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Review Article

Evaluation of Post-Traumatic Stress Disorder using Brain View Imaging

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Abstract

Post-traumatic stress disorder (PTSD) can be severe enough to interfere with patients' daily life and can be associated with co-occurring psychiatric disorders such as depression, anxiety, and substance abuse. PTSD diagnosis is still difficult because many patients may not be willing to disclose their traumatic event, or the symptoms get confused with depression and/or substance abuse. Current methods for diagnosis rely heavily on psychiatrist-patient subjective clinical examinations using standardized questionnaire system. More recently, objective evaluation using electroencephalography (EEG) has been suggested as a better method with higher consistency and accuracy. EEG-based findings can potentially better differentiate PTSD from its overlap with other mental disorders. In this review, we will summarize the evolution of PTSD diagnosis, and how EEG and Brain View can potentially improve the diagnostic field.

Keywords: Post-traumatic stress disorder, Electroencephalography, Diagnostic imaging, BrainView

Introduction

Posttraumatic stress disorder (PTSD) is no longer considered an anxiety related disorder but has been reclassified as a trauma and stress-related disorder. Diagnosing PTSD is difficult because many patients may not recognize their symptoms, are not willing to disclose the traumatic event experienced, or the symptoms that present may be confused with other symptoms that co-occur with PTSD such as depression and substance abuse. Subjective clinical examination of PTSD using standard questionnaires has been the primary method to diagnosis PTSD. More recently, objective assessments such as electroencephalography (EEG) have emerged as a new approach to diagnose PTSD.

EEG-based findings could greatly help in the diagnosis and treatment of PTSD patients because it would be more objective and less symptom-based especially because PTSD symptoms overlap with other mental disorders. Currently, Brainview by Medeia is a new and novel EEG computer-based technology that has been FDA-approved [1,2]. This improved technology is easy to use, universal, and can help aid in the management of brain health and diagnostics of PTSD patients. In this review, we summarize the current subjective and objective methods used to diagnose and evaluate PTSD, discuss how these assessments are used to help manage PTSD symptoms, summarize the changes that occur in electrical activity in the brain of PTSD patients, and review Brainview as a better EEG technology to diagnose and help treat PTSD.

Posttraumatic Stress Disorder

PTSD was first recognized as the term "shell shock" during World War I and "combat fatigue" after World War II. In 1980, the term PTSD was first introduced in the 3rd edition of the Diagnostic and Statistical Manual (DSM) of the American Psychiatric Association [3]. PTSD was originally recognized as 'stress reactions' and 'anxiety neurosis/transient situational disturbances.' After the Korean War, DSM-I characterized PTSD as severe physical or emotional stress that could turn into a chronic neurotic reaction. In 1968 DSM-II eliminated the idea of 'stress reactions' because this era was experiencing a time of global peace. However, when DSM-III was published in 1980 the term PTSD emerged as a distinct clinical diagnosis which resulted from the psychological trauma experienced by soldiers during and after the Vietnam War [4]. Later DSM editions between 1987 and 2000 have refined and improved the diagnosis of PTSD. The most current version of DSM is DSM-5 which was released in March 2022 by the American Psychiatric Association. As of 2018, the World Health Organization (WHO) published the 11th version of the International Classifications of Diseases (ICD-11) which also provides public health perspectives of PTSD and aids in the clinical diagnosis of PTSD [5,6]. Both the criteria described in DSM and ICD-11 are used by clinicians to aid in the diagnosis of PTSD.

Today, PTSD is recognized as a mental health disorder and is associated with significant distress, social anxiety, and emotional impairment [7]. To be diagnosed with PTSD a person must experience PTSD symptoms for longer than 1 month and the symptoms must be severe enough to interfere with an individual's daily life such as their relationships or work. Symptoms of PTSD include avoidance, reactivity, and mood swings. Co-current symptoms that can arise with PTSD also include depression, anxiety, and substance abuse. PTSD can last for several months or in more severe cases, it may last for years. In some cases, PTSD can be triggered by memories of a trauma that cause intense emotional and physical reactions. An individual that experiences PTSD is at a higher risk of suicide and intentional self-harm. The symptoms of PTSD in children and teens, however, may be different than the symptoms experienced by adults. Children under the age of 6 may show signs of bed wetting, the inability to talk, acting out the scary event experienced, or being unusually clingy with a parent or another adult. Older children may have guilt or act out in revenge. In most cases, PTSD is treated by psychotherapy (counseling) and medications to manage symptoms.

PTSD is most common in Veterans because they are often exposed to different traumas and the risk of PTSD varies depending on the war zone, accidents, sexual assault, deployment, and training accidents experienced. Although PTSD was first recognized in veterans, it can occur in all people regardless of their ethnicity, nationality, culture, or age. According to the National Center for PTSD, about 12 million adults in the U.S have PTSD within a given year. Approximately 6 out of 100 people will experience PTSD at some point in their lives. Women (8%) are at a greater risk for developing PTSD compared to men (4%) and this is because women are more likely to experience sexual assault and child abuse. Men are more likely to experience accidents, physical assault, combat, disaster, and witness death compared to women. The National Center for PTSD has found that approximately 5.5 million children and teens are affected by PTSD. Most PTSD trauma in children and teens arises from neglect (65%), sexual abuse (10%), psychological abuse (7%), and physical abuse (18%). According to the American Psychiatric Association, three ethnic groups in the U.S: Latinos, African Americans, and American Indians have higher rates of PTSD compared to other ethnic groups [8]. As of 2020, the National Center for PTSD has recently recognized the effects of the Coronavirus Pandemic on PTSD which led to increased fear of getting sick, concern over loved ones, isolation, job loss, and family demands.

