A Pilot Study of Quantitative EEG Markers of Post-Traumatic Stress Disorder -- Baseline Observations and Impact of the Reconsolidation of Traumatic Memories (RTM) Treatment Protocol.

Jeffrey David Lewine [1,2,3]
Richard Gray [4,5]
Kim Paulson [1]
Denise Budden-Potts [4]
Will Murray [4]
Natalie Goodreau [1]
John T. Davis [1]
Nitin Bangera [1]
Frank Bourke [4]

[1] The Mind Research Network, Albuquerque, NM
[2] The Lovelace Family of Companies, Albuquerque, NM
[3] The Departments of Psychology and Neurology, Univ. of New Mexico, Albuquerque, NM
[4] The Research and Recognition Project, Inc., Corning, NY
[5] Fairleigh-Dickinson University, Teaneck, NJ

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Introduction:

Post-Traumatic Stress Disorder (PTSD) is a potentially debilitating psychiatric disorder that is triggered by exposure to a significantly stressful traumatic event threatening death or physical injury to oneself or others. Core features of PTSD include intrusive re-experiencing (nightmares and flashbacks), avoidance, negative cognition and mood, and disturbances in arousal and reactivity [1]. Available data indicate the lifetime prevalence of PTSD among adult Americans to be just below 8% [2].

Multiple treatment approaches are used for PTSD, including pharmacotherapy and a range of cognitive and behavioral approaches including exposure therapy, cognitive processing therapy, mindfulness and EMDR (eye movement desensitization and reprocessing) therapy. Available data suggest that these various approaches generally provide significant relief of PTSD symptoms in only 25-50% of patients [3-5]. These approaches can also be expensive and time-intensive, with most cognitive-behavioral interventions requiring 15-30+ therapeutic sessions.

Given the current situation, there is mounting hope that a better understanding of the neurobiology of PTSD will lead to the development of better and more efficient therapies [6]. Several lines of human and animal research data converge to demonstrate PTSD-related changes in brain structure and function. Of particular note are reductions in the volume of the hippocampus and ventromedial prefrontal cortex, and increased activity in the amygdala [7-9]. These brain regions are key nodes in brain networks that support the processing of emotional memories. Indeed, PTSD is sometimes considered as a memory disorder in which fear responses over-generalize and fail to habituate because of disrupted memory consolidation and/or reconsolidation mechanisms [10-11]. Recent neuroscience research shows that the retrieval of

memories under certain conditions can open a 1-6 hour window during which reactivated memories can be updated and modified, or even erased [12-16]. This transient process, known as reconsolidation, may have important implications for PTSD treatment [17-18].

These data on mnemonic processing in PTSD have helped to motivate a new treatment approach to PTSD – the Reconsolidation of Traumatic Memories Protocol (RTM) [19-22]. RTM is a cognitive behavioral therapy that explicitly targets the intrusive symptoms of PTSD experienced as sudden and uncontrollable autonomic (sympathetic) responses to the trauma narrative, its elements, or the triggers for flashbacks and nightmares. RTM begins with a brief, quickly terminated recall of the traumatic event that is believed to 'open' the reconsolidation window. The protocol then takes the client through a series of dissociative and perception-modifying visual imagery exercises that are believed to restructure the traumatic memory, especially in relationship to persistent and pathological emotional responses. Typically, this protocol is completed over the course of three to five 90-minute long sessions administered over a 5-10 day window.

Anecdotal reports, published case series, and a published peer-reviewed wait-list control study all indicate that the RTM protocol is remarkably effective at reducing PTSD symptoms for >80% of treated clients [19-22]. For example, in a study of 30 male veterans with PTSD [19], 26 completed the protocol with a mean treatment-related reduction in PTSD symptoms of 33 points as measured at six-weeks post treatment by the PTSD Symptom Checklist Military Version (PCL-M). Given the rapid, medication-free nature of the RTM protocol, the method holds great promise for changing the current landscape of PTSD treatment strategies. In considering this, there is general recognition that clinical evaluations of RTM and other PTSD treatment strategies would benefit from a reliable, easily evaluated and objective biomarker for PTSD.

Prior research has demonstrated PTSD-related alterations in data derived from MRI, Positron Emission Tomography (PET), electroencephalography (EEG) and magnetoencephalography (MEG) methods [7-9, 23-27]. Unfortunately, most of these methods and extracted biomarkers have substantial practical limitations. For example, PET and various types of MRI (structural, functional, DTI, spectroscopy) readily show group differences between PTSD and control subjects, but these measures fail as input variables for accurate classification of individual subjects as belonging to PTSD versus control groups. A viable biomarker for clinical studies must be successfully applicable at the individual subject level. Other limitations include the need for radiation (PET), limited availability (MEG), and/or high cost (>$2000, MRI, PET, MEG). In contrast to the other methods, EEG offers an especially attractive profile with respect to PTSD studies. The method is inexpensive, portable, essentially risk-free and patient friendly, with commercially available normative databases and software for extraction of quantitative metrics and statistical evaluations that provide viable information on how an individual subject deviates from a control population. Given this, the present study sought to (1) identify quantitative EEG (qEEG) metrics for PTSD, and (2) to explore how treatment via the RTM protocol impacts these metric and clinical symptom severity.

Methods:

Subjects: qEEG data were collected and analyzed from (a) 30 neurotypical control (NTC) subjects without PTSD, traumatic brain injury, or other psychiatric, neurological, developmental or learning disorders, and (b) 17 subjects with a diagnosis of PTSD. The NTC population consisted of 24 males and 6 females, ages 24-72. The PTSD group consisted of 12

males and 5 females, ranging in age from 27-74. Inclusion criteria for the PTSD group included a medical diagnosis of PTSD; a baseline score above 20 on the post-traumatic stress disorder symptom interview (PSSI) [28]; a baseline score on the post-traumatic stress disorder symptom checklist (PCL) [29] above 50 for combat related PTSD and 40 for non-service related PTSD; and clinical evidence of sympathetic physiological arousal (flushing, sweating, rapid breathing, etc.) while briefly recounting traumatic events and present month flashbacks or nightmares. In all cases, significant symptoms had been present for at least 12 months. For PTSD subjects, the presence of traumatic brain injury or associated depression were not considered exclusionary factors, as these are very common real-world co-morbidities for PTSD, especially in military populations. A current substance use disorder and other axis I psychiatric disorders were considered exclusionary. Critical demographic data are provided in Table 1. All subjects signed an IRB approved consent form describing the study, prior to any assessments other than a brief phone screen.

