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LORETA Z Score Biofeedback

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Today we are riding the crest of a wave of converging new neuroscience knowledge that includes EEG Neuroimaging Biofeedback (Thatcher, 2000; Congedo et al, 2004; Cannon et al, 2005; 2006; 2007; 2009). In the physics of source localization the forward solution is where a source inside a sphere determines the electrical potential on the surface as calculated using Maxwell's 1864 equations. In contrast, the inverse problem is where the sources are unknown and the location of the sources are estimated by measuring the electrical potential on the surface (Malmivuo and Plonsey, 1995). To solve the inverse equation one must apply physiological constraints such as used in cardiology in the early 1900s and quantitative EEG (QEEG) in the 1980s (Malmivuo and Plonsey, 1995). Low Resolution Electromagnetic Tomography (LORETA) uses physiological constraints related to the human electroencephalogram (EEG) including the use of distributed source smoothing (Pascual-Marqui et al, 1994). LORETA uses a 3D Laplacian spatial operator as a source smoothing constraint where simultaneously active sources distributed in space are used to solve the inverse equation. Importantly, the LORETA solution to the inverse problem was also linked to the standard co-registration used in all neuroimaging modalities including PET, SPEC and fMRI. The linkage to 7 mm cube electrical source volumes co-registered to the standard normative MRI allows for real-time millisecond biofeedback of electrical sources with a similar spatial resolution as fMRI and sufficient for larger volumes such as Brodmann areas that range from 1 to 6 square centimeters (Brodmann, 1909). High-speed computers are essential because the brain is organized in clusters of neurons called Modules and Hubs where groups of neurons are cross-frequency phase locked in re-enterant loops of bursting action potentials conducted by cortical white matter and temporally coordinated by the thalamus and brainstem-limbic systems (Steriade, 2006; Vinogradova, 2001; Thatcher et al, 2008; Sauseng and Klimesch, 2008; Buzsaki, 2006). These important brain dynamics are too fast for fMRI to measure directly.

This is important because structure and function are linked in biology and functional localization in the brain e.g., visual cortex and blindness, deafness and temporal lobe damage, etc, when linked to the patient's symptoms aids in rendering a diagnosis and treatment for him or her. An advantage of LORETA EEG biofeedback is that one can target anatomical regions related to "loss of function" or "weak" function related to the patient's symptoms and complaints (Luria, 1973). This approach has been followed in both LORETA EEG biofeedback (Cannon et al, 2005; 2006) and with fMRI (de Charms, 2008).

