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Clin EEG Neurosci 2012 43: 48
DOI: 10.1177/1550059411428716

The online version of this article can be found at:
http://eeg.sagepub.com/content/43/1/48
The Quantitative Electroencephalogram and the Low-Resolution Electrical Tomographic Analysis in Posttraumatic Stress Disorder

Doran Todder¹, Joseph Levine¹, Ahmad Abujumah¹, Michael Mater¹, Hagit Cohen¹, and Zeev Kaplan¹

Abstract
The electroencephalogram (EEG) is the recording of the brain electrical activity as measured on the scalp. Using mathematical algorithms, the 3-dimensional (3D) distribution of the electrical potential inside the brain can be calculated. One of the methods to calculate it is the low-resolution electrical tomographic analysis (LORETA). In this research, we seek to find the brain structures that differentiate patients with posttraumatic stress disorder (PTSD) from controls. Ten right-handed consenting adult male patients were recruited from a PTSD clinic. All patients fulfilled Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition, Text Revision [DSM-IV-TR]) criteria for chronic PTSD (duration >2 years.) and were on drug treatment regimens that had been stable for at least 2 months (involving only serotonin reuptake inhibitors [SSRIs] and benzodiazepines). The control group consisted of 10 healthy hospital staff members. All study participants underwent 19 channel EEG measurements according to current standards of practice. All artifact-free EEG strips were examined for spectral as well as LORETA analysis focusing on the theta (4-7 Hz) band which is suggested to reflect the activity of the limbic system. The theta band showed a statistically significant difference (P < .05) between the 2 groups in the right temporal lobe and in both the right and left frontal lobes. Our findings support existing research data obtained via other imaging technologies, which demonstrated structural alterations in the right temporal and frontal areas in PTSD. These results indicate that combining quantitative EEG (QEEG) and the LORETA method, among other methods, may improve the neuroanatomical resolution of EEG data analysis.

Keywords
electroencephalography, low-resolution electrical tomographic analysis, posttraumatic stress disorder

Received August 10, 2010; accepted June 6, 2011.

Introduction
PTSD affects about 9% of the general population and is clinically defined by the causal exposure to a significantly stressful experience arousing a certain pattern of response and resulting in a specified number of symptoms of intrusive re-experiencing numbed emotions and avoidance of stimuli, and of hyperarousal, present for at least 1 month after the event. The disorder is often chronic and extremely incapacitating, with long lasting psychological and physiological changes. However, whereas almost all of those exposed to the causal events initially display an acute stress response, the majority do not go on to develop the full-blown chronic clinical syndrome and apparently cope and readjust adequately. Improved means for characterizing the distinctions between patients with PTSD and other populations might reveal possible means for early identification of higher-risk participants and enable the development of more effective methods of primary and secondary prevention.

PTSD has been the subject of numerous studies examining the underlying functional neuroanatomy of the clinical symptoms, generally by means of functional magnetic resonance imaging (fMRI). Most studies have focused on the response to trauma-related versus other stimuli/challenges. Procedures such as the fMRI are costly and complex to perform and have relatively poor time resolution. The EEG on the other

¹ Ben Gurion University, Faculty of Health, Beer Sheva, Israel

Corresponding Author:
Doron Todder, Beer Sheva Mental Health Centre, Hazzadik Miroshlim, Beer Sheva, Israel 84170
Email: dtoder@netvision.net.il
hand offers a potentially valuable complementary source of information for researchers and clinicians, since it assesses real-time electrical activity in the brain and is overall a less costly, time-consuming, and complex procedure. The raw EEG data can be analyzed by direct visual inspection or by computerized quantitative EEG analysis (QEEG). The QEEG is superior to the raw EEG analysis due to its larger reliability and validity.