Assessment of PTSD and Other Symptoms: At baseline, all subjects completed a clinical interview, the PSSI; and the PCL (military or civilian versions, as appropriate). A record was also made of all medications. At one week and one month post-treatment time-points, the PSSI was completed with respect to the total time that had elapsed since treatment, with a focus on symptoms only related to the traumatic events treated during RTM sessions. The PCL was also completed, but this was done with respect to each subject's overall trauma history (that is, without restriction to just RTM treated traumatic events).

RTM Treatment: RTM treatment was implemented across three 90-minute treatment sessions completed during a one week window, as administered by a trained clinician affiliated with the Research Recognition Project where the RTM protocol was developed. Most subjects in this study had multiple traumatic events. Initial treatment focused on each subject's self-identified most distressing event.

Details of the RTM protocol [19-22] are described in the Supplementary Materials. Briefly, each session began with a quickly terminated recall of the traumatic event, intended to reactivate the memory and open the reconsolidation window. Through a series of guided dissociative visual imagery exercises, the client engaged in perceptual manipulation of the traumatic memory (e.g., recalling the event from a third person perspective, viewing it in black and white, in reverse order, and at high speed) in a manner that ultimately allows for recall of the event without triggering emotional hyperarousal. If the protocol for the main traumatic event was completed in fewer than three sessions, additional events were treated, in order of severity. In several cases, 2-3 separate traumatic events were treated.

Quantitative EEG Data Acquisition and Analyses: At baseline, one week, and one month post-treatment, fifteen minutes of eyes closed resting state data were collected using a 21-channel electrode array (International 10-20 system, including left and right mastoids). Data were collected with a left-ear referential montage, with subsequent digital re-referencing to linked-mastoids. Individual electrode impedances were maintained below 10 KOhms. The data stream was digitized at 256 Hz. Data were subsequently read into NeuroGuide (Applied Neuroscience Inc, Largo, FL.) software for quantitative evaluation. As a pre-processing step, the NeuroGuide automated pipeline for selection of time windows without evidence of eye artifacts, drowsiness, and muscle artifacts was run, all with settings at 'very high', indicating the strictest

of criteria for selection of 'clean' artifact free data segments (but see legend for figure 2, describing instances of exception to this rule).

Using only the clean data, the NeuroGuide software calculated the absolute and relative power for delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz) , beta (12-25 Hz), high beta (25-30 Hz) and gamma bands (30-40 and 40-50 Hz), plus additional measures of inter-electrode relationships (phase-lag index, amplitude asymmetry, and coherence). NeuroGuide has a built-in normative database of over 600 subjects across the lifespan. Z-scores were calculated for each subject metric using an age and sex corrected regression model.

Results:

Few of the neurotypical control subjects, but essentially all of the PTSD subjects showed a substantial number of abnormal EEG metrics at baseline. However, within the PTSD group, there was little consistency in the abnormality profile, with the exception of z-scores for absolute high beta power. Figure 1 (top panel) shows z-score maps for high beta activity for the presently evaluated 30 neurotypical control subjects, as compared to the NeuroGuide normative database. High beta maps for these subjects generally did not show deviations from the normative database, an indication of the veracity of the database approach.

Figure 1 (bottom panel) shows the comparable maps for the 17 PTSD subjects. Thirteen (76%) of the subjects showed evidence of increased high beta activity relative to the normative database, whereas only one subject is expected to show such deviation based on chance. Within the PTSD group, there was not a significant relationship between the extent of beta abnormality and baseline symptom severity. In comparison to the neurotypical control group, the rate of

elevated high beta is significantly higher in the PTSD group (Fisher exact test statistic value = 1E-06, $p<0.01$).

Figure 2 shows the impact of the RTM protocol on clinical measures of PTSD severity at 1 week and 1 month post-treatment. As has been reported in other studies, the protocol leads to a substantial decrease in symptoms for the majority of patients. PCL scores fell from an average of 64 at baseline to 31 at one week follow-up (paired-T=9.5, $p<0.001$). These reductions in symptom severity were generally maintained at one month, except in two cases (see discussion below). PSSI scores also showed substantial reduction, falling from a baseline average of 34 points to 12 points at 1 week (paired-T = 11.69, $p<0.001$). At one month post-treatment, the average PSSI score was 11 points, again significantly reduced relative to baseline at $p<0.001$. Figure 3 shows that number of nightmares and flashbacks per month, reported at baseline and at one month post treatment, by each of the 15 subjects with one month follow-up.

Figure 4 shows how high beta contour maps changed as a function of treatment. Of the 13 subjects with increased high beta activity at baseline, ten subjects showed 1-week post-treatment reductions in high beta, with complete normalization of maps in 50% of these subjects. For the other 3 subjects with high beta at baseline, one did not complete the 1-week follow-up session (subject #6), one showed no change in high beta (despite clinical improvement – subject #5), and one showed slightly more high beta than at baseline (in the presence of clinical gains – subject #4). It should be noted that subjects without increased high beta at baseline were nevertheless responsive to treatment. Within the PTSD group, there was not a significant correlation between the magnitude of treatment-related reductions in high-beta and the magnitude of treatment-related reductions in PTSD severity.

At 1-month follow-up, there was evidence of some EEG and clinical rebound, in some subjects. For example, 1-month PCL scores for subjects #2 and #15 returned to baseline levels (with some increase in high beta over 1-week levels). However, in both cases, there were new intervening traumas between the 1-week and 1-month assessments (see Discussion). One subject (#7) showed a significant increase in high beta at the 1-month follow-up, but this is likely attributable to substantial muscle artifact during that evaluation. Finally, subject #5 showed slightly worse than baseline beta at 1-month despite maintenance of a substantial reduction in clinical symptoms.

