Seizure Response Monitoring During Electroconvulsive Therapy

by

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ABSTRACT

Electroconvulsive Therapy (ECT) is used to treat several mental illnesses. Seizure duration is used to determine if the administered stimulus was adequate. Duration is estimated by Electroencephalogram (EEG) interpretation and/or observing motor response. Neither method is universally accepted, nor considered the gold standard; hence both are employed. This study investigated the relationship between the methods. The hypothesis tested was that they would have a strong positive correlation. Previous research suggested that the two methods didn’t result in the same estimate. A case series was carried out using recorded estimates prospectively obtained from 102 ECT procedures on adult Psychiatric inpatients. A strong, consistent, predictable relationship between the methods was not identified. However, using 15 seconds as the minimum for an adequate seizure response, there was agreement in 77% of the cases. In conclusion, this research has demonstrated that while the two methods differ, similar clinical results can be obtained by applying a limiter to both measures.
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I love you all.
Chapter 1. Introduction

1.1 Electroconvulsive Therapy (ECT)

1.1.1 Background and Use

Electroconvulsive therapy was first developed in 1938, and while its exact mechanism of action has not yet been elucidated, extensive research has demonstrated its efficacy in treating various mental illnesses (Enns, 2010). It is the induced seizure, and not the electricity that is thought to be responsible for the benefits of ECT. There are reports of the use of other seizure inducing methods to treat psychiatric illness as early as the 16th century, as well as accounts of camphor being used to induce seizures from the late 1700’s to mid 1800’s (Sadock, 2007). Hungarian neuropsychiatrist Ladislas Von Meduna compared the number of glial cells in the brains of people with epilepsy to those with schizophrenia. He noted a greater number in the former, and theorized that convulsions may antagonize schizophrenia. Based on his work, animal studies were carried out, and injectable camphor was used to successfully treat catatonia in 1934 (Sadock, 2007). While the mechanism of action of ECT remains elusive, there have been several documented changes in the central nervous system post-ECT and subsequent theories which may help explain some of the treatments benefits (Kellner, 2012). These changes include: increased release of multiple neurotransmitters (dopamine, serotonin, norepinephrine, prolactin, thyroid stimulating hormone, adrenocorticotropic hormone, and endorphins), anticonvulsant properties, improved neural plasticity, decreased
metabolic activity in the frontal and cingulate cortex, altered brain connectivity, and altered EEG waveform post-ECT (Kellner, 2012).

Despite the lack of a clear mechanism of action, there exists an abundance of evidence to support the use of ECT for its primary indications, major depressive disorder, bipolar disorder (manic, depressed, or mixed phase), schizophrenia and its related conditions (schizoaffective disorder, schizophreniform disorder) (Enns, 2010). As it is the seizure which is believed to provide the therapeutic effect of ECT, it is important to ensure that each treatment provokes an adequate seizure.

1.1.2 Description of the ECT Procedure

The procedure involves the use of a brief electrical stimulus applied via electrodes placed on the head to induce a seizure. Before the stimulus is applied, the patient is given a general anesthetic. As well, a paralytic agent is administered to prevent the potential violent tonic clonic motor response of an induced seizure. Once the stimulus has been administered the patient is monitored for seizure response. The American Psychiatric Association recommendations for treatment, training and privileging for the practice of ECT state that, “when seizure duration is less than 15 seconds in both motor (convulsive) and EEG manifestations, the likelihood is high that the seizure was limited by insufficient electrical stimulation (or by other factors…) and that the treatment was inadequate.” (Weiner, 2001). Practically speaking, seizure duration estimation is used to determine if
the stimulus administered resulted in an adequate response. The purpose of ECT is to produce a seizure, as this is felt to be the mechanism through which the treatment provides its’ therapeutic benefit. The electricity does not provide the benefit, the seizure does (Sadock, 2007).

1.1.3 Stimulus Response & Seizure Estimation

The two most commonly used methods to measure seizure duration in response to ECT stimulus are by clinical observation of the motor seizure response, or by using an EEG to indirectly measure electrical activity in the brain. To further complicate the situation, there are two methods each to interpret EEG, and to monitor motor response. The simplest method involves looking at the patient and recording the time from stimulus delivery to cessation of any movement. Even with the paralytic agent, there are usually small high frequency tremor like movements in the fingers, toes and/or face. The other way to monitor motor response is to use the “cuff technique” (Weiner, 2001). This involves using a blood pressure cuff as a tourniquet on an extremity. The cuff is placed prior to administration of the paralytic agent, preventing the drug from reaching the muscles distal to the blood pressure cuff. The advantage of this technique is that it allows for an exaggerated tonic clonic response in the area distal to the cuff relative to the rest of the body. The disadvantage is that a single unilateral extremity is focused on, and movement in other body parts may be missed. When using EEG monitoring, an
experienced physician can interpret the seizure duration, or it can be determined by computer automation.

1.1.4 Literature Relevant to ECT Seizure Estimation

Currently there are no clear guidelines in North America as to the exact seizure duration considered to be adequate, or which method of measuring seizure duration is most appropriate. In the United Kingdom, the National Institute for Clinical Excellence publication, “Guidance on the use of electroconvulsive therapy”, does not include seizure duration recommendations (NICE, 2003). It does however reference the Handbook on ECT published by the Royal College of Psychiatrists in the UK for current standards on ECT (NICE, 2003). This handbook states that, “the treating psychiatrist should question whether or not generalized cerebral seizure activity had occurred if at the first treatment the convulsion lasted less than 15 seconds or the EEG recording showed seizure activity lasting less than 25 seconds” (Waite, 2013). The Canadian Psychiatric Association (CPA) recommend a minimum seizure of 15 seconds as measured by EEG, but they also recommend using both EEG and motor response for monitoring during treatment (Enns, 2010). The psychiatry textbook, authored by Kaplan and Sadock, and endorsed by the CPA recommend a minimum seizure length of 25 seconds, but does not specify if this should be measured by the motor or EEG method. They favor neither EEG nor motor response for monitoring; they simply recommend that at least one of the two methods be used (Sadock, 2007). In 2001, The American Psychiatric Association published
recommendations on the practice of ECT. They stated that when seizure duration is less than 15 seconds in both motor and EEG manifestations, the likelihood is high that the seizure was limited by insufficient electrical stimulation and that the treatment was inadequate. They described the motor method as the simplest and most reliable, and recommend using the Hamilton cuff technique. However, they go on to state that EEG monitoring also be used. The reasons they give include: occasionally patients may have adequate seizures without motor manifestations, EEG seizure is commonly of longer duration than motor movements, and rarely patients may have prolonged seizures or return of seizure activity that do not manifest motor movements (Weiner, 2001). The online medical resource DynaMed recommends a seizure minimum of 15 seconds, but does not specify whether this should be measured via EEG or motor response (2011). They recommend that both EEG and motor response be used to monitor the seizure during treatment (DynaMed, 2011). The online medical resource UpToDate recommends a minimum seizure of 15 seconds by EEG. They state that EEG should always be used and the addition of motor monitoring is up to the discretion of the treating physician (Kellner, 2012). DynaMed and the APA publication were the only resources that could be found that specified which technique to use when monitoring motor response; they recommend using the Hamilton cuff technique. None of the resources specified if the EEG seizure duration should be determined by an experienced physician, or by a machine.

