*.NGG) that NeuroStat uses to compute group statistics.

### **Step #1 Organize the EEG Files to be Used in the Batch Process:**

**1a - Create a Batch Input Folder and then copy and paste the \*.ng or \*.dat files that you want to process into this folder.**

**1b - If Group Statistics are planned then individual group folders must be created so that each folder contains only the selected subjects for a given group, e.g., ADD children or Alzheimer's patients, or Stroke patients, normal control subjects, etc.**

**1c - If age has not been specified in the NeuroGuide \*.ng or in the \*.dat files, then one must create a text file using word or notepad that lists the EEG file names and the ages that correspond to each file. The best method is to use the NeuroGuide \*.ng files with age entered in each \*.ng file because one can skip this step and go directly to Step # 2.**

**1d - NeuroBatch assumes artifact free edited EEG files in which all of the EEG data has been selected by a competent person and/or visually verified including the use of test re-test statistics. The competence of the professional is a critical factor in all statistical analyses and NeuroGuide requires a competent operator to select and organize the EEG files in a correct manner. If one does not use \*.ng files, then one must specify the artifact free edit files that are to be used in the batch program. It is unethical to intentionally select artifact and then do analyses on the data without full disclosure that artifact was intentionally selected. Make a folder and then copy and paste each of the subject's artifact free \*.edt EEG edit files for each analyzed EEG which were produced by clicking Edit >Save Edit file in the main NeuroGuide menu. As stated previously the best method is to use the NeuroGuide \*.ng files because one can skip step 1c and go directly to Step # 2.**

**Click Analysis > NeuroBatch to open the NeuroBatch panel. Automatic batch analysis of hundreds artifact free EEG data files is the mission of NeuroBatch. One must specify the file format, file location, Montage, Edits (cannot run NeuroBatch without valid selections of artifact free**



EEG - see [Artifact Free Selection](#)<sup>D31</sup> in the NeuroGuide Manual).

Use the NeuroGuide Batch Analysis Window to Process the EEG files that were organized in Step #1

**NeuroGuide Batch Analysis**

**Input File Parameters**

Input File Format  
NeuroGuide  
Lexicor NRS-24  
QND Tampa Headbox

Input Directory  
Browse...

Input File Extension

**Montage Parameters**

☐ Additional Montage Information Required

Montage  
120deg-outofphase  
30-degree outphase  
60degree-outofphase

**Age Parameters**

☐ Additional Age Information Required

Age Database Text File Name  
Browse...

**Output Parameters**

Output Process  
Generate Subject Reports  
Create Individual Analysis Files  
Create Group Analysis File  
Options...

**Edit Parameters**

☐ Additional Edit Information Required

☐ Select All EEG Time Points

Edit File Format  
NeuroGuide  
QND  
Spectrum 32 Index File

Edit Directory  
Browse...

Edit File Extension

**Eyes Condition Parameters**

☒ Additional Eyes Condition Information Required

☒ Eyes Closed ☐ Eyes Open

**Batch Analysis Monitor**

Run Cancel

**Step # 2b - Select Input File Format by clicking on NeuroGuide for the \*.ng format or Lexicor NRS-24 for the Lexicor \*.dat format (DeyMed, Mitsar and NeuroNavigator all export EEG time series in the Lexicor \*.dat format).**

**Step # 2c - Click Input Directory and then Click "Browse". Browse to the input folder that contains the \*.dat and/or \*.ng files as was organized in Step #1a.**

**Step # 2d - Type ng or dat for the Input File Extension**

**Step # 2e -** The montage parameter (Linked Ears, Average Reference, Laplacian or CSD) is contained in the \*.ng file and the Montage Parameter panel can be by-passed if one does not want to change the Montage. If a \*.dat file was selected in Step #2c then one must select a Montage Parameter such as Linked Ears, Average Reference or Laplacian (i.e., Current Source Density or CSD). If one wants to change the Montage of a \*.ng file from e.g., Linked Ears to Laplacian, then click the "Additional Montage Information is Required" button and then click Laplacian montage.

**Step #2f -** Select Output Parameters that are the processes that one wants performed on the files contained in Step #1.

