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LORETA: An Attempt at a Simple Answer to a Complex Controversy

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LORETA: An Attempt at a Simple Answer to a Complex Controversy

Daniel A. Hoffman, MD

ABSTRACT. QEEG and LORETA have been applied successfully to neuropsychiatric conditions for both diagnosis and treatment guidance using EEG neurotherapy. These techniques aid in providing localization of the sources of normal and abnormal EEG. However, there is confusion about which statistics offer the more accurate data for source density localization. The average clinician is not able to assess the differences in the two most popular data processing programs currently on the market. This paper compares a side-by-side evaluation of NeuroGuide™ and EureKa™ in order to help the reader visualize the differences between these two imaging programs, which have resulted in different maps. This study compares and contrasts both software programs using pathologies with confirmed spatial localization to assess and evaluate their differences and to understand how to use each program to obtain accurate information. doi:10.1300/J184v10n01_05

KEYWORDS. QEEG, LORETA, localization, EEG, NeuroGuide™, EureKa™, neurofeedback, neurotherapy

BACKGROUND

The neurofeedback community is made up of clinicians from various disciplines, the majority of which have not been schooled in the rigors of advanced statistics and mathematics. Nor should it be necessary to know all the sophisticated details as long as the technique is

clinically useful and valid. As a clinician, it is heartening to know that the quantitative electroencephalogram (QEEG) advancement of Low Resolution Brain Electromagnetic Tomography (LORETA) has been successfully applied to neurotherapy and appears to provide localization of the sources of normal and abnormal EEG. Over 138 peer reviewed journal arti-

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Dr. Hoffman expresses his gratitude and appreciation to both Leslie Sherlin of EureKa™ and Robert Thatcher of NeuroGuide™. They were open, encouraging, and helpful in providing guidance and data in this quest for the “Holy LORETA.” Both were interested in the truth and both were hoping, above all else, that there would be no differences.

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cles mark LORETA as well established in the scientific literature. The majority of these studies address clinical issues relevant to the neurofeedback community.

However, this innovation has also brought confusion about which statistics offer the more accurate data for source density localization seen in the LORETA-Key Institute's LORETA Viewer. Extremely bright scientists from around the world extol the rationale behind the different use of statistics in various databases. The ability of the average clinician to accurately assess each argument escapes all but the highly mathematically educated. Even in the hallways of the International Society for Neuronal Regulation (ISNR) conferences, attendees contest the virtues of parametric vs. non-parametric statistics.

LORETA is no different from other sophisticated scientific technology in that most clinicians merely want to know how to use it. Like driving a car, they don't need to know how to build the engine. They want to use it to transport them to where they need to be. When processing data, they want to know that it is correct so that their treatment decisions will lead to accurate neurofeedback and patient improvement. They do not want to be wondering if the data is accurate, or the software program is bug free. They don't want to be concerned about mathematical details. They simply want to know how best to apply this technology clinically.

Fortunately, there are two software programs, NeuroGuide™ (St. Petersburg, Florida; www.appliedneuroscience.com) and EureKa™ (Knoxville, Tennessee; www.novatecheeg.com) which make the application of LORETA available to the ISNR community. A side-by-side evaluation of the two major programs for LORETA analysis may help the reader visualize what they might expect when using the two major LORETA imaging programs. The need to pursue this goal became evident when a problem was discovered when data was processed through the two software programs which ended up with different maps. Therefore, the purpose of this study is to compare and contrast the two LORETA software programs using pa-

thologies with confirmed spatial localization to assess and evaluate the NeuroGuide™ and EureKa™ programs and to understand how to use the programs so as to obtain accurate information.

METHOD

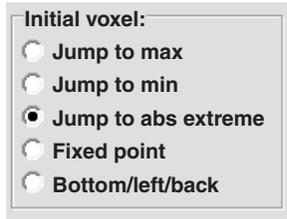
In order to accomplish this analysis, data was procured with confirmed, verifiable pathology, and focused on the question of localization accuracy. Patient A had a right parietal epidural hematoma seen on CT-Scan. Patient B had left temporal epilepsy seen on PET, structural MRI, fMRI, and 128-channel EEG. Data were collected on a Lexicor NRS-24 with the high pass filter off and at a sample rate of 128 Hz.

The data were the same for all reports. It was unartifactual so as not to add any bias, since clinicians span the gamut of artifact ability. The lowest common denominator was chosen. This method was also justified by knowing that the lesions were significant enough that they should still show up regardless of the quality of the data.

The .dat data file was then run through NeuroGuide™ and EureKa™ to visualize the cross-spectral, non-database compared LORETA. EureKa's™ FFT settings in the "Control" menu were set to "Time Domain Tapering = None," "Frequency Domain Smoothing = None" and "Overlapping FFT Windows Advancement Factor I = 32." The LORETA Viewer was set to "Jump to abs extreme" (Figure 1). Theoretically, there should be no difference. However, there was a disparity due to the defaults of each program. NeuroGuide™ uses Absolute images while EureKa™ displays Relative images. In addition, the programs compute FFTs and windowing differently. NeuroGuide™ uses two second epochs of digital EEG data with 75% overlap between successive two second windows. EureKa™ uses an overlapping FFT advancement of 32 samples. However, this had no apparent effect.

For the analysis using the different databases, adjustments and assumptions had to be made. Patient A (Figure 3) was actually 55

FIGURE 1. LORETA'S Initial Voxel Setting



years old and Patient B (Figure 7) was 11 years old. Due to the fact EureKa™ doesn't currently have these ages in their database, all data was run at age 25 for a similar comparison. Another difference was in the bandwidths. NeuroGuide™ was able to process in single hertz bins, while the EureKa™ preset bandwidths used were delta, theta, alpha, and beta, based on the settings in their program. Therefore, the NeuroGuide™ data was run at 3 Hz, 6 Hz, 10 Hz, and 16 Hz which were in the middle of the EureKa™ bands (Figures 4, 5, 8 and 9).

For purposes of this paper, the comparisons to the databases were both run at Absolute Power. However, to address another debate in our field for neurofeedback guidance, EureKa™ was also run in Relative Power (both raw and database comparison) for the reader to assess the differences in localization accuracy (Figures 6 & 10).