A small number of studies have explored QEEG patterns in patients with PTSD and have elicited conflicting results. Begic et al. compared 18 unmedicated PTSD veterans to 20 control participants. They found that the patients with PTSD have both an increased theta power over central brain regions, as well as increased beta activity over frontal, central, and occipital brain regions. No significant differences between the groups were noted for delta and alpha activity. In another study, the same group compared veterans with PTSD to veterans without PTSD. Patients with PTSD displayed predominantly decreased alpha and increased beta power over frontal, central, and temporal areas. No difference was noted for the theta rhythm between these groups. Rabe et al. studied the hemispheric asymmetries among 4 groups. Three of the groups were unmedicated motor vehicle survivors: Full-blown PTSD; subsyndromal PTSD; no PTSD. The participants of the fourth group were healthy controls. No difference was noted between the groups for EEG alpha activity at rest.

Metzger et al. measured the alpha symmetry in a group of female veterans with and without current PTSD. They found some correlation between arousal symptoms and higher alpha activity of the right compared to the left parietal lobe. Finally, Shankman et al. compared the resting EEG of patients with PTSD to highly selected control participants with no history of reported trauma. No statistically significant difference was noted on any of the spectral bands between the groups.

Thus, the existing literature describing QEEG in patients with PTSD shows no consistent trend in findings. With regard to the theta band, although one report suggested that patients with PTSD at rest may demonstrate increased theta activity over central brain regions, another study failed to find such differences.

One of the possible mathematical transformations of EEG data is the low-resolution electrical tomographic analysis (LORETA, see9,10). LORETA uses measurements of the voltage potential over the scalp (raw EEG data) and then estimates the current sources inside the brain that produce the measured signal. This procedure helps to determine the relative contribution of different neuroanatomical structures to the measured EEG. LORETA and other signal processing methods have the benefit of superior time resolution of EEG measurements of milliseconds, which is 3-fold better than that of fMRI, with spatial resolution of approximately 7 mm, which is similar to that of fMRI.11–13

Since it is theoretically possible that 2 EEG measurements with similar visual raw EEG and/or QEEG patterns may differ as to the inner brain electrical dipole distribution, the following study will relate not only to the resting QEEG but also to the LORETA analysis of EEG recordings of PTSD patients as compared to controls.

**Methods**

**Participants**

Ten right-handed, consenting, adult male patients were recruited from the PTSD clinic at the Beer Sheve Mental Health Center (BS-MHC). All patients fulfilled the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition, Text Revision [DSM-IV-TR]) criteria for chronic PTSD (duration >2 years) were on drug treatment regimens which had been stable for at least 2 months (involving only serotonin reuptake inhibitor [SSRI] and benzodiazepines). None had a history of neurological disorder, head trauma, alcohol or substance abuse, or a previous psychotic episode. An equal number of healthy male age-matched volunteer staff members acted as control participants. The study was approved by the ethics committee of the Ben-Gurion University of the Negev.

**Procedure**

The EEG was performed at rest, in a comfortable, quiet, air-conditioned room, for 3 minutes with closed eyes, employing the DeyMed Truescan 32 system with 19 electrodes (http://www.deymed.com), arranged according to the 10 to 20 international conventions, with FPz as a reference. Bipolar eye movement electrodes were applied to the canthus and cheek bone on the right eye in order to monitor the eye movement artifacts. The amplifier bandwidths were nominally 1 to 40 Hz, and the EEG was digitized at 128 Hz. During measurements, the impedance of all electrodes was kept below 5 kΩ.

**Analysis of Data**

Both split-half and test–retest reliability tests were conducted on the edited, artifact-free, EEG segments. Only records with >95% split half reliability and >90% test–retest reliability and a total measurement of more than 1 minute were subjected to the spectral and LORETA analyses. After editing, the shortest EEG length was 1 minute, while the longest was approximately 2 minutes. The removal of artifacts and the calculation of the statistical properties of the segments were performed using NeuroGuide software (http://www.appliedneuroscience.com). The artifacts removal were done both by the automatic algorithms in the NeuroGuide software and by visual inspection.

In order to avoid statistical multiple comparisons, the study focused on one spectral band, namely the absolute theta band, a band suggested to originate mainly from the limbic system, which has previously been reported to play a key role in PTSD symptomatology. The spectral analysis was done using both the linked ears reference montage and the local average (Laplacian) montage. Since most QEEG norms were measured with the linked ears montage, this was used as the standard. In addition, the
Laplacian montage was employed due to its ability to highlight local fields and the fact that it has been suggested to minimize global effects on the brain that drugs usually do.