To better understand what brain regions contributed to the observed increase in high beta activity, group average data were processed using the low-resolution brain electromagnetic tomography algorithm (LORETA), as implemented in the NeuroGuide software suite. Briefly, LORETA is an EEG inversion method that estimates the brain's electric neuronal activity distribution (current density vector field) which gives rise to the scalp recorded EEG profile [30]. Figure 5 (upper left panel) shows that multiple brain regions are contributing to the increased high beta activity in the PTSD group at baseline. Of particular note are contributions from the anterior temporal lobes, including the hippocampal and amygdala regions (left>right), insular and parietal regions (left>right), and bilateral mesial and orbital frontal cortex – all regions commonly considered to be part of the disrupted brain networks for PTSD. At one week and still at one month post-treatment, only minimal high-beta abnormalities were seen (Figure 5, upper right). As shown in the difference map (Figure 5, lower panel) the data indicate post-treatment changes in the high beta activity throughout the brain, but especially for left mesial temporal and parietal regions.

Discussion:

Prior electrophysiological investigations of PTSD have suggested several potential biomarkers of PTSD, including increased theta activity [26, 31-33], frontal alpha asymmetries [34-35] , and increased beta activity [27, 31, 32]. The present study noted some increase in theta for some individual subjects (especially those with comorbid TBI), but this was not consistent across the full group. The present study also failed to find substantial asymmetry in frontal alpha power, but such failure has also been reported by others [34].

In the present work, PTSD related abnormalities in high beta power were identified at both group and individual subject levels. At baseline, 13 of 17 PTSD subjects (76%) showed evidence of abnormally elevated high beta activity. This observation of increased beta activity is consistent with several prior studies of brain electrophysiology in PTSD, including the studies of Begic and colleagues [31-32] that used methods very similar to those employed here.

Using the LORETA algorithm to explore the brain regions giving rise to increased high beta EEG activity in PTSD, the greatest increases were observed for bilateral mesial temporal regions (hippocampus and amygdala, left > right), orbital frontal cortex and the left parietal lobe (see figure 5). The frontal and mesial temporal observations are concordant with those from a completely independent study by Huang and colleagues using MEG [27]. Huang and colleagues found their PTSD group (n=25) to show significantly elevated beta activity arising from several brain regions, with greatest increases seen for bilateral amygdala, left hippocampus, and bilateral posterior lateral orbital frontal cortex. Our data, and those of others [27, 31, 32], thereby converge to show increased beta activity in PTSD, especially in mesial temporal and frontal brain regions (although not all studies have seen increased beta activity in PTSD [26, 33]).

Following clinical intervention with the RTM protocol, all subjects showed clinically meaningful reductions in PTSD symptoms at one week follow-up, with 30% of subjects becoming nearly or completely symptom free. Overall, intrusive symptoms were most impacted by the treatment, but coincident alleviation of avoidance, arousal, and even cognitive problems was seen for the majority of subjects.

At one month follow-up, improvements generally held, except in two cases where at one month, many symptoms had returned to baseline levels (despite a nearly complete cessation of symptoms at one week). Importantly, in both of these cases there was an intervening traumatic event between the 1 week and 1 month follow-up, which caused both of these subjects to revert to pre-treatment avoidance and hyper-arousal behavioral coping mechanisms. However, in both cases, these new traumas did not trigger any re-experiencing of symptoms (flashbacks, nightmares, etc.) relative to the treated traumatic events.

RTM treatment also had a profound impact on brain electrophysiology, and to the best of our knowledge, the present study is the first to demonstrate that a medication-free cognitive behavioral therapeutic approach to PTSD can lead to normalization of relevant aberrant brain activity.

Reconsolidation is believed to be a core neurobiological mechanism for the up-dating long-term memory [11-16], and available data indicate that relevant processes are at least partially distinct from those involved in the original consolidation of a memory [35]. Re-consolidation is also distinct from the process of memory extinction which forms the basis for several PTSD treatment strategies including exposure therapy [17, 36].

Neurobiological data strongly suggest that intrusive re-experiencing of symptoms in PTSD is partly a reflection of perturbed mnemonic processing involving hippocampal and amygdala networks, with the dysfunctional system possibly becoming a recursive intensification loop of triggered traumatic memories, such that the trauma memory dominates conscious and/or unconscious processes in the form of flashbacks and/or nightmares [37-40]. Once the critical trauma memory is re-consolidated into a non-threatening emotional form that no longer causes sympathetic activation, the recursive loop is broken, and no longer able to dominate thought processes.

Through use of the LORETA algorithm, it was shown that post-RTM normalization in the scalp recorded EEG high-beta profile mostly reflects normalization of previously aberrant signals from the left hippocampus and amygdala, a finding fully consistent with above described neurobiological framework suggesting that the RTM protocol impacts memory re-consolidation processes mediated by the hippocampus and amygdala. On the other hand, the strong left lateralization of the findings is a bit puzzling, because other imaging and electrophysiological studies have more typically implicated the right temporal lobe as dysfunctional in patients with PTSD [23-24, 34-35].

In general, one week treatment effects on EEG were maintained at one month although there was a single case (#7) with substantially more beta abnormalities at 1 month than were seen at baseline. However, visual inspection of the data indicate that this most likely reflected muscle artifact during the follow-up examination. There was also an additional case (#5) where high beta activity at 1-month exceeded baseline levels, despite maintenance of clinical gains. The biological basis for this is presently uncertain.

