



Referenced-EEG[®] (rEEG[®]) An Introductory Guide to EEG Recording

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What is Referenced-EEG (rEEG®)?

Referenced-EEG (rEEG®) is a fundamentally new electroencephalographic technology that assists physicians in selecting specific medications appropriate to the specific physiologic abnormalities found in neurobehaviorally disordered patients. Simply put, *rEEG® is the first neurophysiologic assessment tool that helps physicians provide more effective medication management.*

Why is rEEG® needed?

The modern medical model is based upon symptom-based medical practice and pathophysiologic measurement. Psychiatry is unfortunately unique among medical specialties in its lack of such measurement. This has hindered both the advancement of psychiatry in general, and clinical practice in particular. In the current therapeutic model, psychiatrists choose medications based on patient symptoms and behaviors. Significant limitations result since mental illness features do not have a simple relationship with medication response. Without a defined pathologic abnormality to treat and a physiologic marker to guide treatment, psychiatrists and other providers have been forced into the position of choosing between hundreds of psychotropic medications in a somewhat hit-or-miss fashion.

The search for a pathophysiologic marker

Over the last fifty years, many neuroscientists have worked at adapting the medical model to neurobehavioral disorders. Researchers have sought a biomarker to identify differences in brain function and better correlate medical treatment. This can be observed in the growth of various quantitative technologies, including those that depend on blood flow (PET, SPECT and fMRI) and those that measure brain electrical activity (EEG and QEEG). Pioneering research work has resulted in the development of quantitative, age specific values for the resting EEG in *asymptomatic* individuals. Researchers have also documented the reliability of the background resting EEG in clinical settings through stability and reproducibility studies. In addition, automated signal analytic capacity has increased dramatically and ultimately instrument manufacturers have produced reliable equipment suitable for clinical use. The principle thrust of this work was the use of baseline, age adjusted normative values to identify abnormalities that might assist in the objective diagnosis of major disorders.

The Theoretical Basis for rEEG[®]

The hypothesis behind rEEG[®] is radically different: Are there physiological markers of abnormality that associate with effectiveness of specific pharmacotherapies, *independent of DSM or ICD diagnosis*? Testing this hypothesis required an additional dataset of *symptomatic* patients responsive to pharmacotherapy. Over the course of the last fifteen years, the developers of rEEG[®] have collected data from over 2,500 patients and more than 7,500 medication change and outcome data points. The developers used an exhaustive procedure to qualify data points for inclusion in the database, as validity of clinical assessments in the database was crucial. The resulting dataset enabled the definition of mathematical relationships for different medications and made possible a report of the likelihood that a patient with a given abnormality will respond to different medications.

The use of rEEG[®]

rEEG[®] uses proprietary EEG analysis techniques from CNS Response, Inc. It is based upon a standard 19-21lead digital electroencephalographic (EEG) recording completed with a patient in an eyes closed, and alert state. The EEG recording must occur when a patient is medication free and can generally be completed in 30 to 60 minutes. When completed, the digital EEG record is uploaded to CNS Response FTP site for rEEG[®] analysis or send a CD to our Costa Mesa office.

CNS Response essentially acts as a reference laboratory by providing reports to help prescribing professionals determine the most effective medication management for their patients. These reports classify patients based on the 1142 variables calculated in the recording (the FDA – approved neurometric system) and then report on outcome history in treating patients with similar neurophysiologic markers. Reports may indicate single or multiple medications based on the nature of the physiologic abnormality discovered. They may also indicate that brain function is within normal range, suggesting that pharmacotherapy is not indicated or possibly contraindicated. The entire procedure is rapid, non-invasive, and results in a report that is easily used by clinicians given its similarity in format to antibiotic sensitivity testing.

Types of rEEG[®] Testing

An initial rEEG[®] test is called a Type I test and generates pharmacological recommendations based on patient physiology. The Type I test is appropriate for any patient requiring psychiatric medication who is between the ages of 6 years and 80 years of age. It has been studied with treatment resistant

patients, and those who have depression, ADD, eating disorders, as well as addictive disorders. In these cases, in combination with a skilled physician consistently high degrees of efficacy have been reported.