**Step 2g -** Click "Report Generation" to produce topographic maps and tab delimited outputs which are the same as those produced in NeuroGuide Deluxe "Report>Generate Report" by hand. That is, NeuroBatch automates the NeuroGuide Deluxe "r;Report>Generate Report" process for each subject in the folder. A subfolder will be produced within each subject's folder in which the bitmaps and text files are saved.

Click "Individual File Creation" to produce NeuroGuide Individual Analysis Files (\*.NGA) that can be used by NeuroStat for the purposes of Pre-Treatment vs Post-Treatment, or Pre-medication vs. Post-medication comparisons in the same subject. Repeated measures analysis of variance and Paired t-Tests as well as absolute differences and percent differences are the statistical tests performed on \*.NGA files in NeuroStat (see the [NeuroStat Manual](#)<sup>246</sup> for details).

Click "Group Statistics" to produce NeuroGuide Group Analysis Files (\*.NGG) that can be used by NeuroStat for purposes of comparing groups of subjects and not individual subjects. Examples are a group of ADD children vs. a group of Normal children or a group of Alzheimer Patients vs. a group of depressed patients, etc. The user must follow Step # 1b before selecting "Group Statistics". Correct selection and organization of groups by a competent person is necessary in order to obtain valid statistical results.

**Step # 2h -** Select Additional Edit Information or Edit Parameters (Skip this step if you use edited \*.ng files).

**Step # 2i -** Select Additional Eyes Condition Information (Skip this step if you use edited \*.ng files with the eyes open & closed conditions specified)





## **Step #3 Repeat Step # 2 to Process different Montages**

**3a - Parameters and/or Different Output**

**3b - and/or Different Edit Selections**

## **Step #4 Individual Statistics and NeuroStat**

**4a - In NeuroBatch step # 2g Select Individual Analysis File (\*.NGA).**

**4b - Click Statistics > Individual Statistics. Select the type of statistical comparison, e.g., for absolute differences, percent differences, Paired t-Test, Individual t-Test and ANOVA for comparisons between two individual NGA files. See the NeuroStat Manual for details.**

## **Step #5 Group Statistics and NeuroStat**

**5a - In NeuroBatch Step #2f select Group Analysis File (\*.NGG) . and proceed to the end of Step # 2.**

**5b - Click Statistics > Group Statistics for t-Test group statistics. See the [NeuroStat Manual](#)<sup>246</sup> for details**

# Signal Generator

## Manual and Tutorial

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# Part V

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(All EEG Selections and/or Sine Wave Segments are for Illustrative Purposes Only)



# Signal Generator Manual & Tutorial

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## Introduction:

The signal generator is used to calibrate and test the digital signal processing properties of NeuroGuide as well as to serve as an educational program by which the principles of digital signal analyses can be learned and explored. Concepts such as frequency, time, phase delays, noise, amplitude and coherence can be tested and evaluated. EEG data can be simulated by approximating the selected mixtures of signals to match the signal parameters and scalp locations of the EEG.

**Note: Sine Wave Segments were Selected for Illustrative Purposes Only**



## Step #1 Launch NeuroGuide; and

Click File > Open > Signal Generation

The screenshot shows the 'Signal Generation' dialog box with the following components and annotations:

- Select a channel:** Points to the 'Signal' dropdown menu showing 'FP1', 'FP2', 'F3', and 'F4'.
- Select a waveform:** Points to the 'Waveform' dropdown menu showing 'Sine'.
- Select a sample rate:** Points to the 'Sampling Rate' dropdown menu showing '128'.
- Add noise:** Points to the 'Signal Noise (uV)' input field showing '0.00'.
- Select a Pulse:** Points to the 'Pulse' radio button.
- Control pulse duration:** Points to the 'Duration (sec)' input field showing '1.00'.
- Control inter-pulse intervals:** Points to the 'Delay (sec)' input field showing '0.00'.
- Select an peak-to-peak Amplitude uV:** Points to the 'Amplitude (uV)' column header in the 'Signal Parameters by Frequency' table.
- Select a Phase Shift:** Points to the 'Phase Shift (Deg)' column header in the 'Signal Parameters by Frequency' table.
- View the Calibration Signals:** Points to the 'Signal Waveform' plot area.
- Save your Selections:** Points to the 'Save' button.
- Load Selections:** Points to the 'Load' button.