At present, the full relationship between EEG and behavioral observations requires further elucidation, especially because there were 6 subjects (two with increased high beta at baseline, two with normal beta profiles at baseline, and two with slightly reduced high beta at baseline) who showed good clinical response to treatment in the absence of any clear changes in EEG. Nevertheless, the data suggest that increased high beta activity may be a valuable biomarker of PTSD that can be used to provide neurobiological tracking of treatment efficacy. In considering this, it is important to note that approximately 50% of PTSD subjects in this study were on one or more psychoactive medications, most commonly SSRIs and/or anxiolytics. Brain EEG profiles are sensitive to many of these medications, and benzodiazepines are well established to cause increased beta activity. However, the large prior study by Begic and colleagues [32] which also showed increased beta activity in PTSD, enrolled only subjects that had been medication free for at least one month prior to evaluation. Also, none of our subjects changed their medications between baseline and the follow-up sessions which showed dramatically reduced beta levels.

The present study has several limitations, most notably the relatively small sample size and non-blinded pilot design. Prior evaluation of the RTM protocol within the framework of a wait-list control design suggests that RTM clinical effects are real and robust)], but the situation with respect to EEG remains to be determined through future studies using additional randomization and blinding procedures (although prior longitudinal studies suggest that EEG profiles are fairly stable over time, at least for neurotypical subjects).

Whereas RTM appears to be exceptionally effective for eliminating re-experiencing and intrusive symptoms for treated events, and for leading to a reduction in associated aberrant avoidance and arousal behaviors, it does not fully protect against the impact of new traumatic

events, which may trigger a return to aberrant behavior patterns. Combination of RTM (to deal with past events) and inoculation training (to increase resilience to future events) may therefore prove valuable.

Conclusions:

Consistent with prior work indicating PTSD-related structural and functional alterations in hippocampus and amygdala, abnormal high beta activity was seen originating from these (and other) structures, as measured by relatively portable, in-expensive, and easy to use EEG technology. From a treatment perspective, this admittedly open-label study provides additional evidence on the clinical efficacy of the brief RTM protocol, with associated improvements in EEG profiles in a pattern which suggests that RTM does indeed achieve its effect through reconsolidation circuitry involving hippocampal, amygdala, frontal and parietal regions.

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Table 1: PTSD Subject Demographics

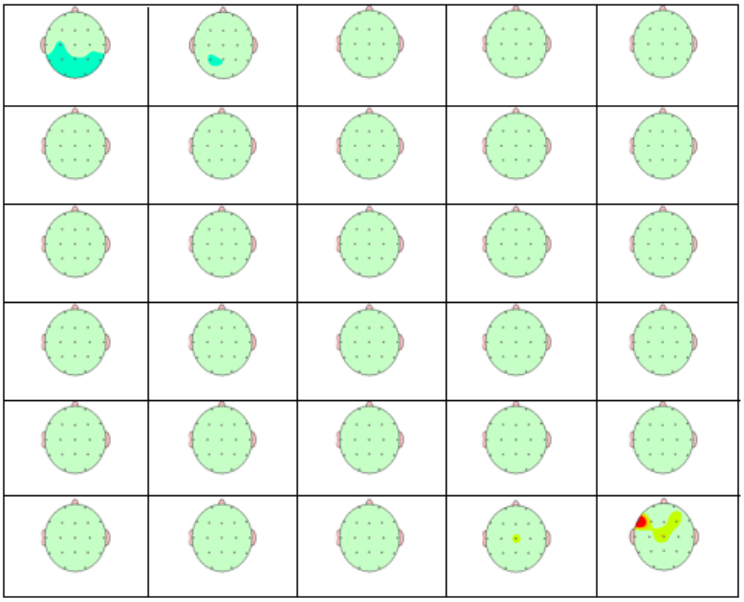
Subject #	Age	Sex	Main traumatic event	Baseline PCL	Baseline PSSI	Flashbacks & Nightmares per month	TBI	Medications
1	50	F	fire	83	46	4F 4N	N	prozac gabapentin alprazolam
2	64	F	medical	74	41	4F 4N	Y	valium
3	37	M	combat	70	39	3F 4N	Y	medical marijuana
4	40	M	combat	69	35	0F 12N	Y	none
5	74	M	combat	68	40	0F 3N	Y	none
6	27	M	combat	67	44	9F 0N	Y	none
7	55	F	sexual assault	66	22	3F 9N	Y	effexor prazosin topamax
8	43	M	combat	67	34	4F 8N	Y	none
9	61	F	domestic violence	64	39	30F 0N	N	lorazepam paroxetine bupropion
10	42	M	medical	64	35	3F 5N	Y	clonidine
11	31	M	combat	63	33	3F 2N	Y	topamax ambien gabapentin buspar abilify cymbalta
12	47	M	combat	61	32	0F 3N	N	none
13	70	M	combat	60	30	0F 9N	Y	none
14	33	M	accident	57	29	8F 0N	N	none
15	66	M	sexual assault	57	43	0F 4N	Y	neurontin seroquel bupropion
16	74	M	combat	51	31	4F 4N	N	none
17	48	F	accident	41	22	0F 2N	N	none

Legend: Table #1

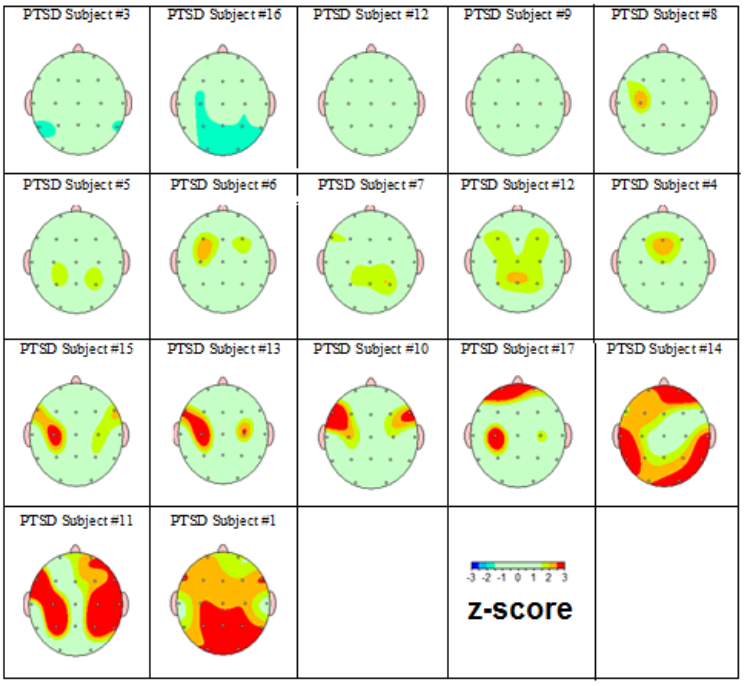
Demographic data for the 17 PTSD subjects. The table provides subject age, sex, nature of the main traumatic event that was treated, PCL and PSSI scores at baseline, baseline frequency of flashbacks and nightmares per month, history of traumatic brain injury (TBI) and medications.

