# NeuroRegulation



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Using Standardized Weighted Low-Resolution Electromagnetic Tomography (swLORETA) to Analyze the Deep Brain Activity for Healthy Adults and Patients with Major Depressive Disorder

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Background. The differences in brain activity between patients with major depressive disorder (MDD) and healthy adults have been confirmed by functional magnetic resonance imaging (fMRI), emission tomography positron (PET), and electroencephalography (EEG), especially at the prefrontal lobe, posterior cingulate cortex (PCC). However, the high cost of fMRI and PET and poor time resolution limited the clinical application. Recently, researchers used high time resolution of standardized weighted low-resolution electromagnetic tomography (swLORETA) to refer to deep brain activity. This study aimed to convert EEG raw signals into swLORETA and explore the differences in deep brain activity between patients with MDD and healthy adults.

**Method.** BrainMaster equipment with a 19-channel EEG cap was used to collect resting EEG data with eyes closed for 5 min. NeuroGuide software was used to remove the EEG artifacts, and swLORETA software was used to analyze the 12700 voxels of current source density (CSD) for 114 patients with MDD comorbid with anxiety symptoms and 134 healthy adults. The deep brain activity at the frontal lobe and PCC in different frequency bands were analyzed for delta, theta, alpha, and beta.

**Results.** There were higher activities at prefrontal lobe (dorsal medial prefrontal cortex [dmPFC], ventral medial prefrontal cortex [vmPFC], dorsal lateral prefrontal cortex [dlPFC], ventral lateral prefrontal cortex [vlPFC], orbital frontal cortex [OFC])

and PCC were found in MDD patients compared with healthy adults, especially for lower delta and theta, and higher beta, beta3, and high-beta.

**Conclusion.** This study indicated that brain hyperactivity at the right prefrontal lobe (dIPFC and vmPFC) and PCC in patients with MDD comorbid with anxiety symptoms, and the dIPFC and PCC were also related to emotion-regulation in MDD. Inhibited high-beta activity or rewarded delta and theta activities at the right frontal lobe and PCC may be a possible neurofeedback protocol for patients with MDD in the future study.

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# Frontal EEG Indices of Attentional Bias and Involuntary Orienting to Pictorial Drug-related Cues in Cocaine Addiction

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Background. Preoccupation with drug and drugrelated items is a typical characteristic of addicted individuals. Several research studies provided support for the hypothesis about the alteration of attention processes in chronic addicts (Hester et al., 2006; Robinson & Berridge, 2001), so-called attentional bias (Franken, 2003), when drug-related cues attain greater salience and motivational significance (Cox et al., 2006). Cue reactivity refers to a phenomenon in which individuals with a history of drug dependence exhibit verbal, physiological, and behavioral responses to cues associated with their preferred substance of abuse (Carter & Tiffany, 1999). One of the cognitive components of cue reactivity in substance abusers is the preferential allocation of attentional resources for items related to drug use (Lubman et al., 2000).

**Methods.** This study explored frontal event-related potentials (ERP) and induced 40 Hz-centered gamma oscillation power to investigate differences associated with responses to attended and unattended drug-related cues in a three-category oddball task using neutral, drug-, and stress-related pictorial stimuli (from the IAPS and matched cocaine images). The study was conducted on 14 individuals with cocaine use disorder (CUD, mean age 44.2 years, 6 females) and 9 age- and gender-matched control (CNT, 36.7 years, 4 females) subjects. A

128-channel EGI-Phillips EEG system was used to record ERP and single trial induced gamma oscillations (30–40 Hz) during the visual threecategory oddball task with three categories (neutral, drug, stress) of affective pictures, when one of the categories was used as a target (attended stimuli, 25%) requiring motor response, while images of other categories including drug images served as unattended nontarget rare (25%) distracters.