The 'Signal Parameters by Frequency' table is as follows:

	Amplitude (uV)	Phase Shift (Deg)
0 Hz	0.00	0.00
1 Hz	0.00	0.00
2 Hz	0.00	0.00
3 Hz	0.00	0.00
4 Hz	0.00	0.00
5 Hz	0.00	0.00
6 Hz	0.00	0.00
7 Hz	0.00	0.00
8 Hz	0.00	0.00
9 Hz	0.00	0.00
10 Hz	0.00	0.00
11 Hz	0.00	0.00
12 Hz	0.00	0.00
13 Hz	0.00	0.00
14 Hz	0.00	0.00
15 Hz	0.00	0.00

The 'Signal Waveform' plot area is empty, showing a grid for visualization.



## Step #2 Use the Mouse to Select:

EEG Channels;

Waveforms (sine, sawtooth, square and pulses);

Frequencies (1 to 30 Hz);

Amplitudes ( $\mu\text{V}$ )

Phase Delays (degrees); and

"Noise" (% S/N ratio)

The screenshot shows the 'Signal Generation' window with the following components and annotations:

- Select a channel:** Points to the 'Signal' dropdown menu showing FP1, FP2, F3, and F4.
- Select a waveform:** Points to the 'Waveform' dropdown menu showing 'Sine'.
- Select a sample rate:** Points to the 'Sampling Rate' dropdown menu showing '128'.
- Add noise:** Points to the 'Signal Noise ( $\mu\text{V}$ )' input field showing '0.00'.
- Select a Pulse:** Points to the 'Pulse' radio button.
- Control pulse duration:** Points to the 'Duration (sec)' input field showing '1.00'.
- Control inter-pulse intervals:** Points to the 'Delay (sec)' input field showing '0.00'.
- Select an peak-to-peak Amplitude  $\mu\text{V}$ :** Points to the 'Amplitude ( $\mu\text{V}$ )' column in the 'Signal Parameters by Frequency' table.
- Select a Phase Shift:** Points to the 'Phase Shift (Deg)' column in the 'Signal Parameters by Frequency' table.
- View the Calibration Signals:** Points to the 'Signal Waveform' plot area.
- Save your Selections:** Points to the 'Save' button.
- Load Selections:** Points to the 'Load' button.

The 'Signal Parameters by Frequency' table is as follows:

	Amplitude ( $\mu\text{V}$ )	Phase Shift (Deg)
0 Hz	0.00	0.00
1 Hz	0.00	0.00
2 Hz	0.00	0.00
3 Hz	0.00	0.00
4 Hz	0.00	0.00
5 Hz	0.00	0.00
6 Hz	0.00	0.00
7 Hz	0.00	0.00
8 Hz	0.00	0.00
9 Hz	0.00	0.00
10 Hz	0.00	0.00
11 Hz	0.00	0.00
12 Hz	0.00	0.00
13 Hz	0.00	0.00
14 Hz	0.00	0.00
15 Hz	0.00	0.00



**2a - Click a channel to select a location in Lexicor format (e.g., O1), then double click a Frequency (e.g., 10 Hz), then double click Amplitude (uV) and type in a value (e.g., 100 uV).**

**2b - Mix sine waves in by double clicking the amplitude of a different frequency, e.g., 5 Hz and type 50 uV.**

**2c - Shift the Phase of the 5 Hz signal by double clicking "Phase Shift (Deg)" at 5 Hz and type 30.**

**2d - Add "Noise" to the 5 Hz signal by double clicking the window below "Signal Noise (uV)" and type 100. This adds 100 microvolts of noise to the 5 Hz signal located at O1.**

**2e - Repeat Steps 2a to 2d for each channel with or without adding phase delays and/or noise or multiple frequencies, etc. Unselect any value by double clicking in the appropriate box and set the value = 0. The Channel is the primary selection and then the amplitude, frequency or mixtures of frequencies and phases and noise are the secondary selections.**