Figure 1: Baseline Z-Score Maps of Absolute High Beta Activity

Neurotypical Control Subjects



Subjects with PTSD

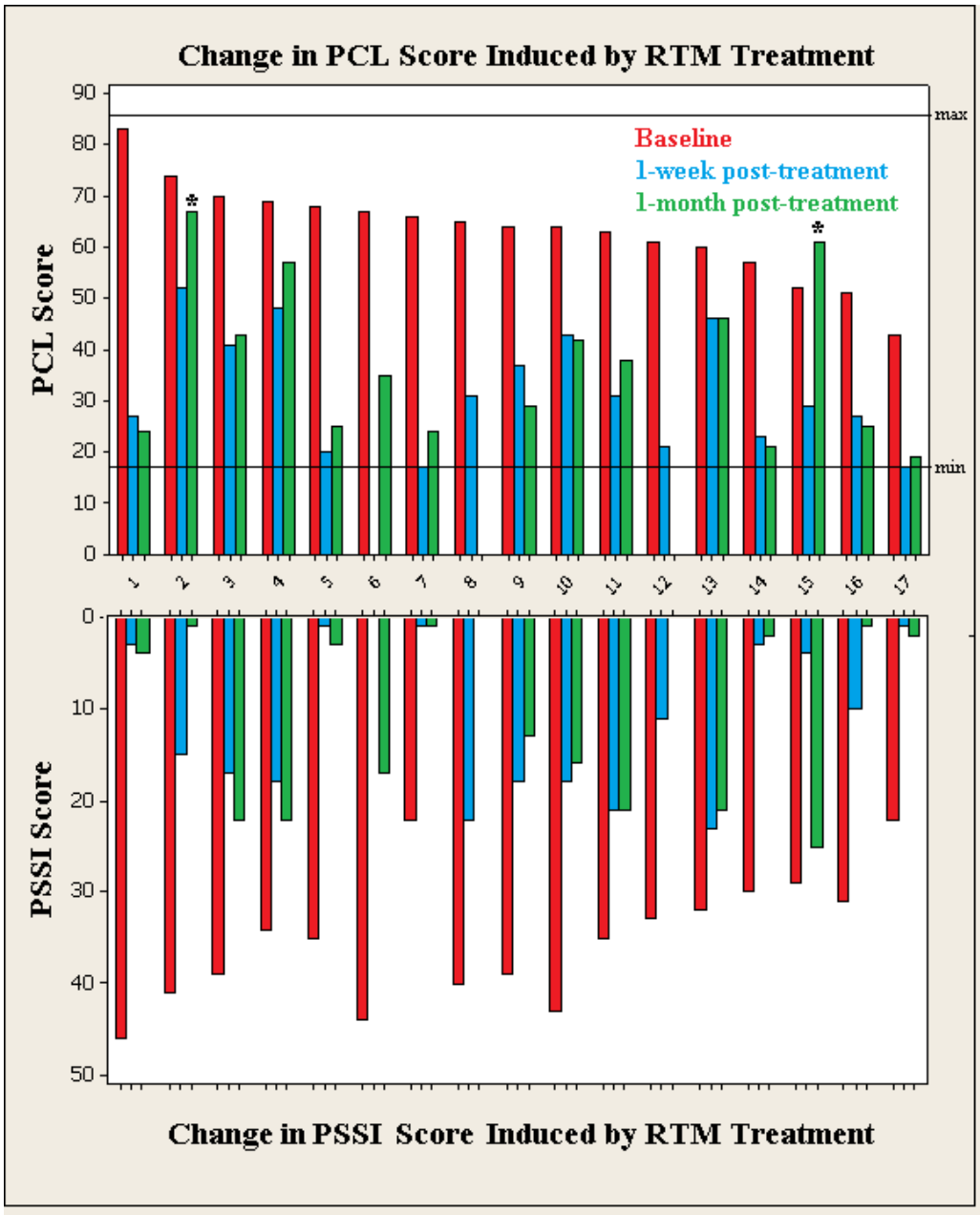


Legend: Figure #1

Baseline qEEG Z-score maps of absolute high beta activity. Maps have a threshold of +/- 1.5 std, so colors other than the pale green indicate statistically significant ($p<0.05$) deviations from normal. Data segments for spectral processing were selected using an automated pipeline that rejects time periods with heartbeat, eye movements, drowsiness, or muscle artifacts, with subsequent visual inspection of selected data to assure that only 'clean' data undergo spectral analyses. For four of the PTSD subjects (but none of the controls), the data stream at baseline contained substantial high frequency activity which the automatic processing identified as muscle artifact, this leading to rejection of almost all of the data. Subsequent visual inspection of the data made it clear, in all but one case (subject #1, second column, last row), that this activity was actually high beta and gamma activity, and not muscle artifact. The data selection pipeline was therefore executed with muscle rejection 'off', or at the 'low' setting (rather than the typical very-high setting).. For subject #1, there appeared to be a mixture of high beta, gamma, and clear muscle artifact. Data were processed with muscle artifact rejection turned off, so some caution is warranted in the interpretation of data from this subject because muscle artifact usually includes some power in the beta and gamma bands. Two of the control subjects showed areas of significantly low values for high beta (upper left hand corner, with blue color), and two show significantly elevated high beta (lower right hand corner, with green and red colors). The false positive identification of abnormal high beta in 4 of 30 control subjects \is within the range of expectations when using a p-value of <0.05. There were thirteen PTSD subjects with high beta (76%), a value significantly above the chance expectation (1 of 17, $p<0.05$). The rate of high

beta abnormalities in the PTSD group is significantly higher than that seen for the control group ($p<0.01$).