The goal of measuring the seizure duration, regardless of method, is to determine if an adequate seizure has been achieved. Given the lack of clear specific guidelines on
which method should be used to monitor seizures, the literature was reviewed with the following research question in mind. Is there a difference in the duration of monitored seizure during Electroconvulsive Therapy when measured by observed motor response versus EEG monitoring?

1.1.4.1 Search Strategy

A literature search began by using the PubMed and PubMed Clinical Query databases. The following keywords were searched: ECT, electroconvulsive, electroconvulsive shock, electroconvulsive therapy, electroconvulsive treatment, EEG, electroencephalography, electroencephalogram, seizure duration, seizure monitoring. Searches using individual keywords yielded large numbers of articles (range of 4868 – 127,716). Combining the terms resulted in more manageable numbers of articles to review. The combination of electroconvulsive treatment + EEG + seizure monitoring yielded the most reasonable number of papers, 54 in total. Review of these papers revealed only 10 articles that were relevant to the research question.

The Cochrane database was also searched using a similar approach, but no relevant results were found.
Information on ECT was then looked up from two online medical information databases DynaMed and UpToDate. Information on monitoring seizure duration was specifically reviewed, and the references listed as the sources of this data were obtained. The single UpToDate source had also been found in the PubMed search, was relevant to the research question, and was included in this review (Kellner, 2012). The DynaMed sources had no relevance to the research question, nor were they found in the PubMed search.

The Canadian Psychiatric Association website contains their position statement on ECT. Upon review of this, the source references for their information on seizure duration/monitoring were also obtained.

The initial search resulted in a total of 57 articles for review. These articles were then scrutinized to ascertain their relevance to the stated research question. Ten articles were identified as potentially valuable. For the purpose of this review, it was decided that a review of the relevant literature published within the last 20 years would be appropriate. Therefore 4 of the 10 identified papers were excluded because they were published before 1993. Part of the rationale behind this decision was that the APA publication containing recommendations on the practice of ECT had included review of publications up to and including December of 1998. Furthermore, this publication was an update of their 1990 recommendations, which was an update of their 1978 recommendations. As well, this major publication was also the sole reference cited for the CPA recommendations on seizure monitoring and duration. The time limitation resulted in six articles remaining.
Two of these articles entitled, “Merits of EEG Monitoring During ECT: a prospective Study on 485 Patients.”, and “EEG Seizure Duration Monitoring of ECT.”, were excluded from the review. Both of these studies looked at the difference in determining adequate versus prolonged seizure when comparing EEG to motor response. Their results are grouped into categories, and the actual seizure durations are not included. The research question in this review is aimed at identifying a difference between measured seizure duration using EEG versus motor response, not which is more reliable for determining adequate or prolonged seizures. Therefore, they were not applicable to this review. It is worth noting that the most recent article identified as relevant to this research was published in 2003.

1.1.4.2 Appraisal of Relevant Publications

1.1.4.2.1 Electroconvulsive therapy clinics in the United Kingdom should routinely monitor electroencephalographic seizures

The first paper, to be discussed, is the one most recently published entitled “Electroconvulsive therapy clinics in the United Kingdom should routinely monitor electroencephalographic seizures.” (Benbow, 2003). This paper was published in The Journal of ECT in 2003. It consists of a retrospective observational case series that was carried out in Central Manchester in the UK.
The introduction criticizes the Royal College of Psychiatrists for not recommending EEG monitoring in their most recent guidelines. They site the American Psychiatric Association Task Force Report (Weiner, 2001), which recommends a minimum of one channel EEG monitoring. They go on to describe the ECT machine used in their clinic, and its seizure monitoring capabilities. They also explain the importance of detecting prolonged seizures so that steps can be taken to avoid the many adverse effects associated with them. No formal hypothesis or research question was posed anywhere in the article. The only prelude to the intentions of their work was the following statement, “Recently, we analyzed the treatment records to investigate the range of seizure thresholds determined using the protocol and the frequency of prolonged seizures.” (Benbow, 2003). This statement makes no mention of comparing EEG and motor seizure response monitoring, nor does it relate to the title of the paper.

The methods were poorly described. In essence they state that information from ECT diaries was obtained, and “The results were analyzed using SPSS…” (Benbow, 2003). One must assume that since no ad hoc statistical plan or intention was described, that the “results” were analyzed post hoc. The authors made no mention of any inclusion/exclusion criteria, nor did they indicate a timeframe over which the data had been collected. The variables obtained from the ECT diaries included patient age at first ECT treatment, ethnicity, seizure threshold, unilateral versus bilateral stimulus, number of treatments, as well as length of seizure (EEG & Motor). EEG seizure endpoint was computer determined. The motor end point was determined by observation only; the Hamilton cuff technique was not employed. It is stated that the physicians involved were
untrained in interpreting the EEG, but it was not stated if they were aware of the computer interpreted duration, which may have been a source of bias. There was more than one physician involved with ECT, and there may have been interrater error affecting motor response estimation. Neither of these potential biases were addressed by the authors.