**Statistics**

As stated before, in order to avoid multiple comparisons only absolute theta band values were compared. The unpaired t test was applied for comparing the data of both the QEEG spectral analysis and the LORETA analysis. Since the EEG strip was divided to 2 second epochs, there were over 30 degrees of freedom and therefore $T > 2.1$ stands for alpha level set at .05.

There was no statistically significant age difference between the study groups ($P = .19$; patients with PTSD—mean age: 44.4, SD: 9 years vs control participants —mean age: 39.1, SD: 9 years).

**Results**

On the QEEG, no statistically significant difference was found between PTSD and control groups for the theta band (4-8 Hz) on both montages (see Table 1). The LORETA analysis, however, revealed distinct patterns for patients with PTSD compared to controls. Patients with PTSD displayed statistically significantly lower activity on the “low” theta band (4-5 Hz), mainly over the right temporal lobe (including Brodmann 13, 20, 21, 22, and 42 areas; Figure 1). On the “higher” theta band (6-7 Hz), patients with PTSD demonstrated lower activity over both the right and left frontal lobes (including Brodmann 9, 10, 44, 45, and 46 areas; Figure 2).

**Discussion**

This study employed 2 methods of brain EEG analysis, namely QEEG and LORETA, in patients with PTSD compared to controls. No statistically significant difference was noted between these groups for the QEEG theta band. However, a statistically significant difference between PTSD and controls was found in the LORETA analysis, particularly on the right temporal lobe and both the right and left frontal lobes.

The significant findings on the LORETA analysis are important. There are relatively few studies reporting brain neuroimaging data at rest, while there is a large number of studies applying provocation paradigms prior to, or at the time of the imaging procedure. In an fMRI study, Lucey et al found that patients with PTSD differ from control participants on the bilateral superior frontal cortices and on the right caudate at rest. Our study also identified different activation of the superior frontal region (Brodmann 9 and 10) between patients with PTSD and controls. The caudate is generally not considered to be an EEG-producing structure and therefore is not a part of the Talairach coordinates serving as the base for the LORETA neuroanatomical identified structures. Therefore, the functioning of this structure cannot be explored by LORETA.

Even if one considers the brain regions relevant to PTSD of these patients while not at rest (ie, subjected to a variety of cognitive tasks), the right temporal as well as the right and left frontal brain areas are reported to differ between PTSD

<table>
<thead>
<tr>
<th>Link ears montage (µV)</th>
<th>8.4 (2.2)</th>
<th>11.8 (3)</th>
<th>NS</th>
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<tbody>
<tr>
<td>Laplacian montage (µA)</td>
<td>221 (61)</td>
<td>434 (149)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations: PTSD, posttraumatic stress disorder; SD, standard deviation; NS, not significant.

The brain maps represent the mean theta distribution over the 19 electrodes for both groups.

Table 1. Comparisons Between PTSD and Control Groups on Both Montages

<table>
<thead>
<tr>
<th>Mean PTSD Group Theta Distribution (SD)</th>
<th>Mean Control Group Theta Distribution (SD)</th>
<th>Mean PTSD Group Theta Distribution Counter Map</th>
<th>Mean control Group Theta Distribution Counter Map</th>
<th>Statistically Significant Difference</th>
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patients and controls. The affected frontal structures were linked previously to the experience and regulation of emotion, while the right temporal lobe dysfunction can elicit the re-enactment and re-living of past experiences that may cause the flashback symptoms.

One of the current neural models for PTSD is associated with deficits in information processing as well as with hypervigilance to salient and threat-related stimuli. This model combines 2 neural processes: hyperarousal on one hand, and the breakdown of an inhibitory function required for attention control and working memory on the other. Evidence for this model came recently from Falconer et al. These authors reported that compared to controls, patients with PTSD activated mostly the left ventrolateral prefrontal brain cortex, while a reduced activation of the right frontotemporoparietal cortical inhibitory network was also noted. Therefore, our results seem to be in agreement with the above model, assuming a compromised cortical inhibitory control brain network in PTSD.