Results and Discussion. Most profound group differences in reactivity to attended and unattended drug-related stimuli were found in the amplitude and latency of frontal P3a and in the relative power of induced (280-380 ms poststimulus) 40 Hz-centered gamma oscillations. At the frontal regions-ofinterests (ROI, left, midline, right; three EEG sites per ROI) amplitude of P3a ERP component was higher to unattended drug cues in the cocaine use disorder group as compared to controls (e.g., mean across all ROIs 3.55 uV in CUD vs. 1.85 uV in controls, F = 8.58, p < .01) and latency was prolonged. Differences in amplitude and latency of P3a in response to attended target drug cues were significant. Prefrontal induced not damma oscillations showed similar pattern of excessive reactivity to unattended drug cues in CUD (at FPz, F = 55.64, p < .001) but not to attended targets. Above described changes of depended variables are indicative of involuntary orienting of attention to highly salient drug-related cues even when subjects are not instructed to attend to nor to respond to them. In the prior studies we reported about usefulness of application of ERP and evoked oscillation measures as biomarkers of substance use and as neurofeedback treatment outcomes (Horrell et al., 2010; Sokhadze et al., 2008).

**Conclusions.** We propose that the employed EEG/ERP cue reactivity variables could be used as valuable functional outcome measures in cocaine drug users undergoing behavioral treatment.

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# Evaluations of Algorithmic Models for Estimations of Current Source Destiny and Electrophysiological Substrates According to LORETA and swLORETA Analyses

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This research examines the mathematical algorithms utilized for electroencephalographic source imaging localization. (ESI) and current source Electrodynamic processes that are evaluated according to source localization analyses and are derived from electroencephalographic assessments are based on the inverse problem. The inverse problem does not have a unique solution as infinite interactions between neuronal generators may yield the same derivation of scalp potentials. Source localization is subject to significant estimation errors of current source density and dipolar sources. The underdetermination of the system influences the significant estimation errors that can arise from small changes in the data related to the three-dimensional montage utilized to derive the estimations of the position and direction of potential electrophysiological generators for the lead field matrix. Common mathematical algorithms proposed to solve the inverse problem include low-resolution tomography electromagnetic (LORETA), weighted standardized low-resolution electromagnetic tomography (swLORETA), minimum norm estimate, and the weighted minimum norm estimate. Statistical evaluations of electrophysiological signals can be applied to evaluate neurocognitive behavior as linear or nonlinear functions. This research specifically evaluates the algorithmic models utilized for source localization according to LORETA and swLORETA

analyses. Thus, the proposed models will be based upon linear estimations of cortical and subcortical activitv that are etiologically relevant to electrodynamic processes. Because arithmetic models that incorporate priors into estimations of source distribution include the Bayesian framework and penalty function, this research examines the calculus related to estimations of source localization according to these models. The penalty function incorporates unknown source dynamics, the number of sensors utilized in the electrophysiological recording, number of samples across time, and a weighted factor. This algorithm utilizes a least squares regression model to estimate the penalty term as a quadratic function. Estimations of EEG sources according to parametric Bayesian models utilize spatial and neural constraints, evaluations of the current, and physical principles related to wave dispersion to derive estimations of localization. The parametric Bayesian model assumes Gaussian distributions and accounts for random fluctuations of sensor and source space. These mathematical models are also included due to the ability to transform one into the other while maintaining the integrity of their core structures.

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# Psychophysiological Indices of Attentional Bias Towards Drug-related Pictures in Visual Cue Reactivity Test in Individuals with Opiate Use Disorder Enrolled in Buprenorphine-Maintenance Program

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Background. Opioid use disorder (OUD) is a major public health problem in the United States that is expected to continue to increase (Blau, 2017; Hadland et al., 2018; O'Donnell et al., 2017). Maintenance treatment with buprenorphine in medication-assisted treatment (MAT) has been associated with reductions in opiate use in individuals with OUD. However, despite low physical symptoms of withdrawal, buprenorphine-treated opioid-dependent still patients demonstrate vulnerability to relapse (Hyman, 2005; Robinson & Berridge, 2001). Craving and attentional bias towards drug-related items may contribute to the high rates of noncompliance and relapse in OUD individuals undergoing MAT. The cue-reactivity paradigm (Carter & Tiffany, 1999) has been among the most prominent methods for investigating drug craving and psychophysiological responses to drug cues.