The results section indicated that data from 67 individuals who had received 95 courses of ECT were used. The number of treatments per course ranged from 1-20, with a mean of 8.4. Given the large number of variables, and lack of any specific goal, the results of several analyses were reported. The only result relevant to this review was the comparison of EEG versus motor response seizure duration. The paper included figure 1, which shows mean length of motor seizure compared with EEG seizure for treatments 1 through 20.
It appears from the bar graph that EEG seizure duration exceeded observed motor seizure across the board. The authors reported EEG seizure length to be greater than motor for treatments 1-6, 8-10, 12, 13 & 16, with statistical significance using the paired t test. It would have been more appropriate to use a scatter plot including all data points to illustrate the relationship between EEG and motor response.

The discussion states that the data shows a marked difference between EEG and motor seizure response. They did not state that EEG is more sensitive than motor response and it was acknowledged that the disparity in seizure duration might not reflect disparity in seizure quality. Regardless, in the conclusion they went on to recommend EEG be used routinely to aid in detection of prolonged seizure.
Key biases potentially affecting this research include the following. Data was obtained from ECT diaries. It is likely that the treating physicians who were observing the motor response were also privy to the EEG interpreted seizure duration; in the absence of blinding this may have affected results. There may have been interrater variability between the multiple treating physicians involved (EEG electrode placement, motor seizure duration observed, etc…) this was not addressed in the article. There may also have been intrarater variability. No selection or exclusion criteria were provided. All analysis was done post hoc, with no specific research question in mind.

Inferences from post hoc analysis are less than ideal. Keeping that in mind, the authors stated that they had demonstrated a marked difference in seizure duration when using computer interpreted EEG monitoring versus simple motor response observation. They went on to recommend current Royal College guidelines be rectified to include EEG monitoring as the standard of practice.

1.1.4.2.2 Motor seizure monitoring during electroconvulsive therapy

The second article to be discussed was entitled “Motor seizure monitoring during electroconvulsive therapy.” (Mayur, 1999). It consisted of a prospective case series that
was published in The British Journal of Psychiatry in 1999. The geographic location of the study was not included in the write up. All of the authors are listed as being affiliated with the National Institute of Mental Health and Neurosciences, Bangalore, India.

The introduction discusses that motor seizure monitoring is well established. They emphasize the importance of EEG monitoring, despite not being included in recent guidelines, and cite several references. There was no research question or hypothesis listed. The following was listed as the aim of the work, “To examine the potential pitfalls of motor seizure monitoring.”. This was in the same vein as this study’s research question, but was less specific.

The methods stated “Consecutive patients referred for ECT over the past one-year period were considered for this study”. Neither specific dates, location of the treatment center, nor the source of the referrals were provided. Exclusion criteria were described, as were the details of the ECT procedure. Patients were excluded if they were under 12 years of age, had a diagnosis of epilepsy or other neurological condition, had received ECT in the last 6 months, or were taking xanthine alkaloids, clozapine or anticonvulsants other than benzodiazepines. A total of 232 patients were included, and only the first electroconvulsive treatment was studied. The motor seizure duration was determined using the Hamilton cuff technique by the treating psychiatrist. An experienced psychiatrist who was not involved with the stimulus administration determined the EEG seizure duration. All patients had to have an EEG seizure of at least 25 seconds duration. The subjects were then divided based on EEG seizure duration into either EEG seizure
less than 120 seconds or, EEG seizure greater than 120 seconds. 120 seconds was used as an arbitrary cutoff for prolonged seizure. All calculations were then based on these two groups. Correlation coefficients for EEG and motor response were calculated. Unfortunately, dividing the sample into the described groups deviates from the research question of this review. I attempted to contact the primary author, P. Mayur, to request access to the studies primary data for comparative analysis, but at the time of submission had been unsuccessful.

The results section was focused on the disparity between EEG and motor readings and placement in the two groups. It is worth noting that a seizure was considered prolonged by EEG standards if it lasted more than 120 seconds, whereas it was considered prolonged if the motor response exceeded 90 seconds. The paper included figure 2, which is directly relevant to the goal of this study.
Figure 2. Scatter plot of motor and EEG seizure duration (Mayur, 1999).

Regarding figure 2, section B (75%) and D (10%) contain the seizure responses that were considered to be adequate or prolonged respectively by both EEG and motor standards. For the purpose of determining whether a seizure was adequate, or prolonged as defined in this study, 85% of the scatter plots were equivalent for EEG and motor estimation. Sections E (6%) & F (<1%) represent seizures that would have been considered prolonged by EEG standards, but not prolonged by motor standard. Section C (3%) showed seizures considered to be prolonged by motor standard, but adequate by EEG standard. It is worth noting again the different cutoff chosen for distinguishing
prolonged seizures for motor (90 seconds) versus EEG (120 Seconds). Using the same
cutoff for each would change the distribution. If arbitrary cutoffs are ignored, there are
no motor seizures that exceed EEG seizures in length. The graph is difficult to interpret
due to the fact that the spacing of time intervals on the x-axis is shorter than on the y-axis.

The discussion section of the paper states that the correlation of motor and EEG
seizure is excellent when a prolonged seizure does not occur. These statements came
from calculations based on arbitrary groups, not duration alone. They go on to say that
EEG seizures exceeding 120 seconds was an arbitrary cutoff, and the clinical relevance of
EEG seizures exceeding 120 seconds needs further prospective study. Yet later they state
that a recommended EEG seizure cutoff of 120 seconds is justified. They also go on to
state that EEG seizure monitoring is essential for at least the first ECT session.
Limitations published in the study include poor generalizability to ECT except first
treatment, as well as not obtaining interrater reliability of motor and EEG seizure
duration.

Some sources of bias present in the study include the following. There may have
been interrater variability between the multiple physicians involved in recording observed
motor seizure response. There may have been intrarater variability for each of these
physicians; as well there may have been intrarater variability for the experienced
physician interpreting the EEG recordings. The paper reports that the physician
interpreting the EEG recordings was not involved in the stimulus administration, but it
doesn’t state if the physician was blinded to any other information regarding the patient
the EEG was recorded from. Nor does it state if the physicians recording the motor response were blinded to the EEG recordings, which may have been displayed during the treatment.