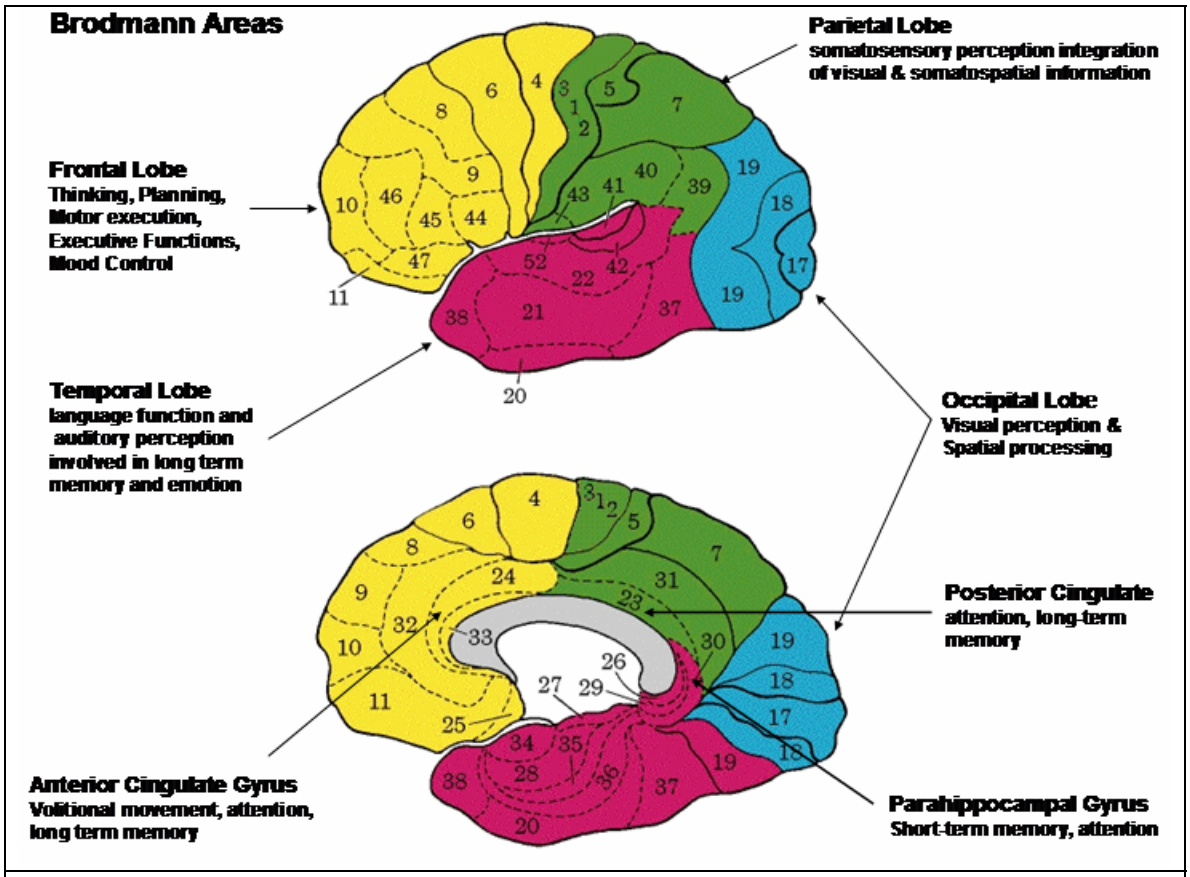

Fig. 1- General structure-function linkages to Brodmann areas (Brodmann, 1909).

fMRI biofeedback involves operant conditioning of groups of neurons where increased action potential bursting is related to dilation of the blood vessels and increased blood flow seconds after the neurons were active. In contrast, LORETA EEG has a sub millisecond time resolution with similar spatial resolution as fMRI (Pascual-Marqui, 1999). In addition to a higher time resolution, there are economic advantages of LORETA biofeedback vs. fMRI biofeedback. For example, an fMRI 3T magnet costs about $3,000,000 with a $40,000 per month liquid helium bill vs < $20,000 for portable LORETA EEG biofeedback with no monthly maintenance costs.

LORETA Normative Database and LORETA Z Scores

A Z score is a statistical measure of the distance an individual is from a reference normal population. The clinical value of EEG Z scores is similar to the clinical value of a blood test, e.g., if a patient is lethargic and jaundice and liver enzymes are 3 standard deviations outside of normal then this helps a clinician link the patient's symptoms to a possible physiological dysfunction. An advantage of real time Z score LORETA biofeedback is instantaneous feedback of age-matched comparisons to a reference database of healthy individuals (Z scores) by which instantaneous deviations in Brodmann areas are linked to a patient's symptoms and complaints. For example, LORETA raw current source density values for each of the 2,394 gray matter voxels was computed for the 678 individuals in the University of Maryland EEG normative database in the eyes open and eyes closed conditions. Means and standard deviations for groups of

subjects separated by 6 months were computed from subjects at 2 months of age to 82 years of age (Thatcher, 2000; Thatcher et al, 2003; 2005). Figure 2 shows an example of significantly deviant LORETA Z scores in a patient with right parietal epidural hematoma linked to the patient's symptoms of spatial neglect.