**Purpose.** We propose that craving and excessive reactivity to drug-related cues could be considered the core mechanisms underlying relapse risk. Comparing central and autonomic nervous systems activity profiles and correlates of craving, drug-cue responsiveness, and more general emotional processes may provide more knowledge towards the comprehension of the interaction between craving, affect-related states, motivational processes, and clinical outcomes of OUD patients enrolled in MAT.

Methods. In a pilot study were recruited 10 participants from outpatient individuals being treated with MAT for opioid addiction. Drug screens were conducted using saliva drug test and eligibility was confirmed by clinical and behavioral evaluations. Pictorial cue reactivity test was conducted using exposure to emotionally neutral pictures from the International Affective Picture System (IAPS: Lang et al., 2001) and drug-related images matching IAPS -pictures by color, size and background. The study used blocked design of presentation (16 images per block, 3 s per image) and each block was followed by subjective rating of craving. Responses were recorded with Nexus-10 psychophysiological monitor with BioTrace+ software (Mind Media, BV, The Netherlands). Photoplethysmogram (PPG). pneumogram, and electrodermal activity were acquired to measure skin conductance level (SCL), time domain heart rate variability (HRV) measures (RMSSD, SDNN), and respiration rate and amplitude. EEG was recorded from four frontal sites referenced to linked earlobes.

**Results.** Analysis of the frontal EEG conducted to assess power of slow (theta, alpha) and fast (high beta, gamma) rhythms in neutral and drug blocks showed higher relative power of gamma (35–45 Hz), along with trends to lower power of theta activity and higher alpha-to-theta ratio in response to drug cues. Autonomic responses to drug cues were featured by increased SCL, higher frequency and lower amplitude of respiration, and increased RMSSD and SDNN measures of HRV with the tendency to phasic heart rate deceleration. This psychophysiological response profile can be considered as indicative of increased attention.

**Conclusions.** Psychophysiological indices of heightened arousal and attention to drug cues were found to be useful objective measures to complement subjective reports of craving. Craving, cue-reactivity, attentional biases are important clinical precipitants of relapse in and their measures may serve as useful objective outcomes of behavioral therapies. Furthermore, they could be used for guiding better targeted behavioral interventions.

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#### Navigating Virtual Neurofeedback Treatment During COVID-19: A Retrospective Analysis James Spears and Cerise Edmonds

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Neurofeedback, or electroencephalography (EEG) biofeedback, is a therapeutic approach that integrates a client's brainwave activity to enhance and empower their specific, individualized growth through self-regulation (Demos, 2005). This modality continues to be applied to decreasing or alleviating symptoms associated with a variety of mental health concerns, including anxiety and posttraumatic stress disorder (PTSD; Gregory et al., 2020; Mennella et al., 2017; Romero et al., 2020). Traditionally, clinicians conduct neurofeedback services in person. Physical presence allows clinicians the ability to assist with certain tasks like correct electrode placement as well as mitigate any questions or technical issues that arise.

On January 30, 2020, the World Health Organization declared a public health emergency in response to the viral COVID-19 outbreak. Shortly after, the United States acknowledged a national emergency (9994Executive Office of the President, 2020), causing many colleges and universities to swiftly transition solely to online platforms (Murphy et al., 2020). Because of this unprecedented transition to virtual learning, collegiate programs that offer or

require student internships as course credit were tasked with developing creative alternatives.