Figure 2



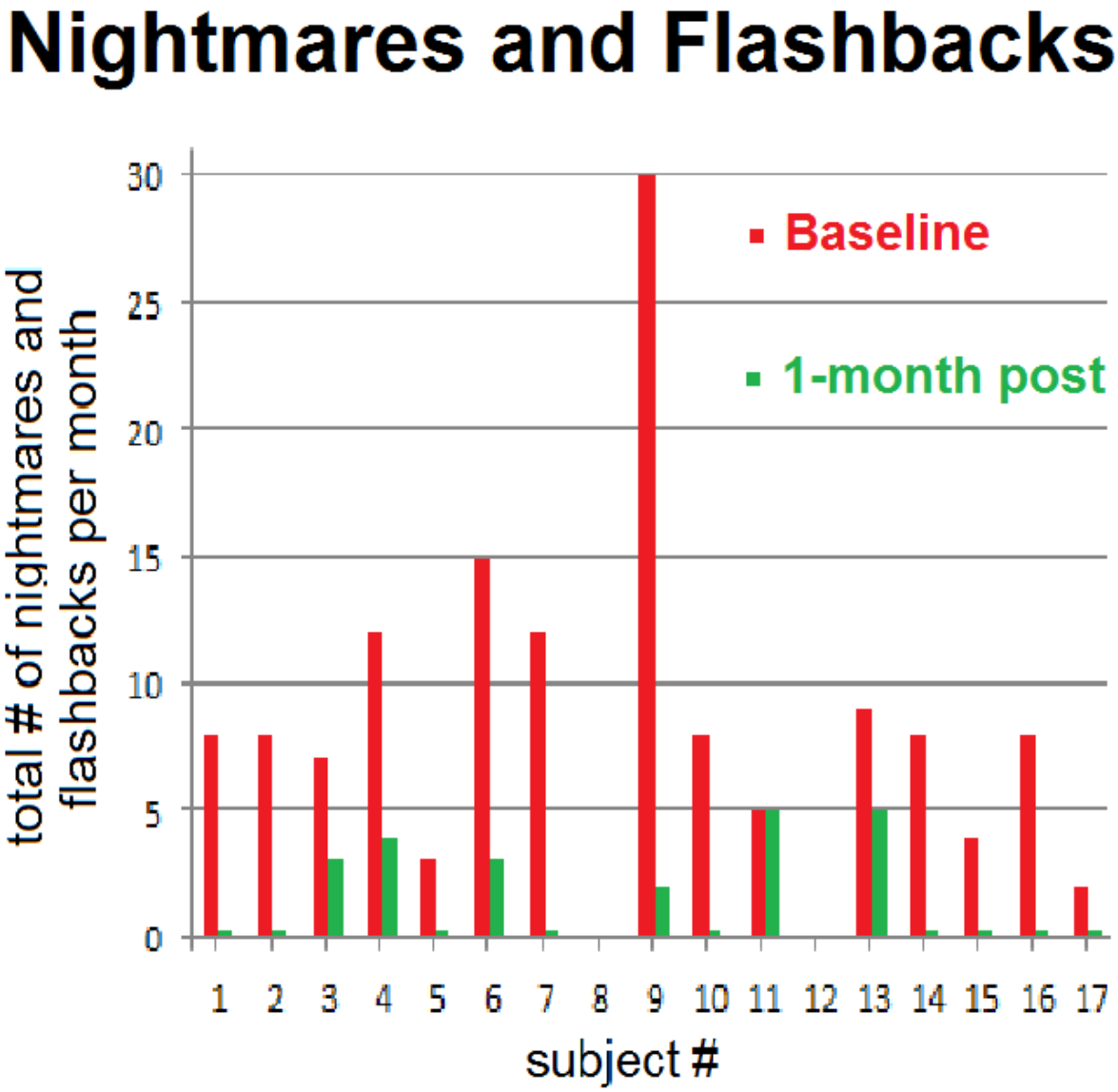
.

Legend: Figure 2

Changes in PCL and PSSI scores following RTM treatment. For the PCL, subjects were asked to provide overall symptom ratings, without restrictions. In contrast, for the PSSI, subjects were asked to provide symptom ratings only with respect to the treated traumas. Note: Subject #6 missed his 1-week appointment and #8 and #12 did not have 1-month appointments.

* Subjects 2 and 15 each experienced new traumas between the 2nd and 3rd weeks post-treatment. In each case, this triggered a return to many prior behaviors related to avoidance and hyper-arousal. However, in neither case did it trigger re-experiencing of the treated traumas (see Figure 3).

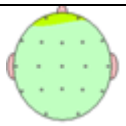
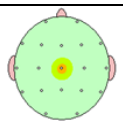
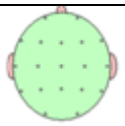
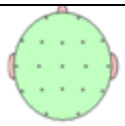
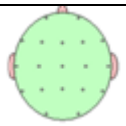
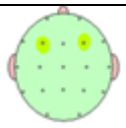
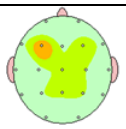
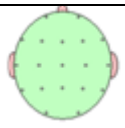
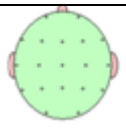
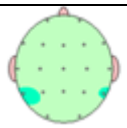
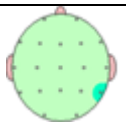
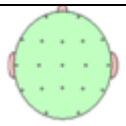
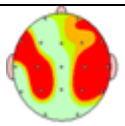
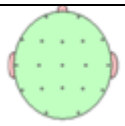
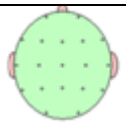
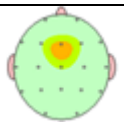
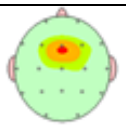
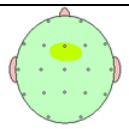
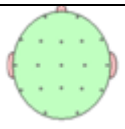
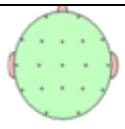
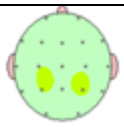
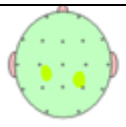
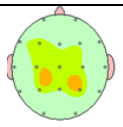
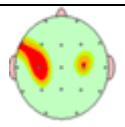
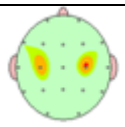
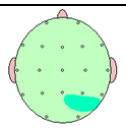
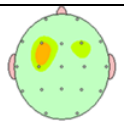
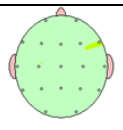
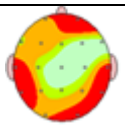
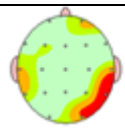
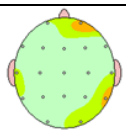
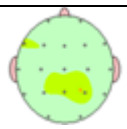
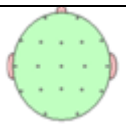
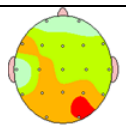
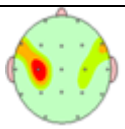
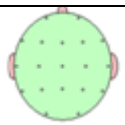
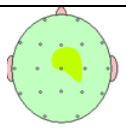
Figure 3