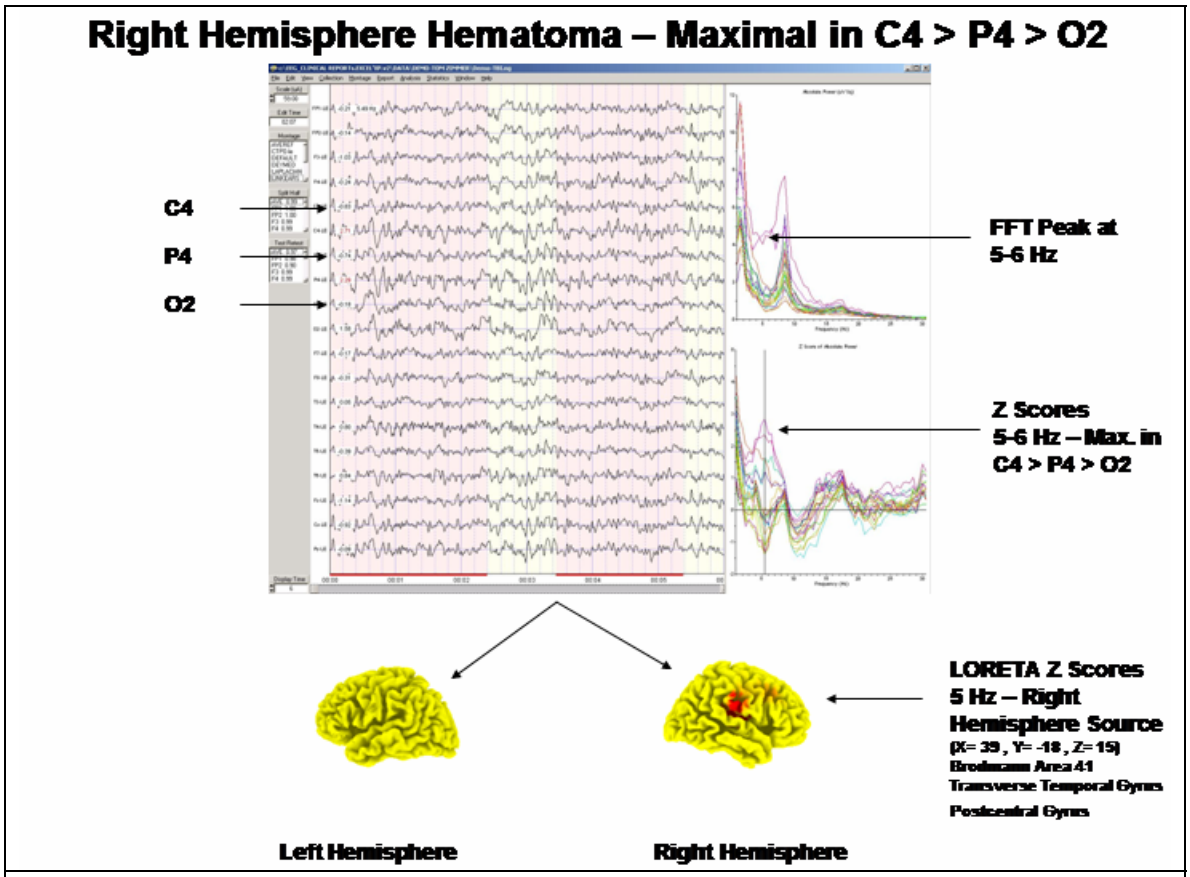

Fig. 2 – Example of deviant LORETA Z scores in a right hemisphere damaged patient. The patient's symptoms included spatial neglect (from Thatcher et al, 2005).

Symptom Check List and LORETA Z Score Biofeedback

Because of computational demands a reduction is necessary in the total possible computations at each instant of time. A reasonable method is to reduce the number of measures by the use of the scientific literature linking symptoms to functional specialization in the brain based on the fMRI, SPECT, PET and EEG/MEG literature. For example, lesions of the occipital cortex (Brodmann areas 17-19) produces blindness, lesions of the temporal lobes (Brodmann areas 20, 21, 38) effect auditory perception, lesions of the hippocampus effect memory (Brodmann area 30), lesions of the left frontal lobe effect speech articulation (Brodmann areas 10, 45, 46), etc. Thus, the total number of EEG measures involved in real-time Z score biofeedback can be reduced by forming apriori hypotheses based on the existing scientific literature. For example, a patient with a history of dyslexia is expected to exhibit deviations in the left parietal lobe based on cytological, MRI, fMRI and EEG/MEG studies. Or a patient with auditory sequencing problems produces the apriori hypothesis of temporal lobe dysfunction, or short-term memory problems with hippocampal, temporal or frontal dysfunction, etc.