**Step #3      Simulate EEG "Spindles" by selecting pulse and then select the frequency and amplitude of the intra-pulse structure, duration and inter-pulse intervals of the simulated spindles.**

**3a - Generate Pulses of different durations and inter-pulse intervals. Use this tool to simulate EEG "Spindles".**

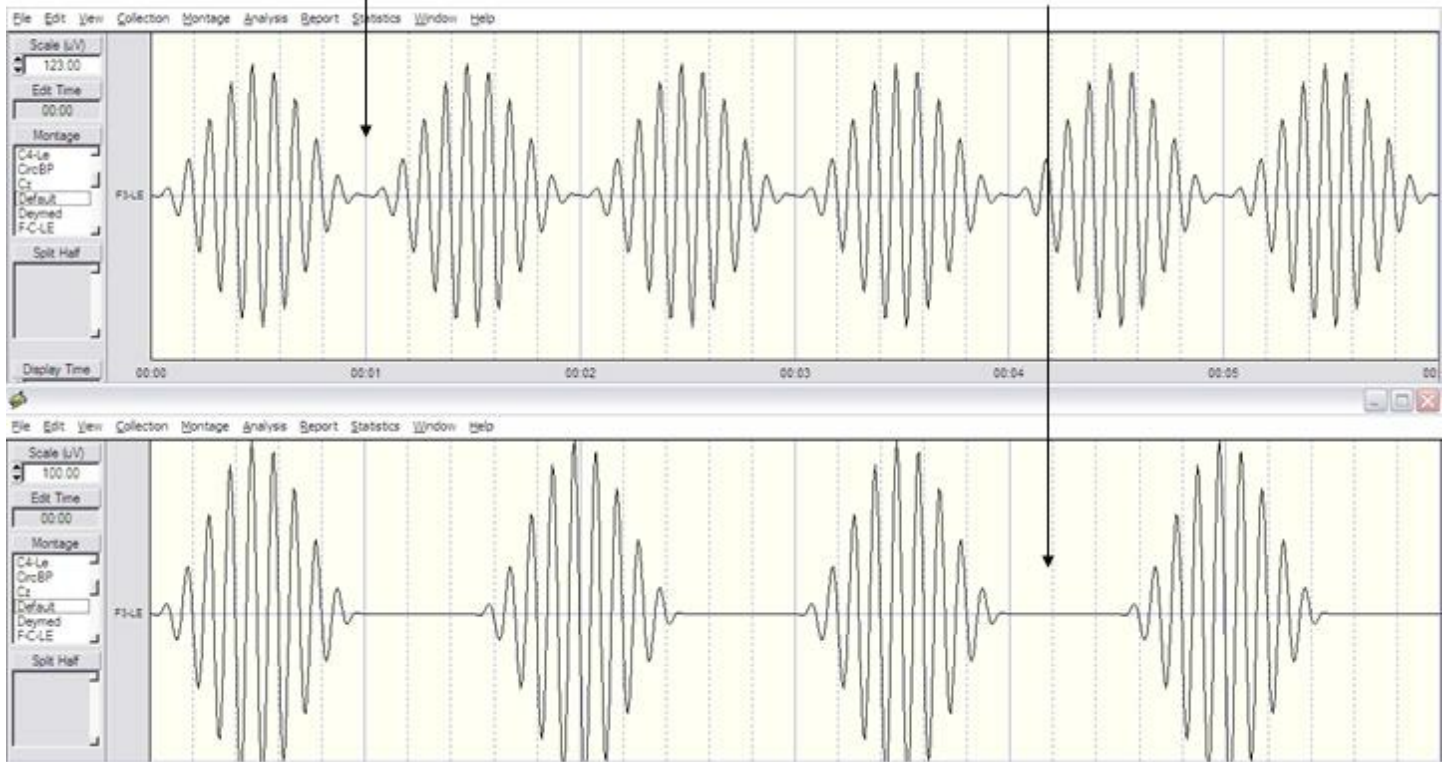




## Simulate EEG 'Spindles' using the Pulse option in the Signal Generator

**Pulse duration = 1.0 second  
Inter-pulse interval = 0.0 seconds**

**Pulse duration = 1.0 second  
Inter-pulse interval = 0.5 seconds**



**3b - Simulate any EEG by comparing the auto and cross-spectral values and then entering these values into the appropriate channels and appropriate parameter selection locations.**

Use the Signal Generator feature of NeuroGuide to learn about digital signal processing in general as well as various analytical programs including LORETA and other inverse solutions.