Nightmares and Flashbacks
total # of nightmares and flashbacks per month
30
25
20
15
10
5
0
Baseline
1-month post
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17
subject #

Legend: Figure 3

Data show the average total number of falshbacks and nightmares per month as reported at baseline and for the month following RTM treatment. Note that subjects #8 and #12 did not have one month follow up evaluations. Subject #8 reported and average of 12 flashbacks and nightmares per month at baseline. At one week followup he reported only one flashback since treatment. Subject #12 reported 9 flashbacks and nigntmares per month at baseline. At one week followup he reported a single nightmare since the end of treatment.

Figure 4

	Baseline	1-week	1-month				Baseline	1-week	1-month
1*						9			
2						10			
3						11			
4						12			
5						13			
6						14			
7*						15			
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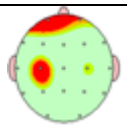
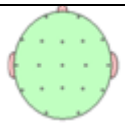
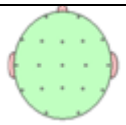
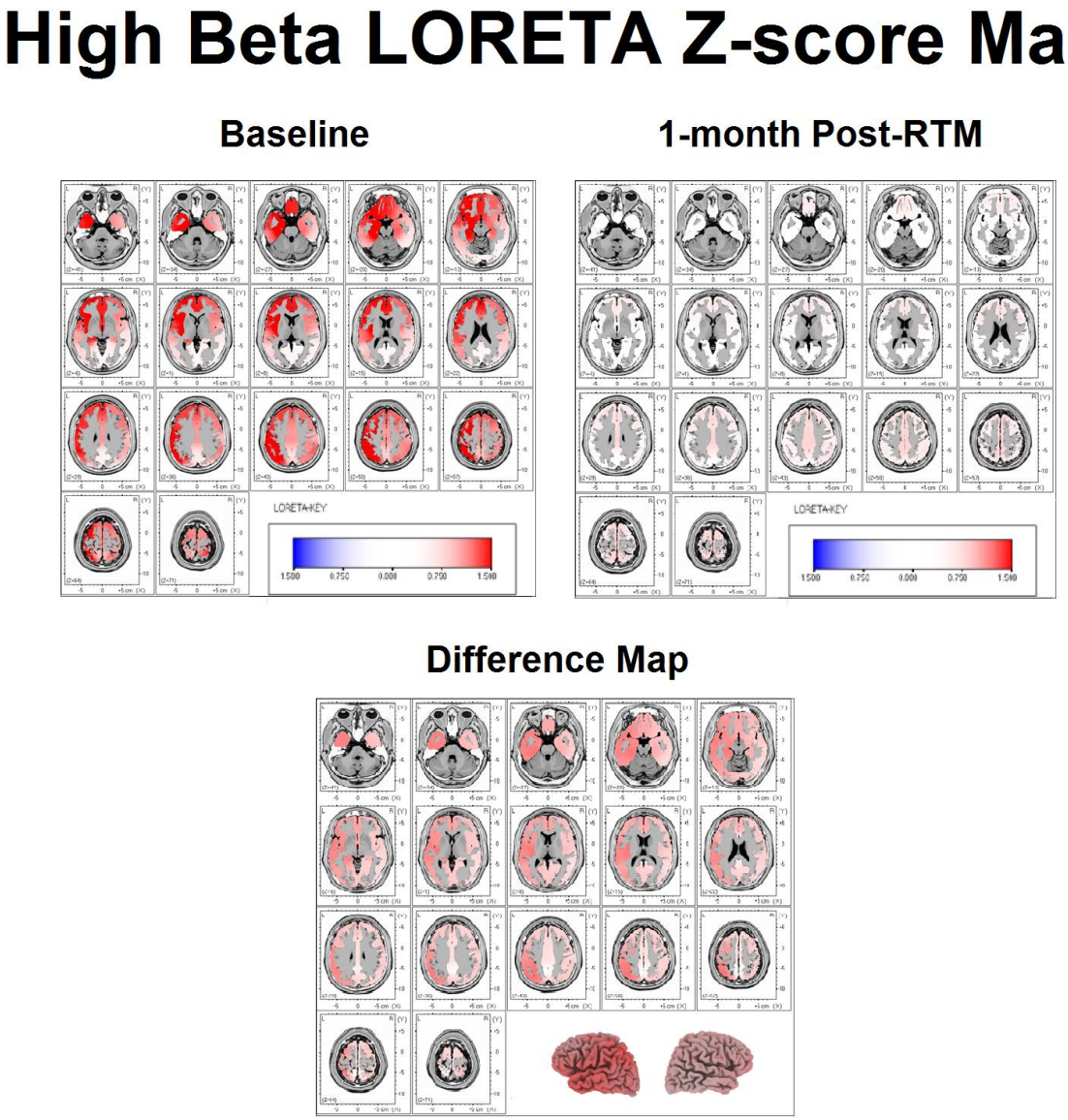
						17			

Legend: Figure 4

Data show how qEEG Z-score maps of absolute high beta activity change following treatment. Maps have a threshold of +/- 1.5 std, so colors other than the pale green indicate statistically significant ($p<0.05$) deviations from normal. All data were processed as described in the methods section and in the legend for figure 1. Some muscle artifact was seen in the baseline scan for subject #1 and the 1-month scan for subject #7, so caution is warranted in the consideration of these datasets. As discussed in the text, subjects #2 and #15 experienced new traumas between weeks 2 and 3 post-treatment. In general, for cases with excessive levels of high beta at baseline, post-treatment maps are more normal in appearance.