While NeuroGuide™ has the ability to run the data as Linked Ear or Average reference, the

data was run as Average reference in order to more closely approximate EureKa™. The LORETA "ScaleWin" linearity settings (Figure 2) were allowed to be moved to 100 while the "Change Max" (Figure 2) settings were kept at their default levels, except when a database value score was below the significance level. In that case it was moved to 1.65 for NeuroGuide™ or 1.0 for EureKa™ to equate with a $p < .05$ value. Statistical significance in Patient B's EEG recording is in the lower frequencies, so it is important to note not only the voxel localization, but whether it is of statistical significance. Therefore, you wouldn't expect to see localization in alpha or beta. This is a similar issue the QEEG field has faced over time regarding the meaning of color changes in topographic brain maps. The color shifts mean nothing clinically if they are not of statistical significance.

FIGURE 2. LORETA's ScaleWin Settings



RESULTS

Patient A—Right Epidural

FIGURE 3. Topographic Map of Patient A

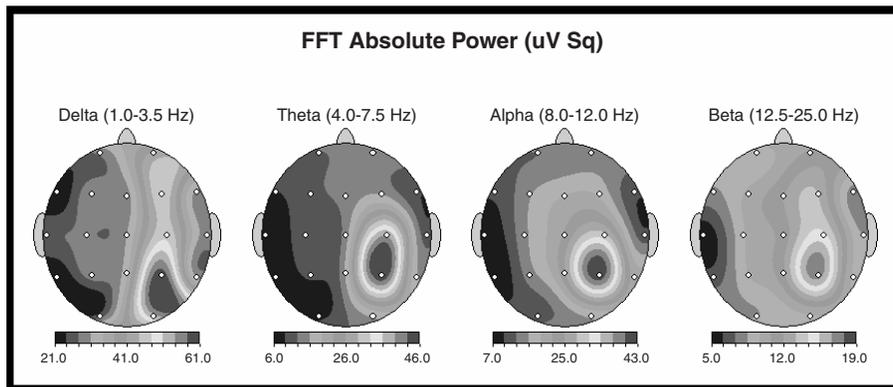
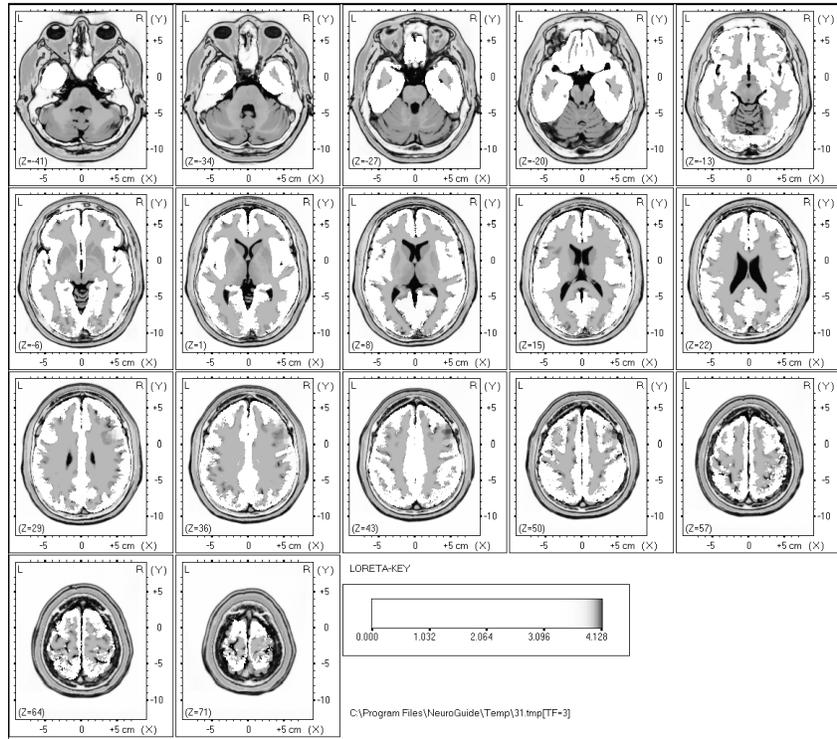
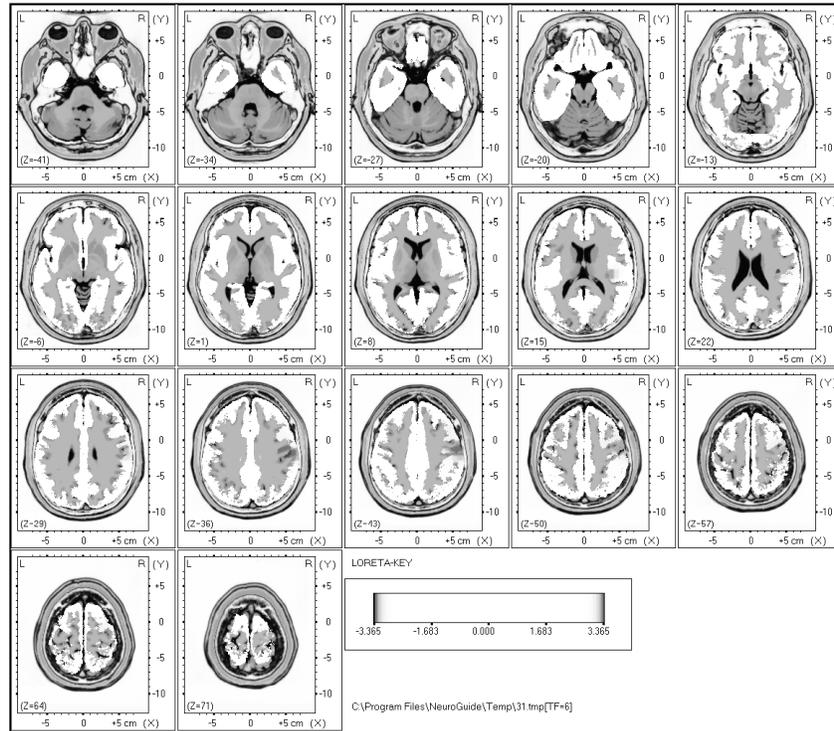