Overall, the write up of the study is more focused on the clinical implications of using motor response with or without EEG monitoring, as opposed to determining the difference between the duration of seizure measure. Similar to the first study discussed, it would appear that when looking at duration of seizure in the absence of arbitrary cutoffs EEG monitoring tended to indicate longer seizure duration than motor monitoring. The major difference was that this study had the EEG interpreted by a person, and the first study used a machine.

1.1.4.2.3 Disconnection of the electroencephalographic, motoric, and cardiac evidence of ECT seizure

The third paper reviewed was entitled, “Disconnection of the electroencephalographic, motoric, and cardiac evidence of ECT seizure.” (Swartz, 1996). It was carried out in the United States, and published in Convulsive Therapy in 1996. It consisted of a case report.

The author, C. Swartz, discusses some of the potential methods of determining seizure quality, including EEG changes, motor seizure, and changes in heart rate. He then goes on to describe some observations made while two separate patients received ECT.
They each received three consecutive stimuli of increasing dosage. The observations were similar for both patients. Following the first stimulus, there was intense EEG seizure activity with a sharp endpoint, but no motor activity, and little increase in heart rate. Following the second stimulus there was 15-21 seconds of motor activity, with negligible seizure activity on EEG, and little increase in heart rate. Following the third stimulus there was typical signs of seizure in all three parameters.

Swartz stated that it is not known which measurements are necessary or sufficient to assure ECT quality. He postulated the question, is it possible that a seizure with signs associated with intense seizure activity such as high EEG amplitude and distinct postictal suppression could still be suboptimal and of questionable quality? He then presented his two cases, which he stated indicate that it is possible.

The EEG seizure duration and characteristics were determined by a physician (the author) for both patients. The author, using the Hamilton cuff technique, also determined the motor seizure duration. The heart rate was interpreted from ECG recordings. The first patient had these particular findings take place during her second ECT session. Her first, and subsequent treatments were more in keeping with what is normally expected. The second patient had these findings observed at his first ECT, and did not continue the therapy afterwards. Swartz does not commit to any particular method of seizure measurement based on his observations, he merely points out that further research is needed to clarify the issue.
Unlike the previous studies that seem to indicate that EEG is more sensitive than motor response for determining seizure activity, this case report gives two instances where they were simply different. Each patient had a motor response in the absence of EEG changes, as well as an EEG response in the absence of motor response. The number of patients involved in the first two studies was substantial compared to this case report, but in overall design all three are similar. As this is a case report, the value of the results in regard to clinical application is poor. The cases were selected on the basis of similar unusual findings. There was no randomization, matching, selection/exclusion criteria, blinding, etc., but one would not expect there to be. The purpose of this type of publication is to present an unusual finding to the scientific/medical community. By doing so, discussion around the findings, current understanding and practice is evoked. This can serve to stimulate more in depth research, which may alter clinical practice, or confirm current accepted practice.

1.1.4.2.4 ECT seizure duration: Reliability of manual and computer-automated determinations

The final study to be discussed was not directly related to the research question as posed. It was entitled “ECT seizure duration: Reliability of manual and computer-automated determinations.” (Krystal, 1995). This study was carried out in the United States, and published in Convulsive Therapy in 1995. The paper was included because it addressed the issue of interrater reliability (person versus person, and person versus computer) of EEG interpretation.
The specific goal laid out in the introduction was “we compared the reliability of Thymatron (Thy) EEG and EMG (Electromyogram) seizure duration measures with seizure duration assessments made by two experienced raters (A.K. and R.W.)”. EMG is a method of indirectly measuring electrical activity in a muscle, for this study it serves as a way to measure motor response duration.

The study subjects were 40 consecutive patients referred clinically for ECT. The method of ECT and EEG recording method was described. Only one seizure per subject was included to maintain independence of data points. They state that attempts were made to let the treatment number studied vary widely, but did not elaborate on how this was done. Manual EEG interpretation was done with the interpreters blind to the subject’s gender, age, treatment type, treatment number, and computer determined seizure duration.

For the analysis, the EEG duration data were assessed for distribution normality and transformed to a normal distribution before subsequent analysis, as indicated. Interrater variability was estimated by calculating pairwise intraclass correlation coefficients (A.K. versus Thy, R.W. versus Thy, A.K. versus R.W.). The correlation coefficients were also calculated with the results divided into groups based on potential predictors of interrater variability. These included presence/absence of EEG artefact, gradual seizure end point, postictal suppression, Unilateral versus Bilateral, single first course versus maintenance, and male versus female.
Mean seizure duration for the physicians was very close, A.K. 53.8 SD 21.1 and R.W. 53.9 SD 21.4. The mean for the Thymatron was slightly different 51.0 SD 19.6. The interrater intraclass correlation was 0.98 for A.K. & R.W., and slightly lower for A.K. & Thymatron 0.86, as well as R.W. & Thymatron 0.83, p < 0.0001 for all three. When the potential predictors of interrater variability were included correlation coefficients dropped for all. The correlation coefficients dropped as low as 0.82 for A.K. & Thymatron, 0.79 for R.W. & Thymatron, 0.95 for A.K. & R.W., depending on which predictors were included. These changes were reported as statistically significant (0.001 < p < 0.01). The question to ponder is, are these results clinically significant? The smallest correlation coefficient was 0.79, which is still very reasonable. When we consider that the range of seizure durations within one standard deviation of the mean (A.K. 32.7 – 74.9, R.W. 32.5 – 75.3, Thy 31.4 – 70.6) all these seizures would be considered both adequate (>25 seconds), and not prolonged (<120 seconds).