Diagnosing PTSD

PTSD can be diagnosed using two methods; subjective assessments that rely on responses from patients during interview questionnaires or objective assessments that rely on electrical signals identified using electroencephalography (EEG).

Subjective Assessments

Subjective assessments are unstructured or structured interviews administered by a trained mental health professional. Some subjective assessments can be used for self-diagnosing before seeking out a professional for a proper PTSD diagnosis. There are several structured diagnostic interviews used for the subjective assessment of PTSD including: the Clinician Administered PTSD Scale (CAPS), the Structured Clinical Interview for DSM-IV (SCID), PTSD symptom scale-interview (PSS-I), the composite international diagnostic interview (CIDI), the Generalized Anxiety Disorder scale (GAD-7), and PTSD checklist (PCL) for civilians. The latter two subjective assessments are often used for the self-diagnosis of PTSD.

Since the 1990s, CAPS has been used to assess PTSD [9,10]. In 2017 CAPS was revised to CAPS-5 (the latest version of CAPS) to correspond to the up-to-date PTSD criteria described in DSM-5 [11]. Weathers et. al., 2017 was the first study to use CAPS-5 to both revise CAPS and use it to evaluate PTSD in two different samples of military veterans. CAPS-5 is a structured 30 question interview that takes approximately 30-60 minutes. There are three versions of CAPS-5 that correspond to different time periods: past week, past month, and worst month over a lifetime. There is also a CAPS-CA-5 version for children ages 7 and above. The CAPS-5 interview assesses the 20 PTSD symptoms listed out in DSM-5 which are grouped into several criteria to score PTSD symptoms of each patient: Criterion (items 1-5), Criterion C (items 6-7), Criterion D (items 8-14), and Criterion E (items 15-20). There is also a Criterion F and G where F is met when a disturbance has lasted for one month and G is met when the disturbance causes distress or functional impairment. The questions asked during the interview target the onset and duration of PTSD symptoms experienced by the patient and evaluates the distress displayed by the subject while the patient is answering each question. A few examples of the questions asked during the interview includes: "In the past month, have you had

any unwanted memories while you were awake?" or "How much do these memories bother you?" If a patient is diagnosed with PTSD, the CAPS test will be administered over periods of time to assess whether symptoms since their previous CAPS test have improved.

SCID was first released in the 1980s as a semi-structured interview for diagnosing mental disorders including PTSD [12]. SCID is based around the criteria in DSM and SCID-5 has been refined and available since 2013 to fit the current version of DSM-5 [13]. During the interview process the patient is asked to describe the history of their illness, past episodes of disturbances, treatment history, and their current day to day function [14]. Diagnostic modules are used to ask yes/no questions related to the diagnosis. Scoring of SCID proceeds in stages and uses a decision tree approach to evaluate a specific diagnosis and skip unrelated questions or entire diagnostic sections. Since the questions evaluate a broad range of mental disorders, SCID can diagnosis symptoms that are co-current with PTSD such as depression, anxiety, or substance abuse [15].

PTSD symptom Scale-Interview (PSS-1) is a 17-item interview with the goal of assessing PTSD symptoms in the past month and the frequency and intensity of those symptoms based on the 20-DSM-5 PTSD symptoms. Patients are supposed to rate their symptoms on a scale of 0 to 4 where 0 indicates no symptoms experienced and 4 is extreme symptoms experienced. The sum of the PTSD symptoms for all 20 questions will yield a total PTSD severity score that will range between 0-80 (80 being the most severe) [16].

The composite international diagnostic interview (CIDI) was developed by WHO and has been used primarily for bipolar spectrum disorders but has also been used for the diagnosis of PTSD [17]. Using algorithms, CIDI provides both lifetime and current diagnosis that is defined by DSM-IV. CIDI focuses on modules during the interview process. Patients are asked questions regarding sadness/depression, feelings of discouragement, and loss of interest. If a patient answers yes to any of those questions they are given a particular module focused on a particular topic [18]. The Generalized Anxiety Disorder scale (GAD-7) is a frequent subjective assessment used for the initial screening, diagnosing, and assessing anxiety disorders including PTSD [19-22]. The assessment consists of seven questions ranked on a scale of 0 to 3. A choice of 0 states that the patient is not experiencing the symptom in the question and a choice of 3 states that the patient is experiencing the symptom nearly every day. A GAD-7 score is obtained by adding the score for each question. A higher score indicates more severe anxiety. GAD-7 scores can range from 0 to 21 and cut-off scores for mild, moderate, and severe anxiety are 5, 10, and 15 respectively.

The PTSD checklist has two versions, the civilian version (PCL-C) and the military version (PCL-M). PCL-C is generally applied to a traumatic event experienced by an individual. The latest version of PCL-C corresponds to DSM-5 [23]. This questionnaire is a self-reporting scale for PTSD and contains 17 questions that correspond to key symptoms of PTSD. Questions are often phrased if the said symptom has bothered the patient in the past month, week, or year etc. Patients indicate how much they have been bothered by a symptom using a 5-point scale (1 is not at all and 5 is extremely bothered).