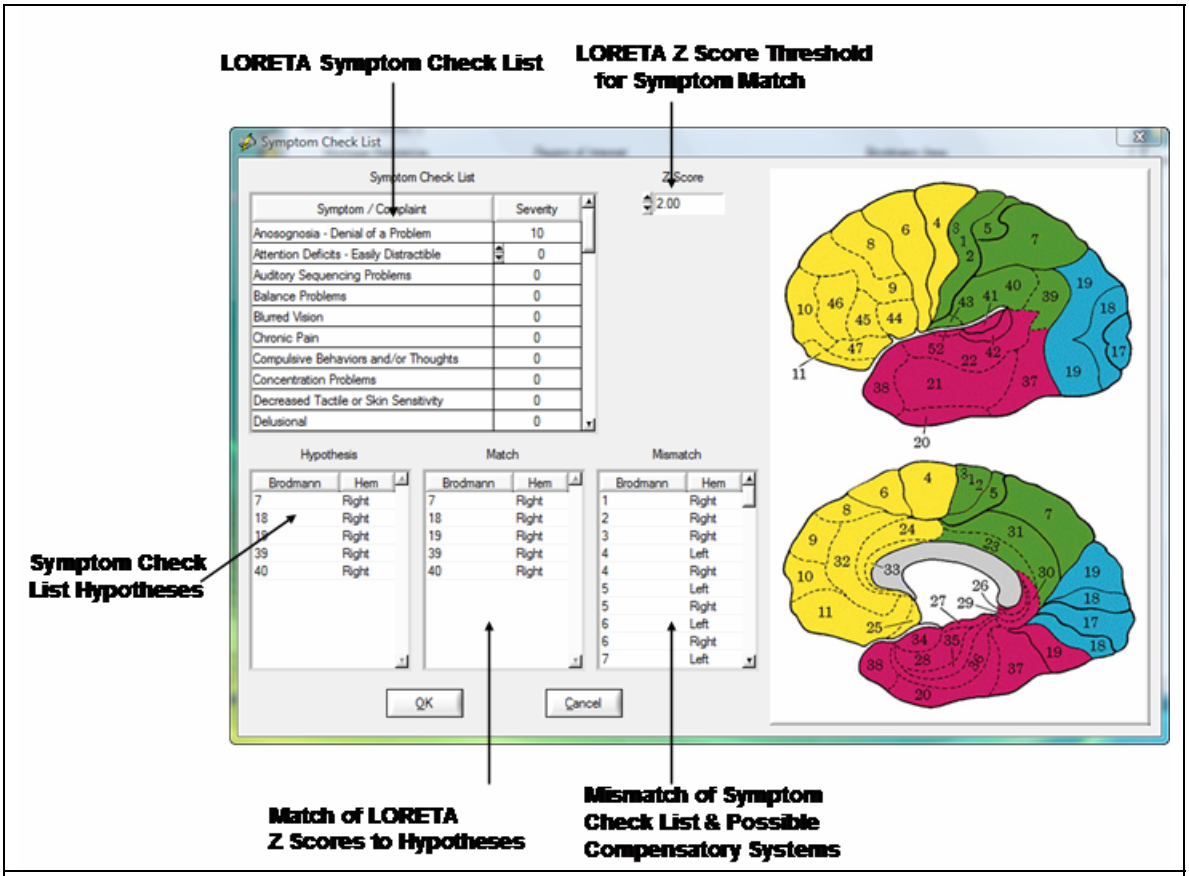

Fig. 3- Example of Symptom Check List to create anatomical hypotheses linked to the patient's symptoms and complaints. The match category is hypothesized as the "weak systems" and the mismatch category are hypothesized to be "compensatory" networks. From NeuroGuide 2.6.4

Thus, planned comparison statistics can be used to individualize LORETA Z score biofeedback of the brain regions (i.e., Brodmann areas) that are hypothesized to be related to the patient's symptoms and complaints prior to training. The LORETA Z scores in the locations of the brain predicted by the symptom checklist are labeled as 'Matches' of the weak systems and the 'Mismatches' are more likely related to compensatory systems. The idea is to identify the most likely brain regions linked to the patient's symptoms vs the least likely brain regions as an initial step toward restoring homeostatic balance within the "weak" nodes and modules of the networks of the brain. The goal is to reinforce movements of consistently deviant brain systems linked to the patient's symptoms toward Z = 0, i.e., reinforce trends that shape behavior as in operant conditioning. Z = 0 is an abstract ideal and is never actually attained for all measures but operates like a set-point around which variations occur. The grand average of healthy normal subjects is a homeostatic average at each moment of time that serves as a reference to help identify high standard deviations in localized brain regions linked to the patient's symptoms.