While the paper does not add to the literature on direct comparison of EEG and motor seizure monitoring, it does help to illustrate one of the main biases in studies that do. The first paper in this review used a computer to determine EEG endpoint, while the second and third paper had a physician interpret the EEG to determine seizure endpoint. It is worth noting that the machine used to determine EEG length in both studies was the Thymatron, and the machines manual states, “These seizure estimates are derived solely by calculation and are proved to aid, not replace, the physician’s judgment”.
1.1.4.3 Summary of Literature Review

The literature review contained three articles that published data directly comparing seizure duration when measured by EEG or via observed motor response. The data from the first study looked retrospectively at 95 courses of ECT in 67 patients, and showed that EEG seizure was of longer duration than the observed motor response to the same stimulus. This was derived from motor observation without using the Hamilton cuff technique, and a computer determined the EEG seizure duration (Benbow, 2003). The second study contained 232 patients, but only used information from the first ECT treatment. EEG seizure duration was determined by an experienced physician, and the motor response was determined with the aid of the Hamilton cuff technique. The resultant data was similar to the first study; the EEG seizure duration was greater than motor response (Mayur, 1999). The third article consisted of a case report of 2 patients receiving 3 consecutive ECT stimuli of increasing dose. The EEG was interpreted by an experienced physician, and the motor response was determined with the aid of the Hamilton cuff technique. The observations reported simply illustrated a difference in EEG versus motor response. They did not show that one was longer in duration than the other (Swartz, 1996). These three articles used varying methods of determining seizure by EEG or motor response, and produced variable results. The fourth article discussed looked at the interrater variability between experienced physicians when interpreting EEG seizure duration as well as interrater variability between experienced physicians and the automated computer determined EEG seizure duration (Krystal, 1995). While this article was not directly related to the research question at hand, it demonstrated that the interrater
variability was less between the physicians than it was between the computer and the physicians. It also demonstrated that in the context of EEG artefact, gradual seizure end point, and postictal suppression there was an increase in the interrater variability for all comers. It is likely that the predictors of interrater variability identified in the fourth study would have also been present in the other studies. This may have contributed to some of the variability in seizure duration as measured by EEG versus observed motor response.

Measuring seizure duration during ECT is universally recommended. There are various methods that can be employed to achieve this. Currently there are no specific guidelines on which method to use. A literature review was undertaken to investigate for a documented difference between measuring seizure by observed motor response, or by using EEG. The results of the included articles seem to suggest that there is a difference in measured seizure duration when comparing EEG and motor response, with most favouring EEG. It is important to keep in mind that the two case series included were poorly designed and written. The case report was well done, but this particular study design is of little direct value to clinical practice. The articles reviewed used variable techniques for measuring seizure duration, and reported varying results. The main issue hindering the research that has been included is the lack of an established gold standard for the diagnosis of seizure during ECT. If one assumes that seizure length correlates to treatment efficacy (not the focus of this review), a valid method of measuring seizure duration is essential. Further research is needed to establish a gold standard for seizure duration measurement.
Chapter 2. Purpose

2.1 Rationale

The purpose of this study was to look for and quantify the correlation between two methods of seizure duration estimation. If it could be demonstrated that the two methods were related closely enough, there would have been positive implications for procedural efficiency. It takes time to, both apply an EEG lead prior to administering the stimulus and, to interpret the final EEG recording. A high level of agreement between the measures could permit ECT without the use of the EEG measure. This would decrease the time required for each ECT procedure. A number of personnel are involved in the administration of ECT (Swartz, 1996). At a minimum, there must be a psychiatrist, an anesthetist, and nursing staff present. The procedure must be carried out in a setting that affords the appropriate level of medical monitoring. Any step towards streamlining the process would have allowed for minimizing the time that these valuable resources are utilized.

2.2 Scientific Question

What is the strength of the relationship between estimated seizure duration when comparing observed motor response and EEG interpretation?
2.3 Hypothesis

The hypothesis of this study was that there would be a strong positive correlation between observed motor response and EEG interpretation when used to estimate seizure duration in response to ECT stimulus.
Chapter 3. Methods

3.1 Research Design

This study was conducted to compare two diagnostic methods. The goal of observing the motor response or interpreting the EEG recording was to diagnose a seizure, as well as to determine the duration of the seizure. It would have seemed logical to carry out a traditional diagnostic test study, and to calculate sensitivity and specificity. The obstacle to carrying out such a study to answer the proposed research question was that there was not a currently accepted gold standard for diagnosing a seizure during ECT. A paper entitled “Evaluation of diagnostic tests when there is no gold standard. A review of methods.” published in 2007 suggests that in cases where there is an acceptable reference standard it may be reasonable to carry out a traditional diagnostic test study without an established gold standard (Rutjes, 2007). However; when there is no acceptable reference standard, such as in the case of this study, carrying out a traditional diagnostic test study has less value. For this reason, the study was designed as a case series. A cohort, or case-control design would not be appropriate, as a single group of patients will all receive the same two investigations. No randomization was required.
3.2 Study Population

The study population included adult Psychiatry Inpatients at the Health Sciences Centre (HSC) in St. John’s, Newfoundland, who were receiving ECT. Adult was defined as anyone 18 years of age or older. There were no exclusion criteria. Any adult patient receiving ECT was included, regardless of age, gender, diagnosis, comorbid conditions, medications, adjunctive therapy, or number of ECT treatments. The reason for not having exclusions based on the previously mentioned parameters was that this study was only interested in comparing two methods of estimating seizure duration during treatment. A more in depth study could investigate for the correlation between seizure estimation by each method and treatment response. This would be challenging, as ECT is used to treat multiple conditions, the number of treatments administered is variable, and measuring treatment response can be subjective in nature. An alternate study design would be more appropriate if using treatment response as the primary outcome, this would require strict inclusion and exclusion criteria.
3.3 Sample Size calculation

Given that this was a case series design and the goal was to look for a correlation between the two seizure duration estimation methods the following formula was used to determine sample size (Bland, 2008):

\[
\left( \frac{1}{2} \log_e \left( \frac{1+p}{1-p} \right) \right)^2 = f(\alpha, P) \left( \frac{1}{n-3} \right)
\]

- \(p\) = the population correlation coefficient
- \(n\) = the sample size
- \(\alpha\) = the significance
- \(P\) = the power

For this study the significance and power limits were chosen as 0.05 and 0.80 respectively. Without knowing the expected correlation between the two seizure duration estimation methods, we could not solve directly for \(n\). Therefore, the minimum detectable correlation coefficients (\(r\)) were calculated for several potential sample sizes (\(n\)). The results are illustrated in Table 1.
Table 1. Minimum Detectable Correlation (r) per Sample Size (n)

<table>
<thead>
<tr>
<th>Sample size (n)</th>
<th>Correlation coefficient (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>0.28</td>
</tr>
<tr>
<td>200</td>
<td>0.20</td>
</tr>
<tr>
<td>300</td>
<td>0.16</td>
</tr>
<tr>
<td>400</td>
<td>0.14</td>
</tr>
<tr>
<td>500</td>
<td>0.11</td>
</tr>
</tbody>
</table>

The purpose of this study was to determine if the correlation between the two methods was strongly positive. Obtaining a large sample size to detect a small correlation coefficient was not necessary. Therefore, a sample size of 100 was chosen. This allowed for the detection of a correlation coefficient as small as 0.28. Although 0.28 is a weak correlation, this sample size allowed for determination of a larger correlation as well. The study required recorded observed motor response times and EEG interpretations from 100 ECT procedures, not necessarily from 100 separate patients.