The QEEG findings are consistent with those of Shankman et al who reported no difference between patients with PTSD and control participants at rest but are in contrast with Begic et al who reported a significant difference for the theta band between patients with PTSD and controls.

There are important differences between the above studies that may account for the conflicting results. Posttraumatic stress disorder is a heterogeneous disorder, and the nature of the traumatic event may be of varying severity and/or expression of symptoms. In the study by Shankman et al, different kinds of events were included, while in the Begic et al study all patients with PTSD were veterans, and it is reasonable to

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**Figure 1.** Group difference between PTSD and controls, in the LORETA analysis. The dark gray areas represent locations with statistically significant differences (T ≤ -2.1) between the study groups. In this figure, the 5 Hz results are shown representing the difference in the lower theta band (4-5 Hz). The LORETA analysis showed a statistically significant lower activity on the “low” theta band (4-6 Hz) in the PTSD group compared to controls, mainly over the right temporal lobe (including Brodmann 13, 20, 21, 22, and 42 areas). PTSD indicates posttraumatic stress disorder; LORETA, low-resolution electrical tomographic analysis.
assume that these participants were exposed to a more limited spectrum of events.

Psychotropic drug treatment may also induce changes in the QEEG. In the study by Begic et al,4 all patients were drug free for at least 2 weeks, while in the study by Shankman et al8 there was no specific mention of drug therapy, and one may assume that the patients were medicated. A third possible difference between the studies is that the patients evaluated by Begic et al4 were not classified according to the clinical clusters of PTSD (intrusive vs avoidance vs arousal clusters), while in Shankman et al8 there was an attempt to correlate the QEEG findings with these clusters as well as with certain personality traits. Another difference is the diagnosis procedure. Begic et al used the DSM-IV4 while Shankman et al relied on clinical interview and the Clinician-Administered PTSD Scale (CAPS) questionnaire.8

While the patients in our study were veterans diagnosed according to the DSM-IV-TR criteria, similar to those in the study by Begic et al, they were receiving medications, in contrast to those participants studied by Begic et al. One may postulate that the lack of drug treatment use by Begic et al contributed to their positive findings. However, SSRIs are usually considered to influence the alpha band, and benzodiazepines are usually considered to influence the beta band, rather than the theta band,14 which is our focus. Therefore, the use of psychotropic medications may thus not explain the difference between our findings and those of Begic et al.4 More research is needed in this regard.

Our study has several limitations: (a) this study consisted of a relatively small number of patients; (b) patients were treated with SSRIs and benzodiazepines and thus were not drug free. On the other hand, the effect of medications is usually considered to cause global changes, while our results show focal affects on the brain, thus making a drug effect less plausible. (c) a state of “rest” is not the same as a “relaxed” state. Some

![Figure 2. Group difference between PTSD and controls, in the LORETA analysis. The dark gray areas represent locations with statistically significant differences ($T \leq -2.1$) between the study groups. In this figure, the 7 Hz results are shown representing the difference in the higher theta band (6-7 Hz). The LORETA analysis showed a statistically significant lower activity in the “higher” theta band (6-7 Hz), for patients with](attachment:image)
of our patients may have experienced anxiety due to a new and unfamiliar examination, although they denied that this provoked anxiety. In the future, objective physiological measurement of arousal may well be applied during the rest condition.

Finally, this research demonstrates the importance of the exploration of the electrical dipole distribution inside the brain. In this regard, McFarlane et al.,26 in a review article describing the neural network model in PTSD, emphasized the importance of short-time resolution brain mapping, since neural function is in the millisecond range, while hemodynamic base brain mapping like fMRI operates on several seconds resolution. The development of EEG analyses such as LORETA could thus provide us with an important brain mapping technique using adequate time and space resolution, which are needed for the study of the neural network function in patients with PTSD.

Declaration of Conflicting Interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The authors received no financial support for the research, authorship, and/or publication of this article.

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