Objective Assessments using Electroencephalography

Standard interviews and questionnaires have been long established and administered by clinicians for decades. Although they are useful in a wide range of clinical settings, there are several disadvantages of using a questionnaire-based approach because words can be misinterpreted, objective and subjective biases can arise, and there could be difficulties in assessing the severity of symptoms [24]. The evaluation of symptoms that are gathered by interviews and questionnaires can however provide a guide for employing both neurocognitive tests and electroencephalography (EEG) based methods.

Originally, EEGs were developed to understand rapid eye movement (REM) during sleep, but it can also be used to detect mental illnesses that affect brain activity such as PTSD. Neuroscientists have taken advantage of EEG methods for the diagnosis, prevention, and treatment of PTSD [25]. EEG is a neuroimaging tool that uses electrodes placed on the scalp to measure electrical activity from the brain over time while the individual is in an uncontrolled resting state or an active task session. The brain processes information by electrical activity in the form of action potentials-nerve impulses that are transmitted from neuron to neuron. EEG scanners measure changes in electrical activity that are graphed over a period of time to indicate the level or degree of activity in the brain.

EEG signals can be extracted and analyzed by either the frequency domain or the time domain. The frequency domain records continuous EEG signals as a function of frequency bands while the patient is in an uncontrolled resting state-eyes closed or open, focusing their attention on a cross in the center of a computer screen [25]. The four types of EEG patterns include: delta, theta, alpha, and beta waves. Clinicians examine two wave patterns: amplitude (intensity or size of an activity) and frequency (speed or quantity of an activity). In the frequency domain analysis, Fast Fourier Transform (FFT) is used to evaluate the range of frequencies occurring and changes in the EEG patterns mentioned earlier. Alpha power is recorded in the left and right hemisphere to evaluate changes in cortical activity. Frontal cortical activity is computed as F7, F3, F4, and F8 while temporal/parietal activity is computed as T5, P3, P4, and T6. These cortical activities are measured based on the placement of the EEG electrodes along the scalp.

The time domain uses continuous EEG data that is segmented into trials that are time locked to a particular response. Patients are provided a stimulus such as visual or auditory that are either neutral, elicit an emotional response, or induce trauma to study the attention, stimulus evaluation, conflict processing, and memory. Each trial is averaged together to evaluate the response toward the event based on what is called event related potentials (ERPs). ERPs are defined as the brain's response to specific stimuli such as sensory, cognitive, or motor. In patients with PTSD, studies often use ERPs to focus on emotional processing abnormalities that are used to

respond to the various stimuli presented. Additionally, ERPs have been used to try to correct ways in which PTSD patients respond to events presented to them that worsen their PTSD [25]. ERPs are analyzed by looking at the differences in the amplitude and latency between stimulus conditions. ERP amplitude is the difference between pre-stimulus (baseline) and the largest waveform peak observed within a particular time frame to the stimulus onset.

EEGs have become a powerful tool in both diagnosing and treating PTSD. EEG recordings of the brain's frontal asymmetry has been considered a useful way to diagnose PTSD. Frontal asymmetry is considered a biomarker of PTSD because changes in the emotions and behaviors of those exposed to stressful situations can be detected in this region of the brain [26]. Changes in frontal asymmetry is the difference between the mean alpha band power between the left and right frontal cortex over several minutes which is measured by EEG. In the literature, there is debate about the degree to which PTSD is associated with frontal asymmetry because changes exhibited by PTSD patients are similar to those with depression or other anxiety disorders. These similarities may make it increasingly difficult to differentiate between PTSD or other psychological illnesses. Second, the EEG data collected by the frontal asymmetry region in PTSD patients is inconsistent. These inconsistencies could be due to differences in the method used across studies [26]. For instance, frontal asymmetry EEG results can differ when patients are at a resting-state versus stimulated by visual cues. At resting-state, EEG measurements failed to show any differences in frontal asymmetry when PTSD patients were compared to controls. However, in another study when patients were subject to emotional interventions such as showing patients pictures which aroused fear or trauma, there were differences demonstrated in frontal asymmetry [27]. The link between EEG frontal asymmetry and PTSD appears to be promising at linking the neuropsychological abnormalities seen in PTSD, however, frontal asymmetry by itself is not sufficient.

EEG recordings are beneficial at diagnosing and evaluating PTSD during resting-state. In one study, resting state EEGs were used to evaluate PTSD caused by blast exposure and mild traumatic brain injury (TBI) in 147 veterans during Operation Iraqi Freedom and Operation Enduring Freedom. During their evaluation, each participant completed the PTSD checklist (PCL) and for 10 minutes, their resting-state EEG was assessed while their eyes were closed. EEG recordings predicted some PTSD symptom factors including avoidance and numbing when observing changes in patient brainwave activity [28]. This study also highlighted that TBIs may increase the risk of PTSD in veterans.

A second study demonstrated that sleep EEGs reveal brain biomarker activity in PTSD patients that could be utilized to determine the presence and severity of PTSD symptoms [29]. EEG data during sleep and wake states was collected from approximately 76 veterans with and without PTSD. Brain coherence markers (BCM) were calculated from EEG recordings to produce an index for PTSD diagnosis as PTSDdx and PTSD severity as PTSDsev. These indexes were used to compute differences in EEG recordings from PTSD versus non-PTSD veterans to determine PTSD markers.