FIGURE 4. Patient A, NeuroGuide™ Database

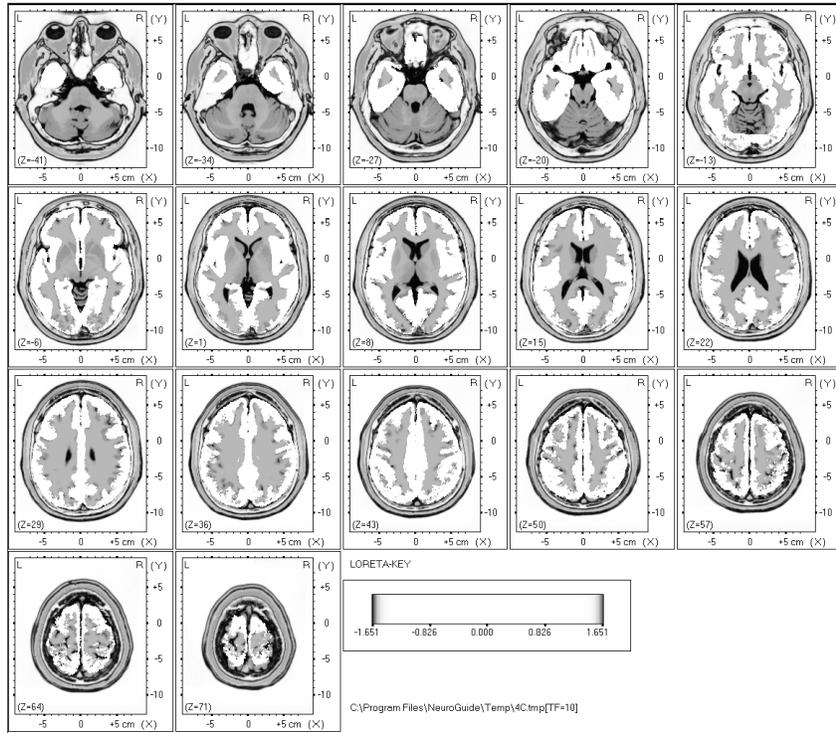
3 HZ



6 HZ



10 HZ



16 HZ

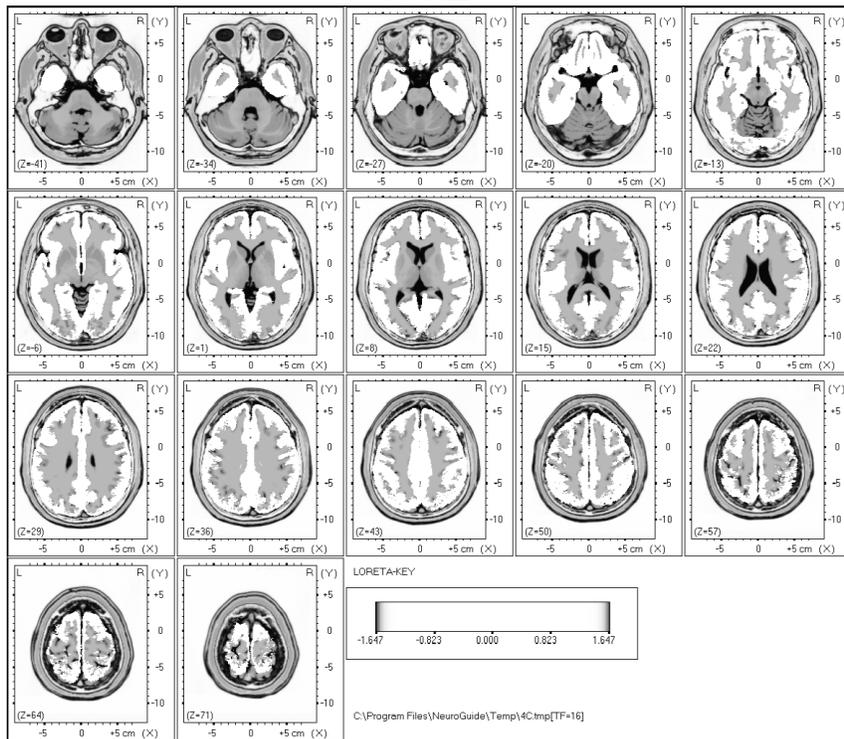
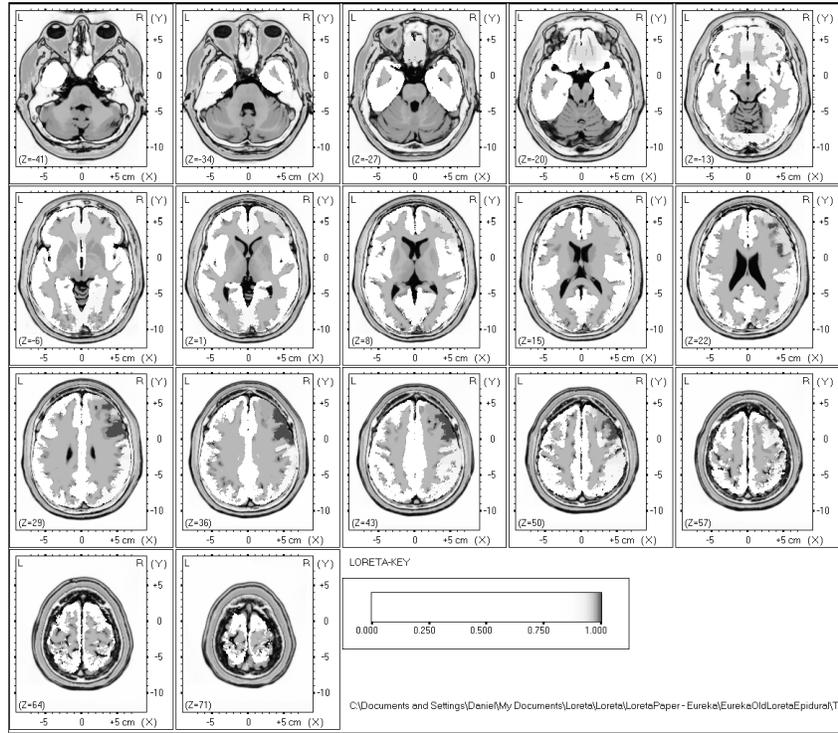
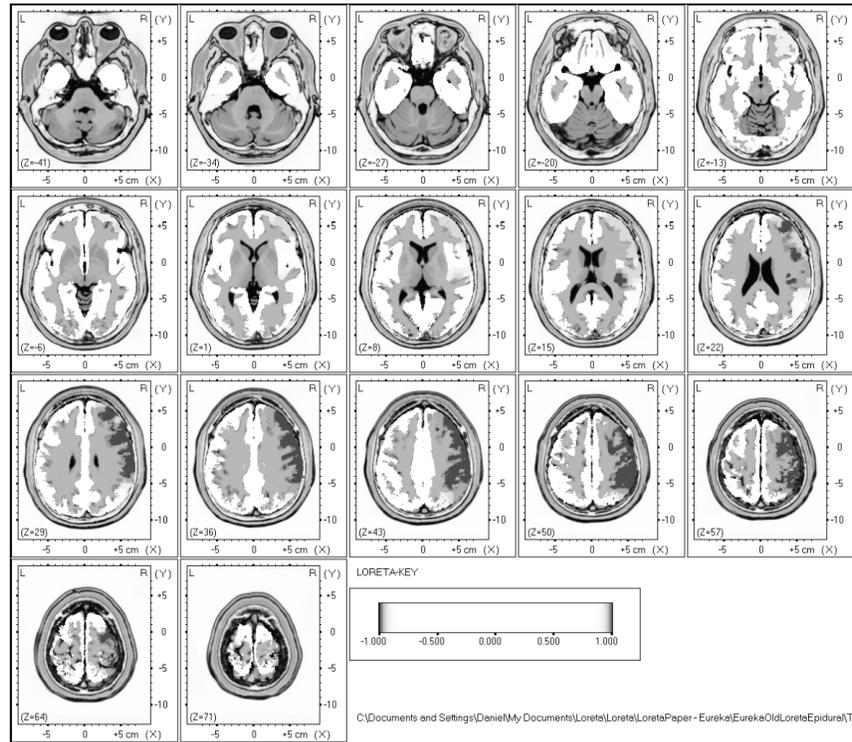