Figure 5


High Beta LORETA Z-score Maps
Baseline
1-month Post-RTM
LORETA-KEY
1.500
0.750
0.000
0.750
1.500
LORETA-KEY
1.500
0.750
0.000
0.750
1.500
Difference Map

Legend: Figure 5

Data show group average high-beta LORETA z-score maps for PTSD subjects at baseline and 1-month post-treatment follow-up. At baseline, abnormal high-beta activity is seen arising from many brain regions, but especially hippocampus and amygdala (left>right), mesial frontal regions, and the left insula and parietal lobe. At one month post RTM, maps show only minimal evidence of high beta abnormalities. Difference maps demonstrate that the post-treatment change is associated with normalization of high-beta activity throughout the brain but especially the left mesial temporal lobe.

Supplementary Materials:

SM1: Detailed Step-by-Step Description of the RTM Process

1. The client is asked to briefly recount the trauma.
2. Their narrative *is terminated as soon as autonomic arousal is observed*. – steps 1 and 2 are believed to open the reconsolidation window.
3. The subject is reoriented to the present time and circumstances.
4. SUDs (subjective units of distress) ratings are elicited.
5. The clinician assists the client in choosing times before and after the event (bookends) as delimiters for the event: one before they knew the event would occur and another when they knew that the specific event was over and that they had survived.
6. The client is guided through the construction (or recall) of an imaginal movie theater in which the pre-trauma bookend is displayed in black and white on the screen.
7. The client is instructed in how to find a seat in the theater, remain dissociated from the content, and alter their perception of a black and white movie of the index event.
8. A black and white movie of the event is played and is then repeated with structural alterations as needed, see SM2.
9. When the client is comfortable with the black and white representation, they are invited to step into a two-second, fully-associated, reversed experience of the episode beginning with the post-trauma resource and ending with the pre-trauma resource.
10. When the client signals that the rewind was comfortable, they are probed for responses to stimuli which had previously elicited the autonomic response.
11. SUDs ratings are elicited.
12. When the client is free from emotions in retelling, or sufficiently comfortable (SUDs ≤ 3), they are invited to walk through several alternate, non-traumatizing versions of the previously traumatizing event of their own design.
13. After the new scenarios have been practiced, the client is again asked to relate the trauma narrative and his previous triggers are probed.
14. SUDs ratings are elicited.
15. When the trauma cannot be evoked and the narrative can be told without significant autonomic arousal and a SUD of only 1 or 0, the procedure for that traumatic event is over.

Table is adapted from reference #21. It is used with the permission of the authors.

SM2: Perceptual modifications for the black and white movie		
Specific Association-dissociation manipulations		
Distance (increasing)	Move screen farther away- (from a few yards to as far back as two football fields, or farther as needed)	
	Variant	Vary distance of the self in booth from the self seated in theatre
Size	Shrink move screen so that the images/persons in movie get smaller	
Brightness/contrast	Vary brightness (white out detail--or provide sufficient light to see detail)	
	Variant	Decrease brightness (darken and obscure detail)
	Variant	Fuzz out distinctions (Decrease contrast / sharpness)
Angel/God Position:	Have the self in the projection booth float up above the theater watching the self in the booth (top of head and shoulders) watch Self in theatre (top of head and shoulders) as the self-in-the-theater watches the movie.	
Intermittent intervals	Watch every third (3^{rd}) second all-the-way through then watch every second(2^{nd}) second all-the-way-through, then watch every first (1^{st}) second	
Point of Focus	Focus upon different parts of the movie	Top half only
	Variant	Watch bottom half only[1]
	Variant	First watch top half all-of-the-way-through, then watch the bottom half all-of-the-way-through
Aspect ratio	Screen made taller and narrower or wider and shorter.	
Screen to Picture Ratio	White screen in background with small black and white movie in middle (Like a matted picture)	
Sequencing/simultaneous	Andreas (July 2016) Pick a point in middle of movie, run it rapidly from the middle of it to both ends--beginning and end--	

	simultaneously. Instruction: "Imagine all events are like dominoes, so when you tip over the dominos at the worst moment of the movie, they will trigger the dominos on both sides so they go from middle to both ends at the same time."	
Angles	The screen turns, or the client in theater moves so that self in theatre is watching movie at an oblique angle.	
Angled Booth	With the observing self in the projection booth, move the booth higher, to the left or to the right corner of the theater and view the side of Avatar's face/body in theatre	
Angle of movie	Imagine that the movie was taken from the side of the actors—a perpendicular third position.	
Speed/tempo of movie	Increase or decrease.	
Tilted screen	Screen/movie tipped forwards or backwards (tipping forward may invoke looming and should only be used with caution)	
	Variant	Screen/movie tipped sideways at skewed angle
Auditory Sub-modality distinctions (speakers next to screen)		
Tempo, Pitch, (Timbre) combo		
	Variant	Quick, high pitch, staccato (sounds like cartoon mice devouring cheese)
	Variant	Moderate tempo, Moderate pitch (sounds like Mae West--if voice or white noise--if sound)
	Variant	Slow, low pitch, elongated/stretched.
Olfactory Sub-modality Distinctions		
Adding smell in theatre when client fixates on movie smell	Popcorn smell added, smell of client's favorite movie food item added, etc.	
Notes: [1] Viewing the bottom half only may be dangerous for victims of sexual assault.		