Overall, EEGs are beneficial for diagnosing PTSD in a clinical setting because it is (1) non-invasive, (2) has excellent temporal resolution that can facilitate studying cognitive and emotional processes, (3) has large-scale spatial resolution to pick up on where signals occur in the brain, and (4) mobile EEG systems are becoming more readily available and accessible [25].

Techniques such as real-time EEG neurofeedback or using functional magnetic resonance imaging (fMRI) concurrently with EEG have been used to help patients reduce their PTSD symptoms and restore brainwave responses. Real-time EEG neurofeedback is a technique that provides patients with a set of instructions to either increase or decrease an activity within a certain frequency band at a particular cortical region [30]. These activities are usually emotional or cognitive strategies performed by the patient such as thinking about a positive memory or engaging in a particular task. Real-time EEG protocols often focus on training related to the alpha/theta brain wave ratio or alpha brain waves only. As the patient performs their activity, EEG data is processed during the recording and patients will immediately know whether they succeeded to change their brain wave activity output [31,32].

Another technique is fMRI, an imaging method that detects changes in the brain metabolism that results from changes associated with task-induced cognitive state changes. Using fMRI with EEG helps to enhance spatial targeting of neurofeedback to lower hyperarousal symptoms experienced by PTSD patients [33-35]. For example, one study used EEG and fMRI to measure anxiety and arousal in a group of 21 individuals that have PTSD resulting from childhood abuse [35]. These individuals underwent 30 minutes of EEG neurofeedback training followed by a resting-state fMRI scan. For the first time, this study found a spontaneous EEG 'rebound' state after neurofeedback. This result demonstrated that there are compensatory mechanisms operating in the brain to alleviate PTSD related symptoms such as increased calmness.

Although fMRI is promising in examining PTSD, the procedure is costly, complex to perform, and has a poor time resolution. EEG techniques such as quantitative EEG analysis (QEEG) and low-resolution electrical tomographic analysis (LORETA) is less complex and costly. Raw EEG data can be analyzed visually or by computerized QEEG analysis which is more reliable and valid. However, the issue with QEEG analysis is that there are several studies with conflicting results. One study compared 18 unmedicated PTSD veterans to 20 controls [36]. They found that PTSD patients had an increase in theta power and beta activity with no significant difference for delta and alpha activity. On the contrary, a second study measured the alpha activity in a group of female veterans with and without PTSD [37]. They found that there was higher alpha activity in the right parietal lobe. Due to conflicts in existing literature for QEEG, another possible EEG technique is using low-resolution electrical tomographic analysis (LORETA). This technique mathematically analyzes EEG signals over the scalp to determine their source wi-

thin the brain's cortex. The LORETA time resolution is considered 3-fold better than that of fMRI. One study used QEEG and LORETA to compare EEGs differences between PTSD and control patients [38]. QEEG did not detect any significant difference for the theta band between PTSD and control groups. LORETA found that the lower theta band was significantly lower in PTSD patients and that the higher theta band had lower activity in the right and left frontal lobes. This study demonstrates that combining QEEG and LORETA methods may improve the resolution of EEG data analysis. Additionally, LORETA could provide an important brain mapping technique to detect changes in the neural network of patients with PTSD which may go undetected when looking at QEEG alone.

Posttraumatic Stress and the Electrical Activity of the Brain

The most reliable and suitable assessment of PTSD is looking at the P300 (P3) wave because it is well documented and conveys information about attention and working memory. P3 is an event related potential associated with cognitive function in decision-making processes. The signal is measured most strongly by electrodes covering the parietal lobe and the P300 refers to a spike detected approximately 300ms following a target stimulus. The target stimulus is then altered to create an 'oddball' paradigm which is most commonly auditory. During the paradigm, the patient responds to the infrequent target stimulus. The patient's P300 response is based on the devotion they give to the task and the degree of information processing required. People with PTSD were found to have an increase in P3a (involuntary attention) amplitude compared to those that do not have PTSD when a trauma-related distractor was used. P3b (voluntary attention) amplitude was also increased in people with PTSD. When neutral distractions were used, the P3b amplitude was reduced in people with PTSD compared to those that did not have PTSD. Additionally, P3wm (working memory) was reduced in the parietal region of those that have PTSD.

As mentioned previously, alpha, beta, delta, theta, and gamma frequency bands are measured by objective assessments to assess changes in the electrical activity of the brain in PTSD versus non-PTSD patients [25]. The most studied frequency band is the Alpha band which looks at alpha power, peak frequency, asymmetry, and connectivity. It has been said that having a higher alpha power leads to the suppression of task-irrelevant processing. A decreased alpha power is a release from inhibition or degree of cortical activation [39,40]. Patients with PTSD are said to have a lower alpha power [41,42] and higher alpha peak frequency [42,43] compared to those that do not have PTSD. In one study, 184 EEG studies were reviewed that reported differences in frequency bands in the resting state condition (eyes closed versus eyes open) [44]. This study observed these differences across a wide spectrum of psychiatric disorders including PTSD. When eyes were closed there was no significant difference detected in the delta, theta, alpha, or beta bands. However, when eyes were open, PTSD patients showed a significant decrease in all bands except the beta band. Magnitude results for PTSD patients were reported to be 21-22% higher with eyes open for PTSD patients compared to eyes closed. Alpha brain asymmetry looks at hemispheric differences of alpha band activity using an EEG asymmetry score which is scored by subtracting left from right alpha power. A positive score on the asymmetry metric indicates increased activity within the left hemisphere. Negative scores indicate increased activity within the right hemisphere [45,46]. Greater left activity is said to correspond to heightened approach-related motivation/emotional response where greater right activity reflects a more withdrawal response. PTSD patients associate more with relative right frontal asymmetry [47]. However, EEG asymmetry results can be somewhat inconsistent. In one study it was shown that boys who experienced increased trauma had increased left frontal asymmetry rather than right symmetry [48]. The same result was obtained for mixed gender studies [49]. It is suggested that these differences could be due sex differences, depression linked with PTSD, recruitment of wrongful controls to compare PTSD patients to, or differences in the trauma experienced.