3.4 Data Collection: Instruments and Procedures

Data was collected from patient charts over a four month period. At the time of data collection, there were four psychiatrists administering ECT at the study site. Each of the psychiatrists agreed to the data recording for the purpose of this study. The procedure was carried out three times a week (Monday, Wednesday, Friday), and up to four patients were treated on each day. Both the motor response and EEG method were used to
estimate seizure duration. Prior to stimulus administration, a single EEG lead was applied to the patient’s mastoid process. The psychiatrist observed the patient from the time of the stimulus delivery until there was no more observable muscle movement. This period was timed and then recorded in the patient’s chart. The Hamilton cuff method was not employed. The ECT machine produced a print out of the EEG response once the procedure had been completed. The psychiatrist then interpreted this recording. The motor response was recorded before the EEG was looked at, making it independently determined. The EEG was interpreted once the psychiatrist already knew the motor response time; therefore, it was not interpreted independently. For this reason, the EEG interpretations of the psychiatrists were not included in this data set. To circumvent this potential source of bias this investigator interpreted the EEG recordings, prior to looking at the recorded motor response time in the chart. As such, the two methods of seizure duration estimation were assessed independently.

Following the ECT procedure, the patient, and their chart were returned to the inpatient unit. The data was collected directly from the chart by this investigator. As mentioned, the EEG was interpreted prior to looking at the recorded motor response. The only data that was recorded was the interpretation of the EEG print out, and the recorded motor response duration as document in the patient’s chart. No patient identifying information was included, nor was any information on age, gender, diagnosis, comorbidities, treatment number, type of ECT (Unilateral or Bilateral), ECT settings, or medications. The purpose of this study was to examine the relationship between estimated seizure duration when using observed motor response and physician interpreted
EEG. To use an analogy, a similar approach could be used to examine the correlation between blood pressure measurement when using an automated machine, or a manual sphygmomanometer. One would not be interested in information about the patient being tested, they would simply be interested in comparing the estimated blood pressure. This point is supported by the design of a randomized crossover trial which compared automated versus manual blood pressure measurement (Heinemann, 2008). The inclusion criteria described by the authors were that the subjects be clinically stable, lucid, English speaking and over 18. The exclusion criteria were based on factors that would prevent bilateral blood pressure measurements only. Similarly, for this study, any patient that was receiving ECT, and having seizure response estimated was eligible for inclusion.

Consent was not sought from the patients whose data was included in this research. This was made clear in the proposal for ethical approval, which was successful. The rationale behind proceeding without consent involved a number of reasons. First, participation in this study did not involve any alteration to the intervention they were receiving. Second, as the sole data collector was often present on the study site hospital unit no additional unauthorized personal data was accessed. Third, often patients receiving ECT are doing so involuntarily, and would therefore not be capable of giving consent. Finally, no personal information of any kind was recorded aside from the estimated seizure durations.

The data was entered into an excel spreadsheet (Microsoft® Excel for Mac 2015, Version 15.17). Two copies of the data were stored electronically. One was stored on a
password protected encrypted USB drive. The other copy was stored in a password protected university email account. As mentioned, no patient identifying data was included in the database. All data will be retained for a period of 5 years, and the data will only be accessible by this researcher.

3.5 Data analysis

The statistical analysis was conducted according to a priori determination. All statistical analysis was carried out using SPSS (IBM® SPSS® Statistics 2012, Version 21). After determining that the dataset was normally distributed, a paired T-Test, a Pearson correlation coefficient and a linear regression analysis were employed. The T-Test was used to compare the two variables. The Pearson Correlation Coefficient calculation was carried out to measure the strength of the association between the two seizure duration estimation methods. The Linear Regression analysis was calculated to attempt to quantify the association between the two methods.

The paper “Statistical Methods for Assessing Agreement Between Two Methods of Clinical Measurement”, describes an approach for assessing agreement based on graphical techniques and simple calculations (Bland, 1986). The authors highlighted several limitations of statistical techniques commonly used to assess agreement. Given that the purpose of this study was to assess the agreement between two methods of seizure duration estimation, this technique was well suited for the data analysis. The
method described by the author supplemented the previously mentioned analysis to aid in making clinical extrapolations. The decision to include this supplemental analysis was made prior to the data collection phase.

3.6 Ethical Approval

Approvals were granted by the Health Research and Ethics Board (HREB) of the province of Newfoundland and Labrador and the Research Proposal Approval Committee (RPAC) of Eastern Health.
Chapter 4. Results

4.1 Descriptive Statistics

Seizure estimates based on EEG and observed motor response were obtained from 102 ECT procedures, Table 2 contains the descriptive statistics derived from the data. The average seizure duration estimate based on EEG interpretation was 29 seconds and for observed motor response it was 24 seconds. EEG estimates ranged from 0 to 79 seconds, and the motor estimates ranged from 0 to 54 seconds. The average difference (EEG - motor estimate) between the two measures was about 5 seconds. The motor estimates were anywhere from 38 seconds longer to 42 seconds shorter than their respective EEG estimates.