The Type II test occurs after implementation of a medication regime from a Type 1 rEEG[®]. About four to six weeks after achieving a stable therapeutic dosage, a second eyes closed, alert EEG, may be completed with the patient on their current medication. This Type II rEEG will assess the effect, or effects of medication on EEG features, as well as the adequacy of treatment. The Type II rEEG[®] report comments on brain activity and medication dosing. In some ways this report is comparable to a bioassay as used in other fields. A patient is a candidate for Type II testing when the physician has followed original pharmacological recommendations and a sufficient time on those agents has elapsed. If the patient is on only one medication and it is a medication needed in the CNS Response outcomes database, the Type II rEEG[®] may be provided at no cost other than recording fees.

How is the EEG recording involved in the rEEG[®]?

The rEEG[®] requires a clean digital EEG in order to provide an accurate report to the physician for medication response. The person recording the EEG is critical in facilitating an accurate report. In Quantitative EEG (QEEG) there is a saying that "junk in means junk out." This is certainly true for the rEEG[®]. Therefore, one who understands the importance of collecting an EEG that meets the technical requirements for rEEG[®] is essential. It is our hope that in reading this manual, you will understand those requirements and your role in helping patients receive the most accurate report possible.

How can CNS Response, Inc. help you?

It is the goal of CNS Response, Inc. to make working with us as easy as possible. To that end, we hope that you will not hesitate to contact us with any questions, concerns or suggestions that you have to assist you in helping your patients.

What to expect in this manual

In the next few pages, you will find help in how to become a rEEG[®] collection site. You will also find the technical requirements for data collection, as well as some helpful hints we have collected from different rEEG[®] sites. We have addressed specific instructions when they are known and if you are using equipment that is not listed, we will be happy to work with you to get more specific guidelines to assist you.

CNS Response, Inc. Referenced-EEG® (rEEG®) Quick Reference Guide

This guide is to be used as a quick reference for the data collection requirements for a rEEG®. This guide assumes that you have already gone through the rEEG® registration process. If you have not completed the registration process, please contact CNS Response at (888) 545-2677 prior to collecting any patient data for an rEEG® report.

- rEEG® Requisition Form received and signed by referring physician
- Confirm medications the patient has taken, both prescription and over the counter (OTC) and verify that the patient has been off those medications as per the physician's instructions.
- Specifically ask about any herbal supplements the patient may be taking
- No alcohol for at least 2 days
- No nicotine for at least 10 hours
- No caffeine for at least 15 hours
- No street drugs for minimum 5 half lives (See 5 half lives chart)
- Specifically asks about Electro-Convulsive Therapy (ECT)
- 19-21 channel according to the international10/20 system
- Ear lobes used to allow for a linked ear montage
- Sensitivity setting: approx. 7 μ v
- Filter settings: pass all data between .5 and 35 Hz.
- Digitization rates: Must be at least 100 Hz/channel
- Calibration recorded prior to test, according to manufacturer guidelines
- 10-20 minutes of Eyes closed, relaxed, alert data collected
- rEEG® Requisition Form is completed, signed, and faxed to CNS Response, Inc. at: 866-294-2611
- EEG data uploaded to the CNS Response, Inc. FTP Site per instructions

Digital EEG Manufacturers

CNS Response does not endorse any manufacturer over any other.

There are many adequate, commercially available, digital EEG machines that can be used for rEEG[®] recording. The key to an acceptable data base comparison is that the machine must allow data to be output in a format that is supported by Insight or is exportable to Lexicor, EDF or EDF90 file formats.

<http://www.eeg-persyst.com/web/FormatsSupported.html>

At present, the following formats are not supported: Oxford/Teca/Medelec DG compressed

Sites using Neuroscan[®] must record in 16 bit mode.

rEEG[®] Data Collection Guidelines

The rEEG[®] database was collected in a standardized format, using relaxed, but alert, eyes closed data collected using a linked ear reference. The standardization requires that all EEGs that are going to be compared against the database, be collected in this standardized format. This format is not intended as a standard neurological EEG exam, it is a very specific format meant to demonstrate specific results.