FIGURE 5. Patient A, EureKa™ Database (Absolute Power)

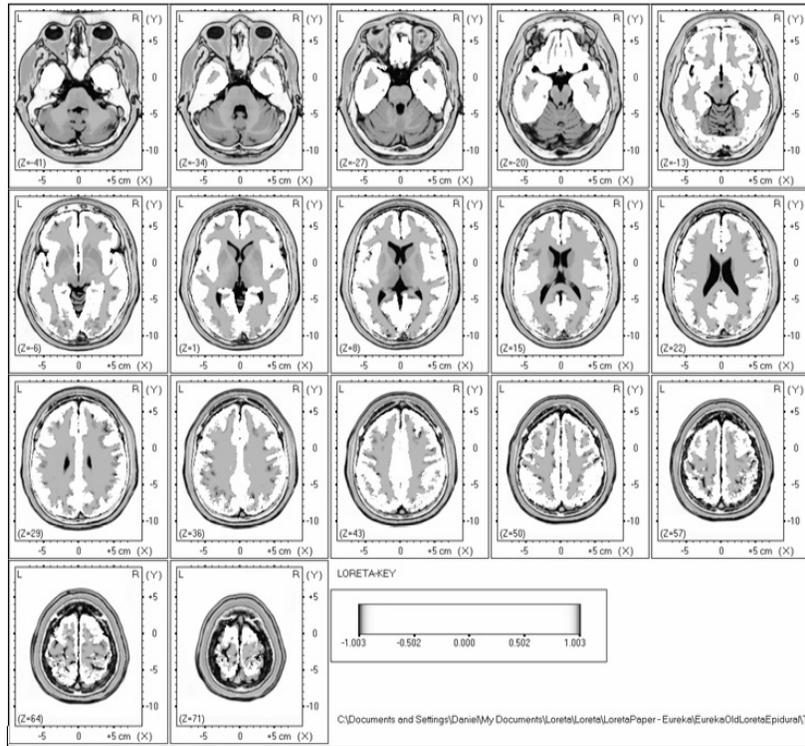
Delta



Theta



Alpha



Beta

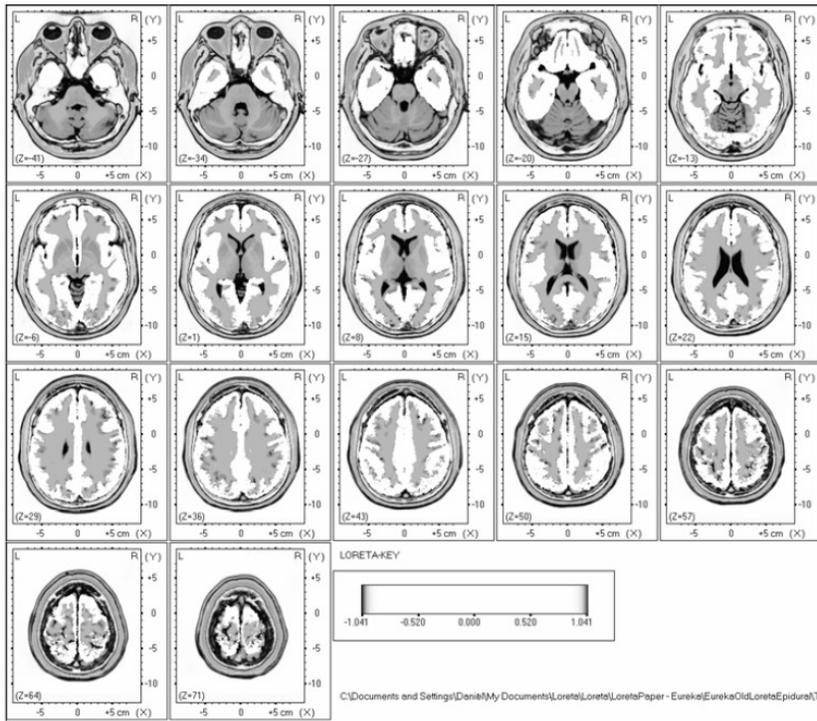


FIGURE 6. Patient A, Eureka™, Relative Power