**Step #4 Click OK, then Click Edit > Select All to view FFT results**

**Step #5 Click File > Save As to Save the signals in NeuroGuide or Lexicor format (\*.ng or \*.dat).**

**Step 5a - Follow the NeuroGuide Manual Instructions to Save As NeuroGuide (\*.ng) or Lexicor (\*.dat) files.**



**Step 5b - Follow the NeuroGuide Manual Instructions to save Power Spectra and Cross-Spectra and to Export to LORETA in the NeuroGuide Manual).**

**Step #6      Example Tutorial by replicating the publication: Gomez and Thatcher "Frequency domain equivalence between potentials and currents using LORETA." *Int. J. of Neuroscience*, 107: 161-171, 2001.**

**6a - Select O1 at 10 Hz at 50 uV and 20 Hz at 25 uV**

**6b - Select O2 at 8 Hz 50 uV and 16 Hz at 25 uV**

**6c - Select F7 at 10 Hz 25 uV and 20 Hz at 50 uV**

**6d - Select F8 at 8 Hz 25 uV and 16 Hz at 16 uV**

**6e - Click OK and then click File > Save As NeuroGuide (\*.ng) or Lexicor (\*.dat) for purposes of further analysis. For example, save the power spectra and/or export the digital time series to LORETA.**

## **Appendixes for the Signal Generator Manual**

**Appendix A: [LORETA](#)** <sup>279</sup>

**Appendix B: [Mathematics of Gomez and Thatcher, 2001](#)** <sup>280</sup>

**Appendix C: [References](#)** <sup>283</sup>



## APPENDIX A: LORETA

Gomez and Thatcher, 2001 used the Key Institute mathematical equations to validate LORETA and cross-validated their math by comparing the forward solution and the inverse solution using MRI 3-D voxel locations and the surface scalp EEG currents and potentials (Based on the Reciprocity Theorem, Helmholtz, 1853). The results of the Gomez and Thatcher, 2001 study is also consistent with Tesche, C. and Kajola, M. "comparison of the localization of spontaneous neuromagnetic activity in the frequency and time domains." *Electroencephalography and Clin. Neurophysiology*, 87(6): 408-416, 1993.

One can test the facts and the science of LORETA for themselves using the NeuroGuide signal generator and the Gomez and Thatcher, 2001 frequencies and locations which is only one of several tools available to test LORETA (see Appendix B and C) not to mention the mathematical concepts of linearity between frequency and time and between electrical potentials and currents (Helmholtz, 1853 physics of "Reciprocity" and the "Lead Field", Malmivuo and Plonsey, 1995).

It makes no difference whether one exports signals in the time domain or in the frequency domain (as demonstrated in the Gomez & Thatcher, 2001 and the Tesche et al, 1993 publications as well as by mathematical simulation in step # 5). Caution must be exercised when using LORETA to be sure to physiologically validate using the surface linked ears, average reference and current source density data. This is not to indicate that LORETA is not a valid mathematical and scientific methodology, to the contrary, it is an important contribution. We are emphasizing the fact that LORETA is valid when used by competent professionals who take the time to validate the source solutions by evaluating the surface EEG distributions and physiology in order to guard against localization error. For example, scalp recorded EEG with large amplitude alpha in O1 and O2 should appear as high current density in areas 17, 18 & 19 in LORETA.



## APPENDIX B: Mathematics and Results of Gomez & Thatcher, 2001

**Note:** There are three instances when multiplication of matrices is commutative: 1- by a null matrix, 2- by an identity matrix and, 3- multiplication by a scalar.

We apply this commutative property in the following manner.