The general requirements are as follows:

- 19-21 channel according to the 10/20 system
- Sensitivity setting: approx. 7 μ V
- Filter settings: pass all data between .5 and 35 Hz.
- Digitization rates: Must be at least 100 Hz/channel
- Calibration recorded prior to test, according to manufacturer guidelines
- Ear lobes used to allow for use of a **linked ear reference**.
- Electrode impedance must be **below 5 K Ω** at each electrode and balanced.

EEG Recording Montage

Digital EEG Systems typically allow for scalp recordings to be made using an arbitrary monopolar reference. Analysis software then typically allows for a variety of display montages for viewing and interpretation.

The rEEG[®] database was constructed in a standardized manner using a linked ear reference. Therefore, all data that is compared against the rEEG[®] must

also allow for a linked ear reference. This procedure differs according to different manufacturers specific instructions. Where possible, we have tried to outline more specific instructions for allowing the use of a linked ear reference, but please verify your equipment's instructions prior to any recordings. Please use ear lobes instead of mastoids for these reference locations. (A1A2).

Length of Recordings

In general, EEG recordings should be between 10-20 minutes long. If there is movement by the patient and the EEG record contains significant amounts of artifact, the recording time should be extended to at least 20-25 minutes to help ensure that adequate artifact free EEG is available for analysis. In general, 2 minutes of eyes closed alert, artifact free EEG conforming to these guidelines is required for a rEEG[®] analysis.

Please note that EEG records not meeting the technical requirements, which contain inadequate data, or are rendered un-analyzable due to the presence of artifact, cannot be processed and patients will need to be re-tested.

The rEEG[®] database was only recorded using alert, eyes closed data, therefore, only this state will be analyzed. Please do not include any Eyes Open, Hyperventilation, or Photic stimulation EEG records.

Impedance Checking

All impedances must be balanced and below 5K ohms throughout the recording. If impedances are checked during the recording, please ensure that your equipment **DOES NOT CHANGE THE RECORDING REFERENCE FOLLOWING IMPEDANCE CHECKING**. Changing the recording reference electrode during recording will interfere with, and may invalidate the quantitative analysis and reporting process.

Recording Location

EEG signals are very sensitive to electrical noise that is present in the recording environment. It is important to control the amount of electrical interference in EEG recordings that are made for the purposes of transmission to CNS Response for rEEG[®] analysis. If there are any questions regarding your data collection site, we may work with you to verify that there is no excess electrical interference.

Electrical interference (noise) can come from a variety of sources including:

- Fluorescent lighting
- Computer equipment

- Microwave ovens
- Electrical equipment operating nearby such as elevators or lab equipment
- Cordless phones
- Wireless networks

Choose a recording site away from as many of these potential interference sources as possible. The noise source that is probably the easiest to influence is the type of lighting. Incandescent lighting should be used in the testing room whenever possible. Other potential sources of interference should be turned off or moved as far away from the EEG recording equipment as possible. It may also be valuable to move electrical equipment that cannot be turned off to another outlet in the room provided that outlet is on a different electrical circuit other than the one being used for the EEG recording equipment.

Patient Factors

Medications

In general, accurate comparison to the rEEG[®] database requires one to be medication free. The ideal situation is for the patient to have discontinued all medications for at least 5 half lives of the longest acting agent. All medications can potentially influence the EEG and must be known so that the EEG can be properly interpreted and compared to an appropriate database.

At the time of testing, it is critically important that you record an accurate list of all medications the patient has taken recently, or is currently taking. You will need to note the name, the dosage and the date and time the last dose was taken (date & time). Please note that this also includes all “over the counter” drugs, herbal remedies, drugs of abuse (e.g. cigarettes, alcohol, cannabis, and other drugs) and vitamins and supplements both prescribed and over the counter.