Beta bands correspond to an individual's current cognitive or motor state. An individual who is in an active conversation would be in beta. Beta waves are high when a person is actively engaged in a task. Beta waves can be split into three sections: low beta waves (12.5-16Hz, "Beta 1"), Beta Waves (16.5-20Hz, "Beta 2), and High Beta Waves (20.5-28Hz, "Beta 3"). The Beta 2 band is useful in helping diagnose PTSD and it is very common to see patients with anxiety have an abnormal increase on Beta2 [50]. Excessive beta activity can cause an individual to become tense, nervous, and sweaty. Physical symptoms present as sweaty palms and racing heart. These symptoms are often associated with PTSD as many patients with PTSD also experience an increase in anxiety levels. Generally, a higher beta power is thought to be cognitive or behavioral inflexibility [25]. There are conflicting findings regarding beta band oscillations in those with PTSD. Two studies suggest that beta power is negatively correlated in those with PTSD [42,51]. A separate study reported that there are no differences in the beta band when comparing those with and without PTSD [52].

Delta band activity is associated with rapid eye movement during sleep [53]. In one study it was reported that delta band activity has no differences between PTSD and non-PTSD patients [36]. On the contrary, a second study demonstrated that there is a decrease in delta sleep activity and endocrine response to metyrapone challenge in male subjects with PTSD [54].

Theta bands are neural oscillations that occur in the brain that have to do with various aspects of cognition and behavior processing such as learning, memory, and spatial navigation. Again, results for changes in the theta band for PTSD patients are mixed. There are several studies that show higher theta power in PTSD patients that were exposed to trauma compared to non-PTSD patients [36,55,56], other studies reported an opposite pattern where the theta power in PTSD patients was lower [38,42], and other studies report no differences in theta power [43,52]. Generally, patients that experience PTSD have a cognitive decline because of alcohol

abuse, depression, and anxiety. All these sub-related clinical conditions are related to an increase on Theta and a decrease on alpha brain waves [57,58].

Gamma bands are used for various cognitive processes and multisensory stimulus. Two separate studies report on two different results, one study demonstrates that PTSD patients have lower gamma bands [59] and another study shows that PTSD patients have higher gamma bands [60].

Brainview

Brainview by Medeia is a new and novel EEG computer-based technology that has been FDA-approved and can help aid in the management of brain health and diagnostics [1,2]. The Brainview system is a software that acquires, displays, and stores electrical activity of the patient's brain. The built-in software can assess multiple EEG wave forms including alpha, beta, theta, and gamma frequency bands during resting state. The patient is required to wear an electrode cap as they take a cognitive assessment test that obtains EEG recordings by scoring their brain's performance on memory, attention, information processing, and executive function. The test is approximately 25 minutes and is non-invasive. The output provided by the system is a neuro-functional physiology report of the results, data summary, raw data, and images. The purpose of Brainview was designed to help both the physician and patient with their diagnosis. Additionally, Brainview can help measure biomarkers related to PTSD that can aid in the diagnosis of a patient experiencing PTSD symptoms. Before Brainview was invented, EEG technology was not portable, the software was complicated and not practical to use in a medical practice. Brainview is a more ideal EEG method because it can be used by primary care physicians rather than specialty physicians only.

Brainview has been used recently to investigate two age groups with PTSD and compare them to individuals without PTSD. These age groups include 38 patients in the age group 17-35 years old and 55 patients in the age group 30-60 years old. In the PTSD age group from 17-35 years old with eyes closed, we have found that there is a difference in: the Alpha2 (10-12Hz) Z-Score increasing with a sensitivity of 62.63 and specificity of 59.81, the Alpha/Beta2 ratio increasing with a sensitivity of 61.07 and specificity of 62.45, the Beta1/Beta2 ratio increasing with a sensitivity of 59.33 and specificity of 67.86, the Beta2a Z-score increasing with a sensitivity of 68.83 and specificity of 61.24, the Beta2/Beta3a ratio increasing with a sensitivity of 61.61 and specificity of 58.32, the Beta2/Beta3 ratio increasing with a sensitivity of 61.91 and specificity of 57.55, the Beta2 Z-Score increasing with a sensitivity of 61.80 and specificity of 62.08, and the Theta/Beta3a ratio increasing with a sensitivity of 51.21 and specificity of 50.78. In the same age group with eyes open, we have found there is a difference in: Beta1/Beta2 ratio increasing with a sensitivity of 59.59 and specificity of 60.87, Beta2 Z-Score increasing with a sensitivity of 59.79 and specificity of 59.20, Beta3 relative power increasing with a sensitivity of 60.53 and specificity of 59.64, and Theta1/Beta2 ratio increasing with a sensitivity of 59.38 and specificity of 60.10.