The counseling department at the University of Texas at San Antonio offers students the unique opportunity to complete an introductory-level and two advanced practicum neurofeedback courses, intentionally designed to fulfill most requirements for certification through the Biofeedback Certification International Alliance. Each course contains a hands-on component, ranging from weekly class labs to conducting no-cost neurofeedback sessions with clients from the community. With the transition to virtual learning regarding the pandemic, these specific classes were challenged with discovering avenues that continued to provide kinesthetic learning for students. Fortunatelv. through collaboration and donations from practitioners and organizations, the department's neurofeedback program offered virtual, distance neurofeedback services to clients that adhered to ethical guidelines postulated by the American Counseling Association (American Counseling Association, 2014). Neurofeedback equipment and laptop computers outfitted with BioExplorer software were distributed to each participant, while clinicians were able to access and operate client computers from the leisure of their homes.

If accepted, the poster presentation will illustrate a retrospective analysis of results and demographics gathered from the client's (N = 17) twice-weekly virtual sessions during the summer academic term of 2020. Those served stated having negative symptoms associated with either anxiety, PTSD, or attention-deficit/hyperactive disorder. Individualized treatment protocols developed were using preliminary theta/beta power ratio data collected scheduled neurofeedback before sessions commenced (Hernández et al., 2016; van Son et al., 2020). Presenters will also discuss the unique advantages and limitations relating to providing virtual, online neurofeedback services.

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## Neurofeedback and Trauma

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Traumatic events do not discriminate and can occur to anyone. The aftermath of the trauma impacts not only the victim but family, friends, coworkers, and their community as well. The numbers are staggering with the PTSD Alliance (2018) reporting that over 13 million or 5% of Americans suffer from PTSD during any moment in time, while the yearly prevalence was reported to be 3.6%. The financial costs of anxiety disorders, including PTSD, amount to well over \$42 billion with many of these dollars being spent on repetitive healthcare visits due to inaccurate diagnoses (PTSD Alliance, 2018).

This qualitative systematic literature review will focus quantitative on the current research on (qEEG), neurofeedback electroencephalography assessment and neurofeedback training with individuals who have experienced psychological trauma. The analysis of the literature surrounding neurofeedback assessment and training will also address the feasibility of identifying the area or areas of the brain impacted by psychological trauma, as well as the magnitude of the impact. Finally, it will attempt to identify areas of the brain that may benefit from training if they were altered by trauma. The overarching goal of the study is to determine if using neurofeedback assessment and training can aid in reducing the time and costs involved in establishing an accurate diagnosis, and ultimately, returning the individual to an increased level of functioning.

The statement of the problem section will identify the high cost of trauma for the individual, family, and society. The purpose of the study is to analyze the literature on neurofeedback assessment and training with individuals who have experienced psychological trauma, identify the psychological impact on the brain, and the manner in which neurofeedback assessment and training may accurately diagnose trauma, facilitate early treatment and decrease the cost of trauma to all involved. The theoretical framework of adaptive information processing theory will provide the lens through which the existing research and findings of the study will be viewed.

Finally, the significance of this qualitative systematic literature review, as well as limitations and delimitations are identified. Key words utilized include neurofeedback, EEG biofeedback, psychological trauma, posttraumatic stress disorder, PTSD, acute stress disorder, electroencephalography, EEG, quantitative EEG, QEEG, brain map, brain computer interface.

Participants were adult individuals with a history of trauma ranging from single incident trauma to chronic and developmental trauma. Findings are revealed and implications for the profession and field are noted.

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# Improving Mental Health Through Z-score LORETA Neurofeedback During a Pandemic Ingrid Valentin and Robin van Osch

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During the COVID-19 pandemic, the general population's mental health has been decreasing around the world. This creates a high need to find efficacious methods to improve mental health. Pharmacotherapy can lead to side effects and its effect subsides when the treatment is withdrawn. The field of neurofeedback, or EEG biofeedback, is over 50 years old. It has proven its efficacy in a wide range of psychological and cognitive symptoms. LORETA *Z*-score neurofeedback training (LZNFB) is a relatively new advancement in this field and, as such, there is a limited body of evidence investigating its efficacy. The aim of this study is to evaluate its effect in an uncontrolled clinical setting.

**Participants.** Thirty-one adult clients (21 men, 10 women, mean age M = 31.63, SD = 9.5) with mental health complaints filled in the Brief Symptom Inventory (BSI-53) before and after their neurofeedback therapy. Nine clients also responded to a follow-up questionnaire 3 months later.