Table 2. Descriptive Statistics

<table>
<thead>
<tr>
<th></th>
<th>EEG</th>
<th>Motor response</th>
<th>Difference EEG – motor</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>102</td>
<td>102</td>
<td></td>
</tr>
<tr>
<td>Mean (sec)</td>
<td>29.08</td>
<td>23.68</td>
<td>5.4020</td>
</tr>
<tr>
<td>Standard deviation (sec)</td>
<td>15.958</td>
<td>11.997</td>
<td>14.26153</td>
</tr>
<tr>
<td>Range (sec)</td>
<td>0-79</td>
<td>0-54</td>
<td></td>
</tr>
</tbody>
</table>
4.2 Tests of Normality

Figures 3 through 8 demonstrate that the EEG estimates, observed motor response estimates, and the difference between these values were all normally distributed. As such, the independent sample paired T-test, Pearson Correlation Coefficient, and Linear Regression calculations were conducted as planned.
Figure 3. Distribution of EEG seizure estimations with normal line superimposed.

Figure 4. Test of normality, Q-Q plot of EEG seizure estimations.
Figure 5. Distribution of observed motor response seizure estimations with normal line superimposed.

Figure 6. Test of normality, Q-Q plot of observed motor response seizure estimates.
Figure 7. Distribution of the difference in seizure estimations with normal line superimposed, as based on EEG minus observed motor response.

Figure 8. Test of normality, Q-Q plot of the difference in seizure estimations, as based on EEG minus observed motor response.
4.3 Paired Samples T-Test

Table 3. Paired Samples Statistics

<table>
<thead>
<tr>
<th></th>
<th>Mean (sec)</th>
<th>N</th>
<th>Standard deviation</th>
<th>Standard error mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEG</td>
<td>29.08</td>
<td>102</td>
<td>15.958</td>
<td>1.580</td>
</tr>
<tr>
<td>Motor response</td>
<td>23.68</td>
<td>102</td>
<td>11.997</td>
<td>1.188</td>
</tr>
</tbody>
</table>

As can be seen in Table 4, the average difference between the two methods of seizure estimation was approximately 5 seconds. In other words, on average, the EEG estimation was 5 seconds longer than the observed motor response estimation. The sample size used resulted in a 95% confidence interval ranging from about 3 to 8 seconds. The t-value generated by the analysis was approximately 4, indicating that the two methods used were different. As well, the likelihood that these results occurred by chance is less than 0.1% based on the significance result.

Table 4. Paired Samples T-test

<table>
<thead>
<tr>
<th></th>
<th>Paired differences</th>
<th>t</th>
<th>Degrees of Freedom</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (sec)</td>
<td>Std. deviation</td>
<td>Std. error mean</td>
<td>95% Confidence interval of the difference</td>
</tr>
<tr>
<td>EEG-motor response</td>
<td>5.402</td>
<td>14.262</td>
<td>1.412</td>
<td>2.601</td>
</tr>
</tbody>
</table>
4.4 Pearson Correlation Coefficient

<table>
<thead>
<tr>
<th></th>
<th>EEG</th>
<th>Motor response</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEG</td>
<td>1</td>
<td>0.510</td>
</tr>
<tr>
<td>Pearson correlation coefficient (r)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significance</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Motor response</td>
<td>0.510</td>
<td>1</td>
</tr>
<tr>
<td>Pearson correlation coefficient (r)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Significance</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

The Pearson Correlation Coefficient is a measure of the linear correlation between two variables, and is represented by r. Analysis was carried out to calculate the correlation coefficient between the two methods of seizure duration estimation. The calculated Pearson Correlation Coefficient was 0.510, with a p-value of <0.001. This indicated a moderately positive linear relationship between the two methods of measure, which was statistically significant.
4.5 Linear Regression Analysis

Linear regression analysis is used to illustrate the relationship between a dependent and independent variable. In this case both variables were indirect measures of seizure activity. As well, both measures were independent variables, as neither had been established as the gold standard. For the purpose of completing the analysis the observed motor response was designated as the independent variable and the EEG response was designated as the dependent variable. Figure 9 shows a scatter plot of the EEG and Motor Response seizure estimations with the linear regression line superimposed. The value $R^2$ is a statistical measure of how close the data points are to the illustrated regression line. The calculated $R^2$ value for this analysis was 0.26. This means that the linear regression model explains 26% of the difference between the two measures. Or conversely, that an unknown factor explains 74% of the difference between the two measures. As such, the relationship between the two measures is not robust.
Figure 9. Estimated seizure duration, with linear regression line included.

Table 6. Linear Regression Model Summary

<table>
<thead>
<tr>
<th>Model</th>
<th>r</th>
<th>R^2</th>
<th>Adjusted R^2</th>
<th>Std. error of the estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.510</td>
<td>0.260</td>
<td>0.252</td>
<td>13.797</td>
</tr>
</tbody>
</table>
4.6 An Alternate Approach to Measuring Agreement

The paper “Statistical Methods for Assessing Agreement Between Two Methods of Clinical Measurement”, describes an approach for assessing agreement based on graphical techniques and simple calculations. The authors also explain the rationale behind their stance that commonly used measures of agreement, such as correlation coefficients, are inappropriate (Bland, 1986). Figure 10 is a scatter plot which has the average seizure estimate for each ECT procedure on the x-axis and the difference in seizure estimation between the two methods of measure (EEG-motor response) on the y-axis. The graph also includes three horizontal lines. The middle line represents the average difference between the two methods (5.4 seconds). The highest and lowest line represent the mean plus or minus two standard deviations respectively (33.4 and -22.6 seconds). These upper and lower lines represent the boundaries of where one would expect 95% of the values representing the difference in the seizure estimates of the two methods to lie. Considered another way, for any given observed motor response seizure estimation one would expect that 95% of the time the corresponding EEG estimates would be anywhere from 33.4 seconds longer to 22.6 seconds shorter. As well, on average one would expect the EEG estimate to be 5.4 seconds longer than the observed motor response. The results of this analysis agree with the previous analysis suggesting a strong relationship between the two methods of estimation was not present.
Figure 10. Difference against mean for seizure estimation of both methods.