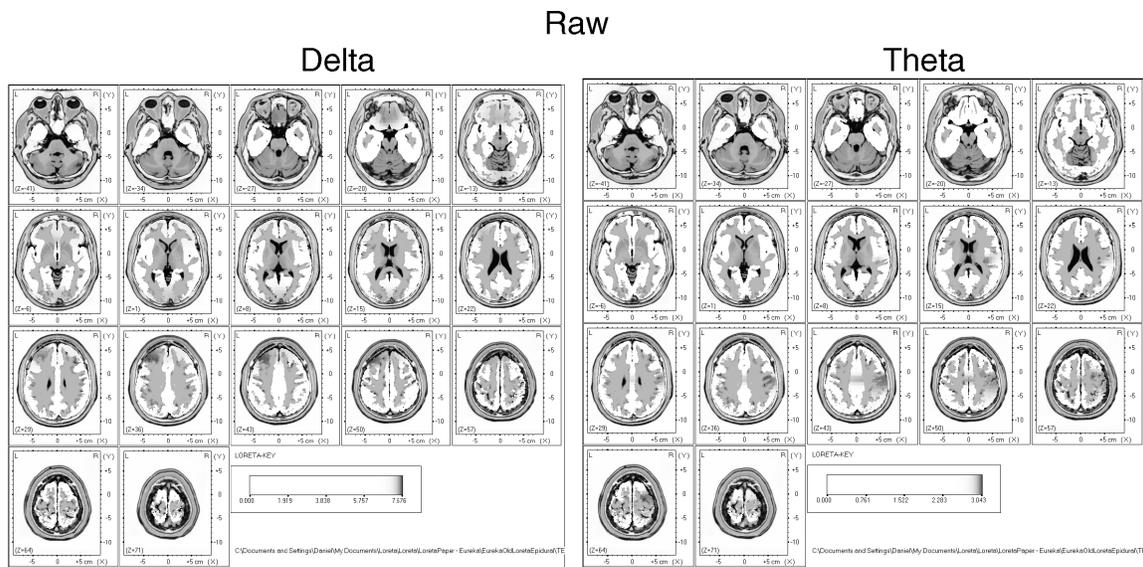
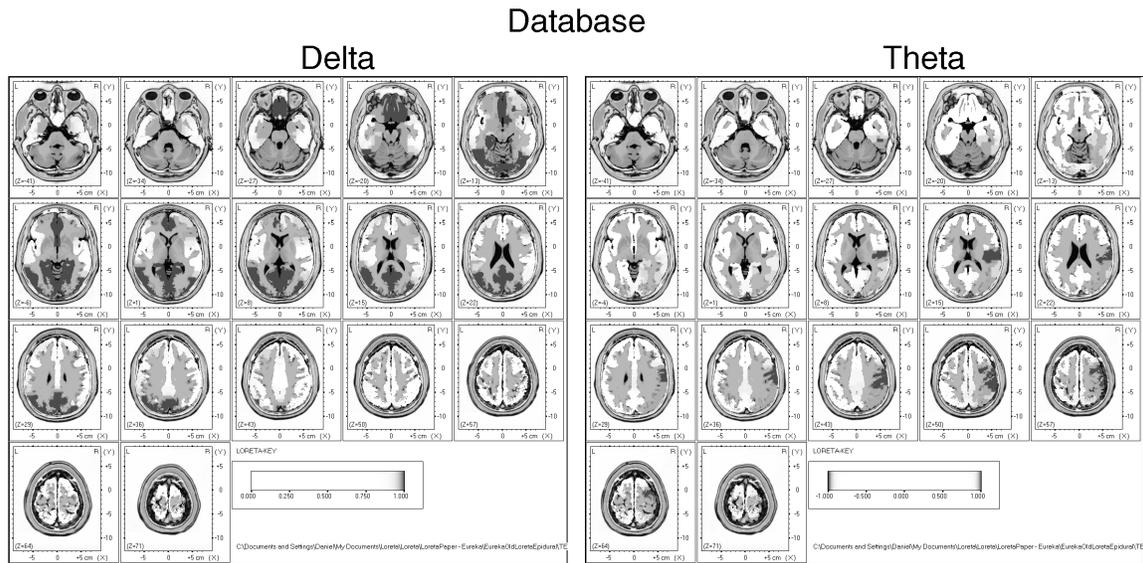


FIGURE 7. Topographic Map of Patient B

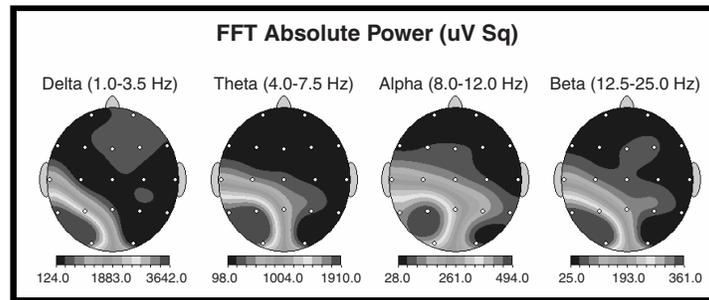
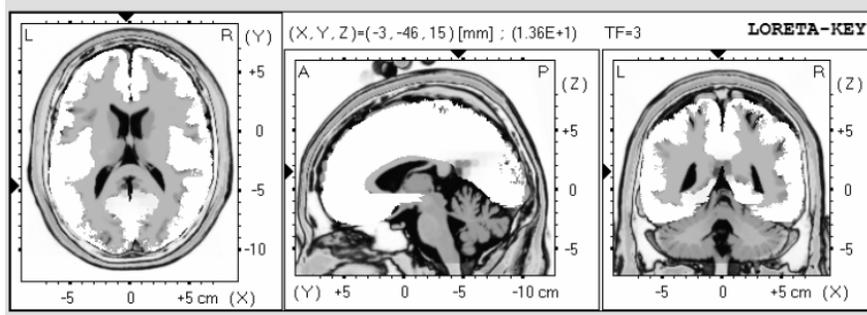
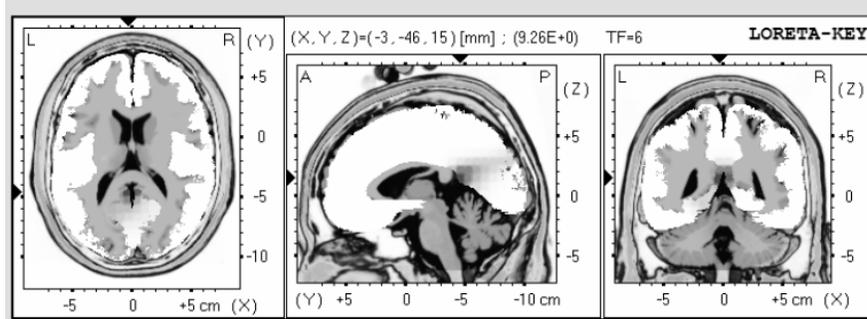