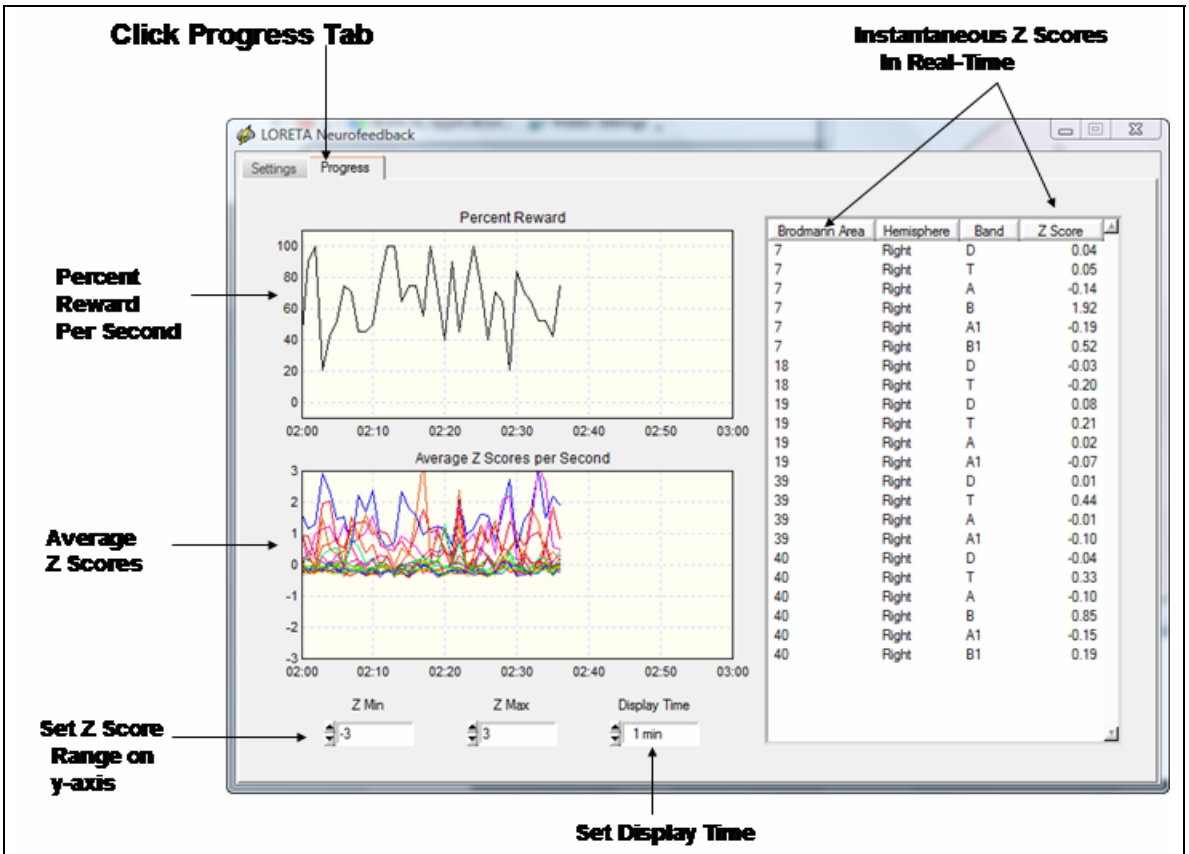

Fig. 4 – Example of LORETA Z Score Biofeedback Progress Chart. The top left are the percent of time that threshold has been met, bottom left are the average Z scores from different Brodmann areas. The right column are real-time Z scores from Brodmann areas selected by the symptom check list. From NeuroGuide 2.6.4

Another advantage of LORETA Z score biofeedback is the issue of co-morbidities that are often present in patients, for example, attention deficit disorder and anxiety. The advantage of linking symptoms to functional specialization in the brain produces hypotheses with common brain regions involved in both an attention disorder and anxiety. For example, attention is mediated by the hippocampus for the creation of memories; the insula and anterior cingulate for attention shift and the bilateral frontal lobes for executive control. Failure of this system may in part be due to insular cortex deregulation which is also involved in anxiety disorders and/or obsessive compulsive disorders. Depression is another disorder that involves the anterior cingulate gyrus and the frontal lobes (Pizzagalli et al, 2002), etc. Thus, a symptom check list linked to neuroanatomy thereby provides deep and underlying hypotheses that can be used for purposes of biofeedback using the QEEG in the same manner as fMRI biofeedback but at a fraction of the cost.

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