**Method.** All clients started with an intake and qEEG assessment on which their LZNFB protocol was based. All qEEG analyses and protocols were executed and designed by one lead clinician. Before the first training session patients filled out the BSI-53 in order to determine symptoms related to the physiological profile. Each LZNFB session lasted between 30 and 40 minutes. A training protocol was

used for at least five sessions before possibly altering it. The training protocol was designed to target a known neural network, that has a significant role in the client's symptomatology. Since this study was made in a clinical setting and received no funding, each client did a number of sessions that was estimated to be the best compromise between clinical efficacy and the possibilities of their financial situation. After their last session, they filled the BSI-53 again. A follow-up BSI-53 measurement was requested 12 weeks after the last session.

Results. The participants did 16 sessions on average (M = 16.16, SD = 6.11). On average, the BSI-53 scores after neurofeedback (M = 46.16, SE =5.77) were lower than before neurofeedback (M =71.71, SE = 6.01). This difference, 25.55, BCa 95% CI [17.43, 33.67], was significant, t(30) = 6.42, p < 100.001, and represented a medium to large effect size of d = .76. Three months after the last session, the scores were still lower than before neurofeedback (M = 42.11, SE = 10.31), which was also significant t(8) = 4.54, p = .002, and represented a large effect size of d = .84. Three out of 31 (9.6%) participants were classified as nonresponders (less than 5% change in scores). The only noticeable side effect was fatigue, which subsided within a day after each session.

**Conclusion.** LZNFB shows promise to improve pandemic-related and unrelated mental health conditions, with a high response rate, potentially long-term health outcomes and side effects limited to a short-lived fatigue. Because of the clinical, uncontrolled design of the study, mitigating factors were difficult to exclude. For example, nine participants changed their psychoactive medication habits during their neurofeedback sessions. Controlled studies are needed in order to replicate effect sizes and confirm the significance of these results.

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# Comparing the EEG Patterns Between Patients with Major Depressive Disorder and Healthy Adults Through a Normalized Database in Taiwan

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**Background.** Brain hyperactivity has been confirmed as a trait marker in patients with major depressive disorder (MDD). Several quantitative electroencephalography (qEEG) databases are available in the United States, patients' EEG data were compared with the qEEG database and transformed into the *z*-score. However, Taiwan has not yet established a qEEG database in healthy populations. This study aimed to collect and develop the qEEG database of healthy adults and compared the qEEG patterns between patients with MDD and healthy adults.

**Method.** This study was based on the EEG collection and development of the qEEG database. All of participants received Beck Depression Inventory-II and Beck Anxiety Inventory. The 19-channel EEG raw signals were recorded for 5 min resting with eyes closed. NeuroGuide software was used to analyze 184 healthy adults, divided into 10-year age groups from 20 to 70, and calculated the mean and standard deviation of each age group. The statistical analysis was converted 146 raw EEG data from patients with MDD into the *z*-scores.

**Results.** (1) Patients with MDD revealed higher absolute high-beta at prefrontal lobe (F3/F4), parietal lobe (P3/P4), and midline (Fz/Cz/Pz) compared with the healthy adults. (2) The average z-score in high-beta and the absolute value of zscore in high-beta were both greater than 1 at prefrontal lobe (F3/F4), parietal lobe (P3/P4), and midline (Fz/Cz/Pz) in patients with MDD. (3) There were positive correlations between depression and the absolute high-beta of z-score at F3, P3, P4, Cz, Pz; as well as positive correlations between anxiety and the absolute high-beta of z-score at F4, P3, P4, Pz.

**Conclusion.** The brain hyperactivity was confirmed in the high-beta frequency band in patients with MDD. Moreover, the average *z*-score was greater than 1, and the *z*-score of high-beta was correlated with depression and anxiety. This study indicated that the *z*-score can be used as a reference standard for qEEG in patients with MDD.

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