FIGURE 8. Patient B, NeuroGuide™ Database

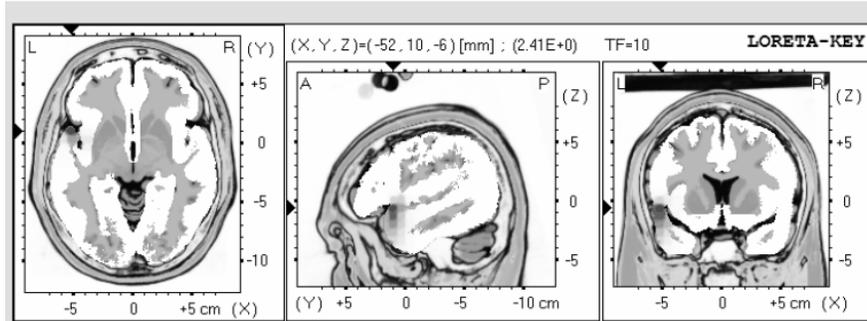
3 HZ



6 HZ



10 HZ



16 HZ

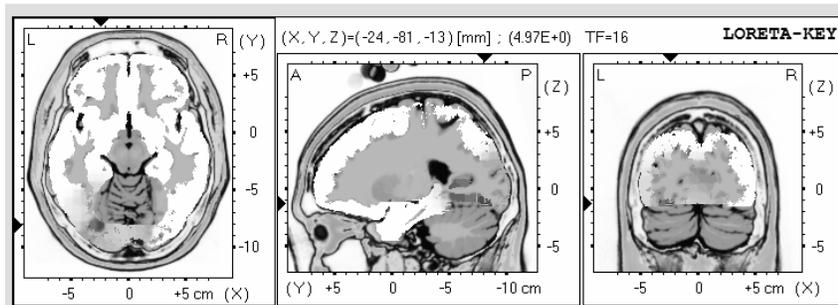
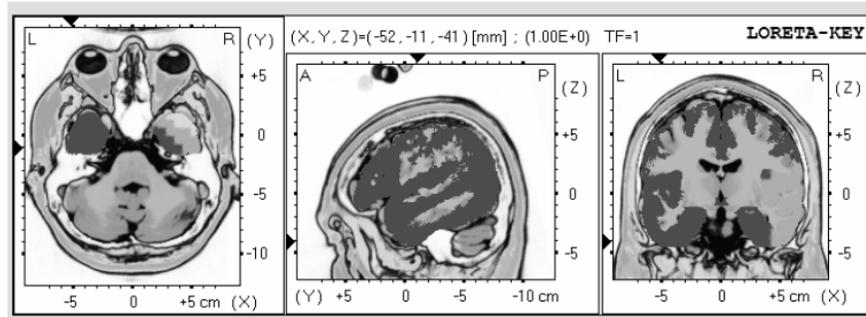
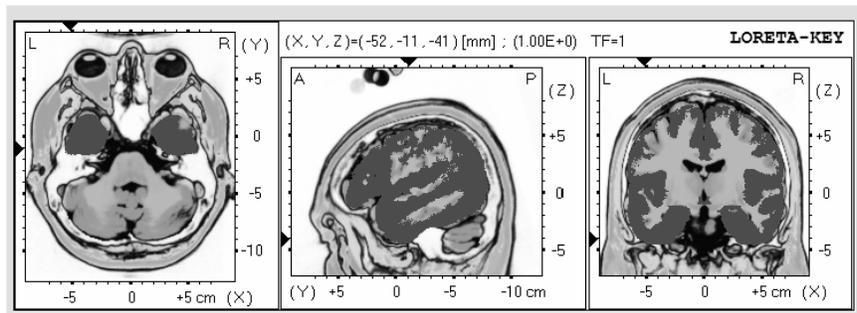


FIGURE 9. Patient B, EureKa™ Database (Absolute Power)

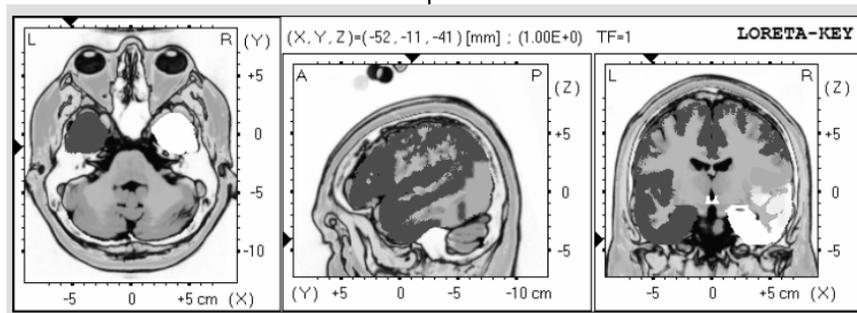
Delta



Theta



Alpha



Beta

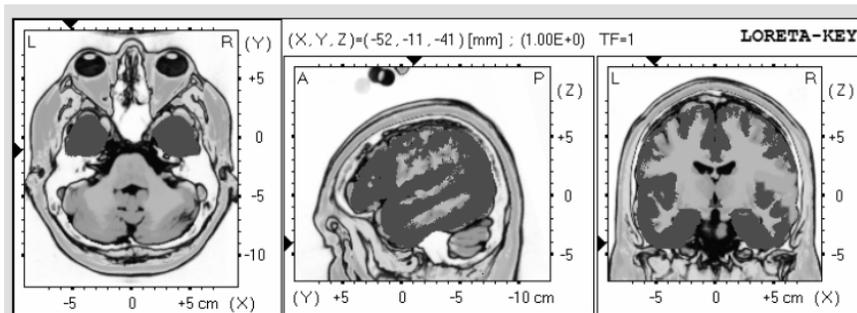
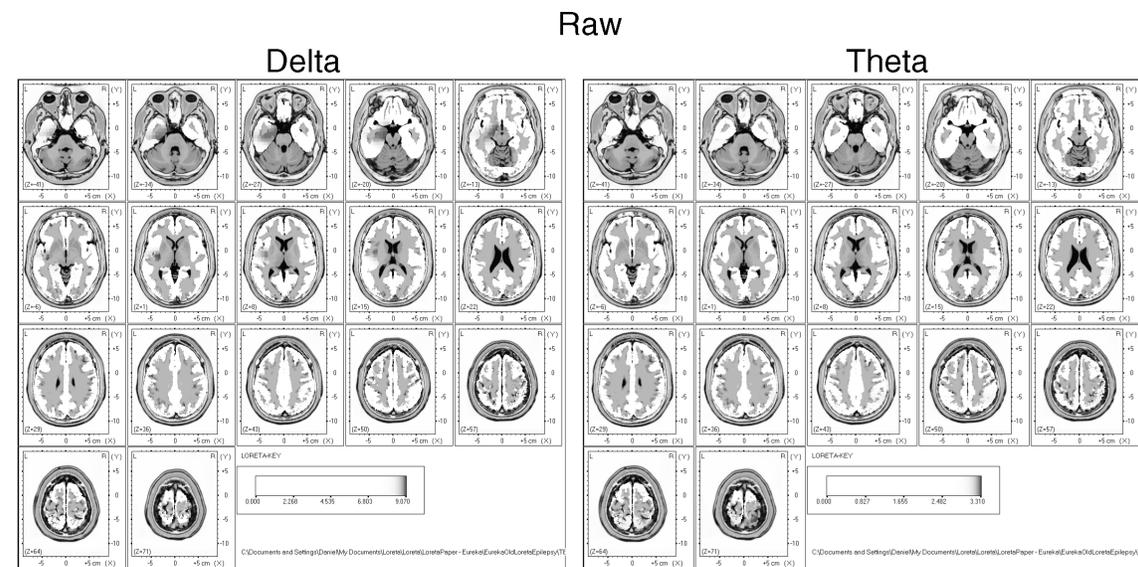
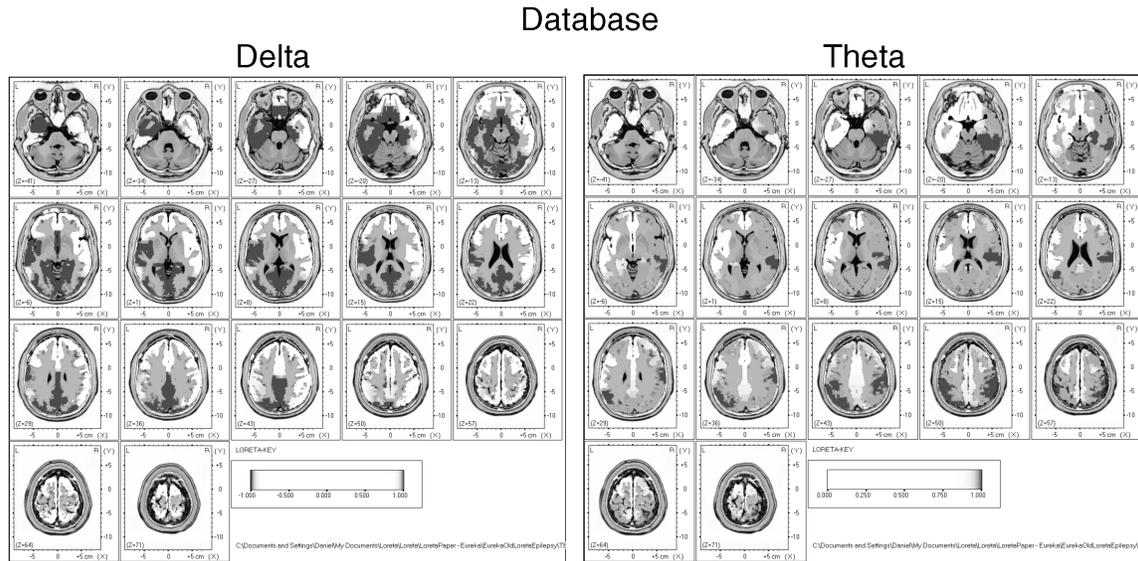