For  $S = KJ$ , where  $K$  is the lead field matrix,  $J$  = current and  $S$  = the sensitivity of the sensors (depending on the model used and the conductivity, etc.).  $S$  is an  $N \times W$  matrix for the scalp potentials (EEG/MEG), where  $N$  is the number of sensors and  $W$  is the number of time samples.  $J$  is a  $3M \times W$  matrix, where  $M$  is the number of sources and  $W$  is the same time samples as for  $S$ . Then the inverse solution is a linear combination of the signal  $S$  in the sensors

$$J = T \cdot S \quad \text{Eq. 1}$$

Where  $T$  is some generalized inverse of  $K$ , where the minimum norm solution is

$$T = (\text{pinv}(K' \cdot K = K)) = K' \quad \text{Eq. 2}$$

$K'$  is the transpose of  $K$ , and  $\cdot$  represents matrix multiplication and  $\text{pinv}(X)$  is the Moore-Penrose pseudoinverse (Menke, 1984). Pascual-Marqui et al, 1994 use the mathematical method that they refer to as "Low-Resolution Computed Tomography" (LORETA) to add physiological foundations and to avoid the minimum norms's problems in localizing deep sources by using the Laplacian Operator  $B$  and  $W$  as a weighting matrix. The LORETA equation is

$$T = \{\text{pinv}(WB'BW)\}K'[\text{pinv}(K \text{ inv}(WB'BW)K')] \quad \text{Eq. 3}$$

The critical factor in these considerations is that the real number FFT computed by the cross-spectrum (Hermitian matrix as a scalar real number) as represented in equation 1 is a linear operator such that for any inverse solution of the form in equation 3 is equivalent to:

$$\text{FFT}(J) = \text{FFT}[T \cdot S] = T \cdot \text{FFT}[S] \quad \text{Eq. 4}$$

Equation 5 is the formula that Gomez and Thatcher (2001) used. Gomez and Thatcher (2001) simulated the linear equivalence by a combination of sine waves and confirmed the linearity of equation 5 as any one can do by using the NeuroGuide signal generator as described in step # 5 for oneself.

Figure 1 - From Gomez & Thatcher, 2001. This is the three-shell spherical model of the head used to simulate LORETA. Four electrodes (F7, F8, O1, O2) and the reference electrode (A1) are indicated by black rectangles. The coordinates of the electrodes are according to the best-



fitting sphere relative to cortical anatomy (Towel et al., 1993). The peaks of beta (for F7 and F8) and alpha activity (for O1 and O2) are indicated in parenthesis. Eight sources (1 to 8) indicated by black circles were located in the interior of the sphere to represent the equivalent current sources such as in the gray matter.