The referring physician will have listed a withdrawal schedule for each medication that the patient is currently taking, on the rEEG[®] requisition form (attached). You must verify at the time of the EEG that the patient has followed all instructions regarding medication withdrawal. If the patient has not followed the withdrawal instructions, or has taken any OTC medications, herbal supplements, vitamins, or illicit drugs inside of the allowed timeframe, please contact CNS Response at (888) 545-2677 and we will help you determine if the EEG will be valid for interpretation. Any medications may prohibit CNS Response, Inc. from creating a rEEG[®] report, or may result in spurious results.

Note that some “medications” are really replacement of natural hormones, e.g. thyroid, insulin, or estrogen, and may not require potential discontinuation prior to baseline examination, and these must still be listed on the rEEG® requisition form. Certain antihypertensive agents ARE included in the reference population for individuals over 50 years of age and thus may not have been discontinued. Please contact CNS Response (888-545-2677) for details of the specific agents that do not have to be potentially discontinued for patients in this age group.

Patient State

Recordings are suitable for rEEG® analysis ONLY if the patient is **awake and alert** and at least 120 seconds of clean, artifact free EEG are available for analysis (e.g., free of muscle or body movement, jaw clenching, swallowing, EKG, eye-movement, etc.). EEG recorded during mild patient drowsiness will be edited out of the record prior to analysis. Further, it is useful to explain to the patient the need to remain motionless, awake, and alert during testing. The person recording the EEG must monitor the EEG for effects of drowsiness while the recording is in progress.

Limiting Artifact

There are a number of potential “contaminants” that can obscure the EEG, which must be eliminated at the time of the recording. **The patient must be instructed to remain as still as possible, they may not talk, and they must minimize any eye movements, including blinking and lateral eye movement.** Often clenching the jaw produces muscle artifact over the temporal scalp, contaminating recording from over these regions.

Common Remedies:

- Having the patient gently rest their fingers on their eyelids during the recording
- Placing cotton balls over the eyelids with medical tape or underneath eye masks
- Even with the eyes closed, sometimes asking the client to focus their eyes downward will help still them
- For EMG: often repeated clenching and releasing of the jaws will lower the EMG
- Having patients slightly open their mouths, without the teeth touching, can help. Sometimes patients may rest their tongue between their teeth, which may also help prevent jaw clenching.
- If the EMG is in the frontal leads, you may ask the patient to scrunch their forehead a few times and then relax. You may also request them to position their eyes (closed) in different positions to see if it releases the tension.

Please remember that a rEEG® report may not be produced if the recording does not contain at least 120 seconds of artifact free data.

EEG Data Transmittal to CNS Response

CNS Response has created a secure FTP Site to allow for all digital EEG data to be uploaded for processing of the rEEG® report. After your site has been registered, you will receive a login name and password and instructions for accessing the FTP site.

If you are unable to access the FTP site, please contact CNS Response at (888) 545-2677.

Responsibility for rEEG® Requisition Form

The rEEG® Requisition Form (available at www.cnsresponse.com) is the form that the physician completes to order a rEEG® report. You will coordinate with the referring physician to determine how you will receive the rEEG® requisition. Often, the physician gives the form to the patient with instructions to bring it to the EEG test appointment and give to the EEG tech. It may also be a good idea to receive a faxed copy directly from the physician prior to the EEG testing.

The professional recording the EEG is responsible for reviewing the "Type I" or "Type II" "Medication List" and confirming with the patient that all listed medications were discontinued as directed by the physician. They should place their initials in far right column if patient has been compliant. **All patients must be asked about new medications, prescribed or over-the-counter, alcohol, nicotine, caffeine, vitamins or herbs that may have been taken.** If the patient is medication free, the EEG recording professional signs their name at the bottom of the page. After the EEG recording has been completed, the form is faxed to CNS Response at the number listed at the top of the form, 866-294-2611. **All rEEG® reports cannot be processed until receipt of the rEEG® Requisition.**

HIPPA Requirements: Disclaimer

CNS Response is aware of your and our responsibilities under HIPPA. Our production systems are secure and password protected. Your data will be uploaded to, and downloaded from the secure site. When you fax information to us, the fax arrives in a secure area and is accessed only by CNS Response employees. If you have specific questions about procedures for handling the EEG data you are submitting, please contact CNS Response.

CNS RESPONSE CONTACT INFORMATION

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