FIGURE 10. Patient B, Eureka™ Database (Relative Power)



Patient B—Left Epilepsy

CONCLUSION

The primary purpose of this paper was to take two cases with known pathology and see how each program localized the lesion. While extensive discussions on the rationale for the use of different statistics can be found elsewhere (see reference list), from a clinical viewpoint, the goal was merely for the reader to see

differences in order to know what the different programs output was producing when generating data and to identify settings and assumptions that might account for data errors.

Parametric vs. Non-Parametric Statistics

NeuroGuide™ uses parametric statistics while Eureka™ uses non-parametric statistics. However, a different statistical method for the database comparisons does not appear to be critical because there was little difference be-

tween the two methods in the case of the epidural Patient A. A survey of the literature shows that both statistical methods are commonly used and there is one LORETA study in which parametric versus non-parametric statistics were actually compared with both being found valid.

The difference in Patient B's localization probably has to do with scaling. Since NeuroGuide™ uses parametric statistics, the standard deviation or Z-scores can be set by the user in the "ChangeMax" slider located in the LORETA "ScaleWin" setting (Figure 2). This allows the user to find the voxels with maximum positive or negative standard deviations when compared to the database and view it to accommodate the best clinical use.

EureKa™ works differently. By using non-parametric statistics, a p value is utilized. Once a significance is made (p of .95 or higher) it determines that there is a 100% statistical difference from the database—like a YES/NO response. Apparently, it will not separate between two voxels that are both significantly different from the database. In other words, there is no scaling. In Patient B, since the voltage amplitude was so high, many voxels significantly deviated from the database and thus the all "red" image (Figure 9). It appears that non-parametric statistics, at least as currently displayed in EureKa™, show that the voxel either is or isn't significant.

Therefore, while both NeuroGuide™ and EureKa™ are accurate, in this case, the output is more specific in NeuroGuide™ since the viewer can be set to maximize the degree of localization.

Database Differences

The two programs were accurate in localizing Patient A's right hemisphere epidural pathology (Figures 4 & 5). Clinical treatment decisions would not be different from the data obtained from either program. Where the surface EEG demonstrated a clinically significant deviation, both LORETA's visualized it accordingly. Likewise, when the scaling was set for statistical significance, the lesion was not seen in those frequencies where the surface EEG did not show it. This, again, underscores the importance of knowing that each program's scaling

for the "Max" slider under the "ScaleWin" option is different (Figure 2). NeuroGuide's™ is in Z scores and EureKa's™ is set in p values.

Patient B, the one with the left temporal epilepsy, was difficult for EureKa™ to localize (Figures 8 & 9). Almost all the voxels were colored red, no matter how I set the "Linearity" or "Max" sliders (Figure 2). The reason for this is discussed above under the Parametric versus Non-Parametric section.

Addressing the concern about the age of the patient as it relates to the age the data was processed through the database, the literature does not suggest that an 11-year-old has much higher amplitude than an adult and therefore the database need not distort it to such a degree. NeuroGuide™ was able to localize it, even though the database was set to 25 years old as well. (Appendix A shows the more accurate localization when the correct age is used in the NeuroGuide™ analysis.)

One methodological criticism is the comparison of the EureKa™ bandwidths to the NeuroGuide™ single 1 Hz bands. Does, for example, 6 Hz actually represent the same as a band of 4 to 8 Hz? The single hertz might miss (or oppositely, overemphasize) brain activity while a 4 to 8 band might dilute (or likewise, overstate) pathology, depending upon the actual frequency source of the lesion. Would it, therefore, be a fair representation? To remedy this, for Patient B, a frequency band was created by using Excel to average the NeuroGuide™ 1 Hz Z-scores .lor file from 4 to 8 Hz and saved as a .lor file. At the age bracket of 25, it looked like the 6 Hz band as seen in this paper above and at the correct age, it showed excellent localization. Using broad bands or 1 Hz bands made no appreciable difference in NeuroGuide™ and therefore was not relevant in this case.