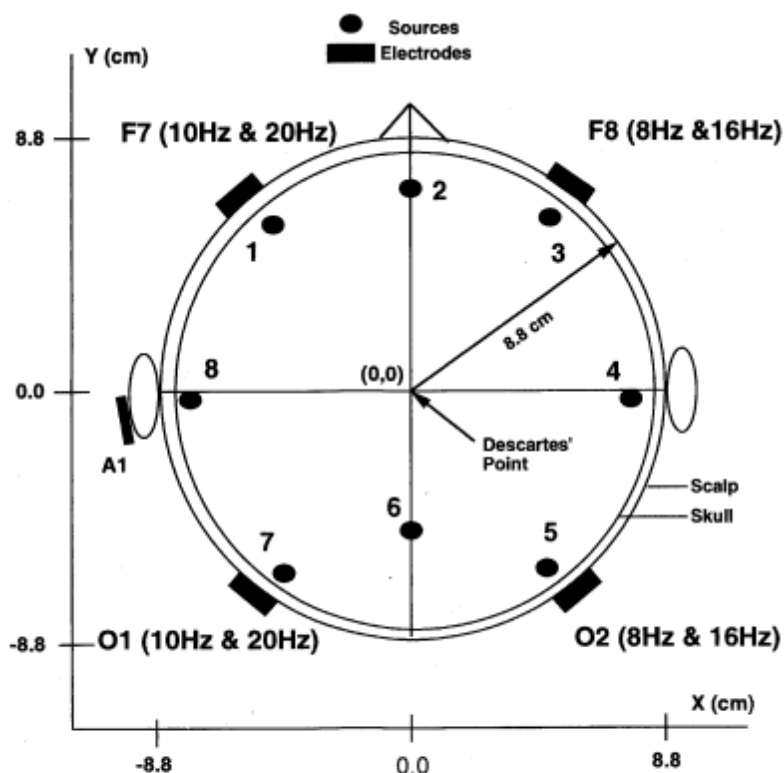
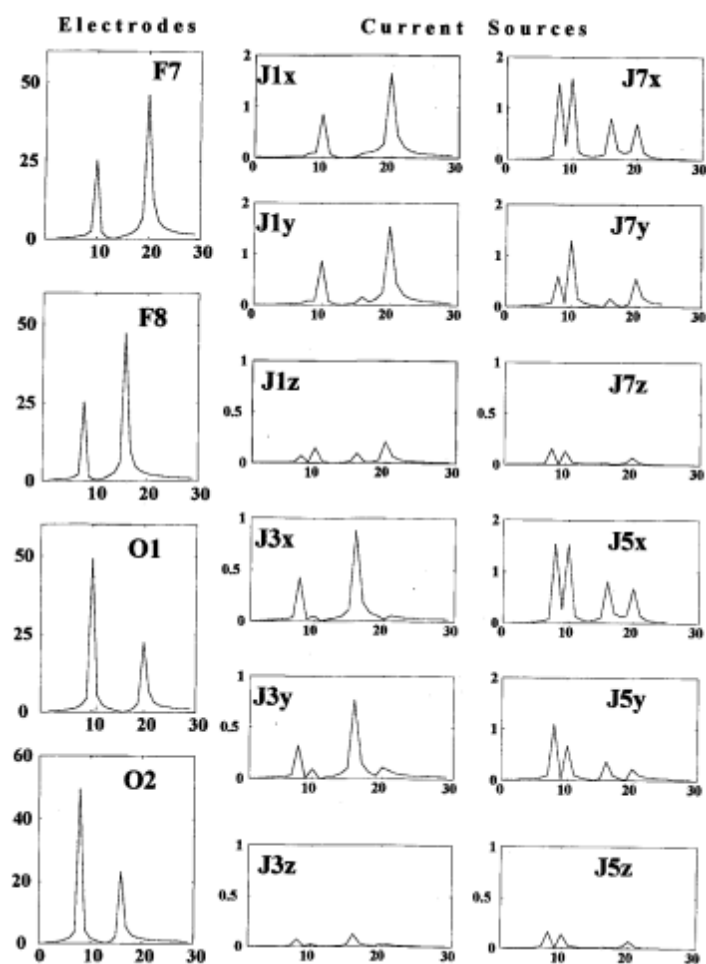


FIGURE 1 The three-shell spherical model of the head used to simulate LORETA. Four electrodes (F7 F8 O1 O2) and the reference electrode (A1) are indicated by black rectangles. The coordinates of the electrodes are according to the best-fitting sphere relative to cortical anatomy (Towel *et al.*, 1993). The peaks of beta (for F7 and F8) and alpha activity (for O1 and O2) are indicated in parenthesis. Eight sources (1 to 8) indicated by black circles were located in the interior of the sphere to represent the equivalent current sources such as in the gray matter.

Figure 2 - From Gomez & Thatcher, 2001. Power spectrum of the signals used to simulate LORETA. The spectrum of the signals in the scalp electrodes is shown on the left (amplitude of beta is higher in the anterior regions, alpha amplitude is higher in the posterior regions and a frequency shift toward the lower frequencies in the right hemisphere). The center and right columns are the spectra of the current sources nearest to the electrodes J1, J3, J5 and J7 after calculating the inverse solution. Each source has three components x, y and z. The y-axis of the electrodes is  $\mu V^2 / \text{cycle/sec}$  for the electrodes and  $\mu A / \text{cm}^2 / \text{cycle/sec}$  for current density at each source location. The x-axis is frequency in Hz in all cases. This simulation confirms the mathematical statements and demonstrates a frequency domain equivalence between the spectra of electrical potentials at the scalp and the spectra of currents in the interior of the head model.





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# **All Comments and Feedback Are Welcome**

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and tell us what you think.**



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