In the PTSD age group from 30-60 years old with eyes closed, we have found that there is a difference in: the Alpha Z-Score increasing with a sensitivity of 62.45 and specificity of 58.45, the Beta1/Beta2 ratio increasing with a sensitivity of 58.75 and specificity of 58.25, the Beta2a/Beta2b ratio increasing with a sensitivity of 69.03 and specificity of 65.53, the Beta2a Z-score increasing with a sensitivity of 57.85 and specificity of 57.24, the Beta2/Beta3a ratio increasing with a sensitivity of 61.70 and specificity of 61.16, the Beta2/Beta3 ratio increasing with a sensitivity of 59.95 and specificity of 59.80, the Beta2b relative power increasing with a sensitivity of 67.10 and specificity of 61.56, the Beta2b Z-score increasing with a sensitivity of 67.67 and specificity of 63.47, the Beta3a relative power increasing with a sensitivity of 63.28 and specificity of 60.74, the Beta3a Z-Score increasing with a sensitivity of 64.65 and specificity of 63.94, the Beta3 Z-Score increasing with a sensitivity of 63.84 and specificity of 62.67, and the Theta3 relative power increasing with a sensitivity of 60.07 and specificity of 65.06.

Currently, a clinical study is planned to be conducted between 2022-2023 using the Brainview QEEG technology, sponsored by Medeia Inc. This study is aimed at demonstrating both the safety and efficacy of EEG Normative Database measurement technology. Data will be collected from 4,000 patients ages 2 to 95 from various neurology offices using Brainview QEEG as a standard diagnostic tool over the last 5 years. During this study, patients will be required to wear an EEG electrode cap to document their brain activity results and they will answer neuropsychological questions. Medeia Inc will receive these de-identified questionnaires and BrainView EEG results to determine whether BrainView results correlates with clinical diagnosis.

Conclusion

Diagnostic techniques for PTSD have evolved with the development of multiple psychometric instruments, including CAPS, SCID, PSS-I, CIDI, GAD-7, and PCL for civilians. Most of these instruments required clinician for administration and subjective interpretation, with the exception of GAD-7 and PCL that can be self-administered and interpreted by the patients. The reliance on subjective tests however means the possibility of missing diagnosis, especially with the frequently co-occurring depression, anxiety, or substance use disorder in these patients. As a more objective instrument, EEG use has been developed to diagnose and differentiate PTSD from other psychiatric disorders. BrainView EEG system is the most current attempt at improving the sensitivity and specificity of EEG for this use.

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References

1. Miranda P, Cox CD, Alexander M, Danev S, Lakey J (2019) Event related potentials (erps) and alpha waves in cognition, aging and selected

dementias: A source of biomarkers and therapy. Integrative Molecular Medicine 6: 1-12.

2. Miranda P, Cox CD, Alexander M, Danev S, Lakey J (2019) Overview of current diagnostic, prognostic, and therapeutic use of eeg and eeg-based markers of cognition, mental, and brain health. Integrative Molecular Medicine 6: 1-9.

3. Turnbull GJ (1998) A review of post-traumatic stress disorder. Part i: Historical development and classification. Injury 29(2): 87-91.

4. Crocq MA, Crocq L (2000) From shell shock and war neurosis to posttraumatic stress disorder: A history of psychotraumatology. Dialogues Clin Neurosci 2(1): 47-55.

5. Brewin CR, Cloitre M, Hyland P, Shevlin M, Maercker A, et al. (2017) A review of current evidence regarding the icd-11 proposals for diagnosing ptsd and complex ptsd. Clin Psychol Rev 58: 1-15.

6. Maercker A, Brewin CR, Bryant RA, Cloitre M, Reed GM, et al. (2013) Proposals for mental disorders specifically associated with stress in the international classification of diseases-11. Lancet 381(9878): 1683-1685.

7. Goldstein RB, Smith SM, Chou SP, Saha TD, Jung J, et al. (2016) The epidemiology of dsm-5 posttraumatic stress disorder in the united states: Results from the national epidemiologic survey on alcohol and related conditions-iii. Soc Psychiatry Psychiatr Epidemiol 51(8): 1137-1148.

8. Taylor Desir M. What is posttraumatic stress disorder (ptsd)?.

9. Weathers FW, Keane TM, Davidson JR (2001) Clinician-administered ptsd scale: A review of the first ten years of research. Depress Anxiety 13(3): 132-156.

10. Blake DD, Weathers FW, Nagy LM, Kaloupek DG, Gusman FD, et al. (1995) The development of a clinician-administered ptsd scale. J Trauma Stress 8(1): 75-90.

11. Weathers FW, Bovin MJ, Lee DJ, Sloan DM, Schnurr PP, et al. (2018) The clinician-administered ptsd scale for dsm-5 (caps-5): Development and initial psychometric evaluation in military veterans. Psychol Assess 30(3): 383-395.

12. Spitzer RL, Williams JB, Gibbon M, First MB (1992) The structured clinical interview for dsm-iii-r (scid). I: History, rationale, and description. Arch Gen Psychiatry 49(8): 624-629.

13. Brodey B, Purcell SE, Rhea K, Maier P, First M (2018) Rapid and accurate behavioral health diagnostic screening: Initial validation study of a web-based, self-report tool (the sage-sr). J Med Internet Res 20(3): e108.