Absolute versus Relative

Since there is much discussion in the neurofeedback community about the value of Absolute versus Relative Power, and the fact that the developers of the software have different technical preferences (as well as the fact that NeuroGuide™ only calculates in Absolute Power) the addition of EureKa's™ Relative Power maps were included—both from the raw and database comparison statistics (Figures 6 & 10). This can be used by the reader to not only

compare the relative raw with the database, but to compare both relative raws with either the EureKa™ or NeuroGuide™ absolutes.

s-LORETA

While I also had the opportunity to make these same comparisons using the new *s-LORETA*, I did not include them in this paper as the differences were visually unnoticeable in these cases.

SUMMARY

The LORETA literature is filled with publications demonstrating excellent localization, validation and clinical utility. The concern that instigated this paper was the discrepancies between the applications of the two available software programs for clinicians. The following are the conclusions drawn from these comparisons:

1. LORETA is a well established clinical tool that continues to grow and add value for the neurotherapist.
2. Based on these cases, the best agreement between the software programs is in absolute power and while some relative power maps localize well, it should not be solely relied upon. The option of also viewing relative power in NeuroGuide™ just for the sake of completeness as well as the ability to view data with all options is recommended. The use of relative power should be viewed with caution and, as this paper demonstrated, it failed to localize as well as the absolute power maps. Nevertheless, there are times when absolute power may need to be augmented, such as with metal plates, staples or screws in the scalp or, as in Patient B, where absolute power doesn't distinguish between the statistically significant voxels.
3. Using correct age matching localizes better. A more complete age group in the EureKa™ database would be valuable.
4. Specificity of the frequency may make a difference, depending upon how focal a lesion is. This is seen in the 1 Hz bins of topographic brain maps. It would be helpful to see EureKa™ develop the abil-

ity to show LORETA in 1 Hz bands and likewise, to see NeuroGuide™ provide greater ability to create bandwidths.

5. Both parametric and non-parametric statistics are valid. This is demonstrated in the literature and specifically in the case of Patient A where both programs, using different statistical methods, localized equally well. The differences in Patient B reflect the lack of scaling or rank of the deviations from the use of non-parametric statistics.
6. It would be unifying to see the debates in our field turn into constructive advancements, since the divisiveness causes confusion and distraction from important clinical evidence, resulting in a lack of confidence.
7. Despite the rhetoric of a clinician's favorite program, knowing how to use the program along with what it can or cannot visualize is of significant importance. Becoming more educated about what each program does and how it does it (such as Max scaling units or that raw data is displayed in Absolute images in NeuroGuide™ and Relative images in EureKa™), can make all the difference in whether something is clinically accurate or not. A "Primer" or "Quick Start" mini-manual from each of the developers giving very basic information on how to set the LORETA options, what purpose each setting offers and the definitions and significance of scaling units, for example, would make for more consistent and reliable data and treatment options. This, in fact, was partially responsible for the conflicting data output obtained when others ran a patient's QEEG through the two programs, and which was ultimately responsible for the writing of this paper. While much of this can be found in the electronic Help sections, it is buried within technical portions that make it difficult for the average clinician to differentiate. This coupled with the fact that most people never read manuals (a fault more of the clinicians than the software developers), causes errors in data processing that could be easily mitigated. This level of complexity should not have

to be researched and learned by every clinician wanting to use LORETA, yet without understanding the basics, “garbage in, garbage out.” Without this understanding, it is difficult to make use of the two available programs’ differences, yet these questions have been asked, literally for years. It should be distressing to all of us that therapeutic decisions may be made by many based on not understanding some basic fundamentals and suggests that those using LORETA should take courses from the developers where the significance of these settings are well understood. Likewise, it is incumbent upon the instructors of these courses that the attendees clearly understand the differentiations contained in the programs.

8. Finally, demonstrating more cross-validation, publications on the issues discussed above and FDA regulations are all elements that would enhance LORETA and benefit the entire field. To date, NeuroGuide™ has received a FDA registration.

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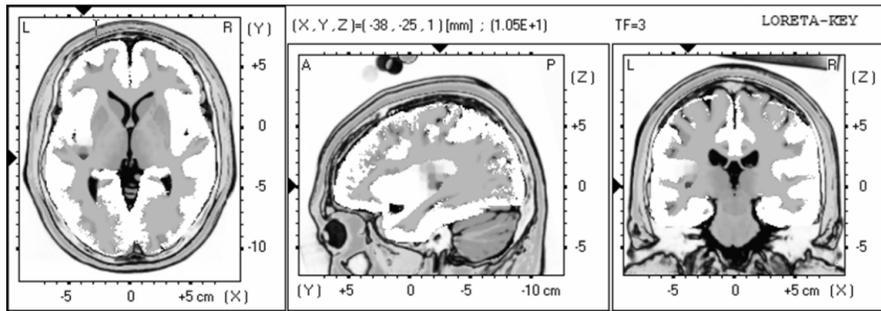
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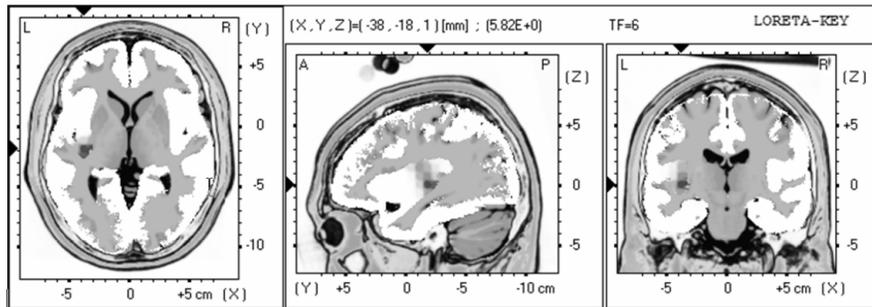
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APPENDIX A. NeuroGuide™–Database Patient B Age = 11

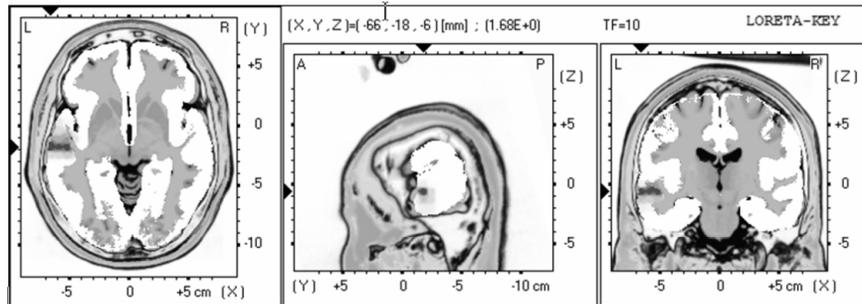
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