14. Roelofs J, Muris P, Braet C, Arntz A, Beelen I (2015) The structured clinical interview for dsm-iv childhood diagnoses (kid-scid): First psychometric evaluation in a dutch sample of clinically referred youths. Child Psychiatry Hum Dev 46(3): 367-375.

15. Renaud F, Jakubiec L, Swendsen J, Fatseas M (2021) The impact of co-occurring post-traumatic stress disorder and substance use disorders on craving: A systematic review of the literature. Front Psychiatry 12: 786664.

16. Foa EB, Tolin DF (2000) Comparison of the ptsd symptom scale-interview version and the clinician-administered ptsd scale. J Trauma Stress 13(2): 181-191.

17. Kessler RC, Akiskal HS, Angst J, Guyer M, Hirschfeld RM, et al. (2006) Validity of the assessment of bipolar spectrum disorders in the who cidi 3.0. J Affect Disord 96(3): 259-269.

18. Gelaye B, Williams MA, Lemma S, Deyessa N, Bahretibeb Y, et al. (2013) Diagnostic validity of the composite international diagnostic interview (cidi) depression module in an east african population. Int J Psychiatry Med 46(4): 387-405.

19. Jordan P, Shedden Mora MC, Lowe B (2017) Psychometric analysis of the generalized anxiety disorder scale (gad-7) in primary care using modern item response theory. PLoS One 12(8): e0182162.

20. Plummer F, Manea L, Trepel D, and McMillan D (2016) Screening for anxiety disorders with the gad-7 and gad-2: A systematic review and diagnostic metaanalysis. Gen Hosp Psychiatry 39:24-31.

21. Kroenke K, Spitzer RL, Williams JB, Monahan PO, Lowe B (2007) Anxiety disorders in primary care: Prevalence, impairment, comorbidity, and detection. Ann Intern Med 146(5): 317-325.

22. Spitzer RL, Kroenke K, Williams JB, Lowe BA (2006) brief measure for assessing generalized anxiety disorder: The gad-7. Arch Intern Med 166(10): 1092-1097.

23. Blevins CA, Weathers FW, Davis MT, Witte TK, Domino JL (2015) The posttraumatic stress disorder checklist for dsm-5 (pcl-5): Development and initial psychometric evaluation. J Trauma Stress 28(6): 489-498.

24. Hall JA (2011) Clinicians' accuracy in perceiving patients: Its relevance for clinical practice and a narrative review of methods and correlates. Patient Educ Couns 84(3): 319-324.

25. Butt M, Espinal E, Aupperle RL, Nikulina V, Stewart JL (2019) The electrical aftermath: Brain signals of posttraumatic stress disorder filtered through a clinical lens. Front Psychiatry 10:368.

26. Meyer T, Smeets T, Giesbrecht T, Quaedflieg CW, Smulders FT, et al. (2015) The role of frontal eeg asymmetry in post-traumatic stress disorder. Biol Psychol 108:62-77.

27. Rabe S, Beauducel A, Zollner T, Maercker A, Karl A (2006) Regional brain electrical activity in posttraumatic stress disorder after motor vehicle accident. J Abnorm Psychol 115(4): 687-698.

28. Sheerin CM, Franke LM, Aggen SH, Amstadter AB, Walker WC (2018) Evaluating the contribution of eeg power profiles to characterize and discriminate posttraumatic stress symptom factors in a combat-exposed population. Clin EEG Neurosci 49(6): 379-387.

29. Modarres MH, Opel RA, Weymann KB, Lim MM (2019) Strong correlation of novel sleep electroencephalography coherence markers with diagnosis and severity of posttraumatic stress disorder. Sci Rep 99(1): 4247.

30. du Bois N, Bigirimana AD, Korik A, Kethina LG,Rutembesa E, et al. (2021) Neurofeedback with low-cost, wearable electroencephalography (eeg) reduces symptoms in chronic post-traumatic stress disorder. J Affect Disord 295:1319-1334.

31. Panisch LS, Hai AH (2020) The effectiveness of using neurofeedback in the treatment of post-traumatic stress disorder: A systematic review. Trauma Violence Abuse 21(3): 541-550.

32. Reiter K, Andersen SB, Carlsson J (2016) Neurofeedback treatment and posttraumatic stress disorder: Effectiveness of neurofeedback on posttraumatic stress disorder and the optimal choice of protocol. J Nerv Ment Dis 204(2): 69-77.

33. Zotev V, Phillips R, Misaki M, Wong CK, Wurfel BE, et al. (2018) Real-time fmri neurofeedback training of the amygdala activity with simultaneous eeg in veterans with combat-related ptsd. Neuroimage Clin 19: 106-121.

34. Nicholson AA, Rabellino D, Densmore M, Frewen PA, Paret C, et al. (2018) Intrinsic connectivity network dynamics in ptsd during amygdala downregulation using real-time fmri neurofeedback: A preliminary analysis. Hum Brain Mapp 39(11): 4258-4275.

35. Kluetsch RC, Ros T, Theberge J, Frewen PA, Calhoun VD, et al. (2014) Plastic modulation of ptsd resting-state networks and subjective wellbeing by eeg neurofeedback. Acta Psychiatr Scand 130(2): 123-136.

36. Begic D, Hotujac L and Jokic Begic N (2001) Electroencephalographic comparison of veterans with combat-related post-traumatic stress disorder and healthy subjects. Int J Psychophysiol 40(2):167-172.

37. Metzger LJ, Paige SR, Carson MA, Lasko NB, Paulus LA, et al. (2004) Ptsd arousal and depression symptoms associated with increased right-sided parietal eeg asymmetry. J Abnorm Psychol 113(2): 324-329.

38. Todder D, Levine J, Abujumah A, Mater M, Cohen H(2012) The quantitative electroencephalogram and the low-resolution electrical tomographic analysis in posttraumatic stress disorder. Clin EEG Neurosci 43(1): 48-53.

39. Roux F, Uhlhaas PJ (2014) Working memory and neural oscillations: Alpha-gamma versus theta-gamma codes for distinct wm information? Trends Cogn Sci 18(1): 16-25.

40. Klimesch W (2012) Alpha-band oscillations, attention, and controlled access to stored information. Trends Cogn Sci 16(12):606-617.

41. Veltmeyer MD, McFarlane AC, Bryant RA, Mayo T,Gordon E, et al. (2006) Integrative assessment of brain function in ptsd: Brain stability and working memory. J Integr Neurosci 5(1): 123-138.

42. McFarlane A, Clark CR, Bryant RA, Williams LM, Niaura R, et al. (2005) The impact of early life stress on psychophysiological, personality and behavioral measures in 740 non-clinical subjects. J Integr Neurosci 4(1): 27-40.

43. Wahbeh H, Oken BS (2013) Peak high-frequency hrv and peak alpha frequency higher in ptsd. Appl Psychophysiol Biofeedback 38(1): 57-69.

44. Newson JJ, Thiagarajan TC (2018) Eeg frequency bands in psychiatric disorders: A review of resting state studies. Front Hum Neurosci 12: 521.

45. Smith EE, Reznik SJ, Stewart JL, Allen JJ (2017) Assessing and conceptualizing frontal eeg asymmetry: An updated primer on recording, processing, analyzing, and interpreting frontal alpha asymmetry. Int J Psychophysiol 111: 98-114.

46. Allen JJ, Coan JA, Nazarian M (2004) Issues and assumptions on the road from raw signals to metrics of frontal eeg asymmetry in emotion. Biol Psychol 67(1-2): 183-218.

47. Tang A, Miskovic V, Lahat A, Tanaka M, MacMillan H (2018) Van Lieshout, R.J.; Schmidt, L.A. Trajectories of resting frontal brain activity and psychopathology in female adolescents exposed to child maltreatment. Dev Psychobiol 60(1): 67-77.

48. Cicchetti D, Curtis WJ (2007) Multilevel perspectives on pathways to resilient functioning. Dev Psychopathol 19(3): 627-629.

49. Meyer T, Quaedflieg C, Weijland K, Schruers K, Merckelbach H (2018) Frontal eeg asymmetry during symptom provocation predicts subjective responses to intrusions in survivors with and without ptsd. Psychophysiology 55(1).

50. Ribas VR, Ribas RG, Nobrega JA, da Nobrega MV, Especie JAA (2018) Pattern of anxiety, insecurity, fear, panic and/or phobia observed by quantitative electroencephalography (qeeg). Dement Neuropsychol 12(3): 264-271.

51. Cowdin N, Kobayashi I, Mellman TA (2014) Theta frequency activity during rapid eye movement (rem) sleep is greater in people with resilience versus ptsd. Exp Brain Res 232: 1479-1485.

52. Falconer EM, Felmingham KL, Allen A, Clark CR, McFarlane AC, et al. (2008) Developing an integrated brain, behavior and biological response profile in posttraumatic stress disorder (ptsd). J Integr Neurosci 7(3): 439-456.

53. Knyazev GG (2012) Eeg delta oscillations as a correlate of basic homeostatic and motivational processes. Neurosci Biobehav Rev 36(1): 677-695.

54. Neylan TC, Otte C, Yehuda R, Marmar CR (2006) Neuroendocrine regulation of sleep disturbances in ptsd. Annals of the New York Academy of Sciences 1071: 203-215.

55. Bangel KA, van Buschbach S, Smit DJA, Mazaheri A, Olff M (2017) Aberrant brain response after auditory deviance in ptsd compared to trauma controls: An eeg study. Sci Rep 7(1): 16596.

56. Imperatori C, Farina B, Quintiliani MI, Onofri A, Castelli Gattinara P (2014) Aberrant eeg functional connectivity and eeg power spectra in resting state post-traumatic stress disorder: A sloreta study. Biol Psychol 102: 10-17.

57. Dunkley BT, Sedge PA, Doesburg SM, Grodecki RJ and Jetly R Theta, et al. (2015) mental flexibility, and post-traumatic stress disorder: Connecting in the parietal cortex. PLoS One 10(4):e0123541.

58. Rangaswamy M, Porjesz B, Chorlian DB, Choi K, Jones KA, et al. (2003) Theta power in the eeg of alcoholics. Alcohol Clin Exp Res 27(4): 607-615.

59. Lee SH, Yoon S, Kim JI, Jin SH, Chung CK (2014) Functional connectivity of resting state eeg and symptom severity in patients with post-traumatic stress disorder. Prog Neuropsychopharmacol Biol Psychiatry 51: 51-57.

60. Ehlers CL, Hurst S, Phillips E, Gilder D A, Dixon M (2006) Electrophysiological responses to affective stimuli in american indians experiencing trauma with and without ptsd. Annals of the New York Academy of Sciences 1071: 125-136.