The APA has designated 15 seconds as the minimum seizure duration considered to be adequate. Keeping this in mind, the significant difference between the two methods becomes apparent (Weiner, 2001). An average difference of 5.4 seconds is large when dealing with a threshold of 15 seconds. As well, the range one would expect corresponding values to fall 95% of the time was large at 56 seconds. This suggests that the two methods are not closely related.
4.7 Post Hoc Analysis

4.7.1 Addressing Zero Values

Upon examination of figure 9 there was an obvious number of points that contained estimates of zero for EEG and/or observed motor response. Zero values indicated that the method of seizure duration estimation used did not identify any seizure activity. In an attempt to investigate the impact of these zero values multiple calculations were carried out with several exclusions considered. The analysis started with excluding all points that contained an observed motor response of zero, then only points containing EEG values of zero were excluded, and finally any point that included a zero value was excluded. The calculations included mean difference, 95% confidence interval of the mean difference, standard deviation, Pearson correlation coefficient (r), and finally the linear regression value $R^2$. Table 7 shows the results of these calculations along with the values from the original analysis without exclusions for comparison.
Table 7. *Summary of Results Obtained from Analysis with Exclusions Based on Zero Values*

<table>
<thead>
<tr>
<th></th>
<th>No exclusions</th>
<th>No motor response zero values</th>
<th>No EEG zero values</th>
<th>No zero values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean difference (sec)</td>
<td>5.40</td>
<td>4.26</td>
<td>6.76</td>
<td>5.57</td>
</tr>
<tr>
<td>95% Confidence interval (sec)</td>
<td>2.60-8.20</td>
<td>1.40-7.13</td>
<td>4.12-9.41</td>
<td>2.94-8.20</td>
</tr>
<tr>
<td>Std. deviation (sec)</td>
<td>14.26</td>
<td>13.84</td>
<td>13.06</td>
<td>12.42</td>
</tr>
<tr>
<td>r</td>
<td>0.51</td>
<td>0.47</td>
<td>0.53</td>
<td>0.52</td>
</tr>
<tr>
<td>R²</td>
<td>0.26</td>
<td>0.23</td>
<td>0.28</td>
<td>0.27</td>
</tr>
</tbody>
</table>

Regardless of exclusions the variation in mean difference was about 2.5 seconds, with rounding the Pearson correlation coefficient was consistently 0.5, and the variation in R-squared was 0.05. It would appear that altering the analysis based on zero values had very little impact on the results.

4.7.2 Consideration of Agreement Regarding Adequate Versus Inadequate Response

As was set out from the start, this analysis was based on the continuous variable of time. However, after considering the previously detailed analysis the decision was made
to further investigate the data in an alternate fashion. The American Psychiatric Association task force report on the practice of ECT states that when seizure duration is less than 15 seconds in both motor and EEG manifestations the likelihood is high that the seizure was limited by insufficient electrical stimulation and that the treatment was inadequate (Weiner, 2001). The Canadian Psychiatric Association (CPA) recommend a minimum seizure of 15 seconds as measured by EEG. As such, 15 seconds was chosen as the cut off to separate adequate and inadequate seizure response. Using SPSS, the seizure estimate variables were converted from actual time value to either adequate response (15 seconds or more) or inadequate response (less than 15 seconds). The next step was to quantify the number of procedures which resulted in seizure response being deemed adequate by each measurement modality, and the amount of agreement between the two.

Figure 11 is a graphical representation of the agreement between the two measures. For 79 cases (77%) both EEG and observed motor response agreed. For 10 cases (10%) the EEG identified the response as adequate, while the observed motor response identified it as inadequate. For 13 cases (13%) the observed motor response identified the response as adequate, while the EEG response identified it as inadequate.
Figure 11. Number of cases in which EEG and motor response agreed regarding adequate seizure response of 15 seconds or more.

The scatter plot of Figure 12 includes a vertical and horizontal line representing the 15 second mark for observed motor response and EEG response respectively. These lines indicate the minimum seizure duration considered to be adequate. The graph has been divided into four quadrants by the intersection of these reference lines. Quadrant A represents the seizure responses considered to be adequate by EEG response, but not observed motor response (10 cases). Quadrant B represents the seizure responses
considered to be adequate by both methods of estimation (73 cases). Quadrant C represents the seizure responses considered to be inadequate by both methods of estimation (6 cases). Quadrant D represents the seizure responses considered to be adequate by observed motor response, but not EEG response (13 cases).

Figure 12. Scatter plot of EEG and motor response including reference lines that represent the minimum duration of adequate seizure duration (15 seconds).
Both methods agreed that the seizure response was adequate for 73 cases (72%). Had observed motor response been used alone, 86 cases (84%) would have been identified as adequate. Conversely, had EEG response been used alone 83 cases (81%) would have been identified as adequate.

As mentioned previously, neither EEG nor observed motor response have been universally accepted or recommended as the gold standard for estimation of seizure duration and therefore response to ECT administration. Considering this, the number of ECT procedures that would have been deemed adequate can be determined for a number of scenarios. If one were to use both measurement modalities and define an adequate ECT response as a seizure duration of 15 seconds or longer, regardless of method used, then 96 of the 102 procedures would have been deemed adequate. Conversely, if one defined adequate ECT response as a seizure duration of 15 seconds or longer in both EEG and observed motor response then only 73 of the procedures would have been deemed adequate. If only EEG was used, then 83 procedures would have been considered adequate. Finally, had only observed motor response been used then 86 of the procedures would have been considered adequate.
Chapter 5. Discussion

5.1 Addressing the Hypothesis

The null hypothesis of this study was that there would be a strong positive correlation between observed motor response and EEG interpretation when used to estimate seizure duration in response to ECT stimulus.

5.1.1 Traditional analysis

The traditional statistical approaches used to quantify the correlation between both methods of seizure duration estimation did not establish a strong positive correlation between them.

The calculated Pearson correlation coefficient of 0.51 was moderately positive at best. Further examination of the relationship between the two measures via linear regression analysis yielded similar results, with a $R^2$ value of 0.26. This means that the linear regression model can account for a mere 26% of the difference between the two measures, and that 74% of the difference can be attributed to unknown factors.

Despite the fact that both methods of seizure duration estimation are essentially indirect measures of the same thing, seizure activity, the statistical analysis using traditional approaches did not identify a strong relationship between the two.
5.1.2 Alternative Approach to Quantifying Agreement

As per the recommendations laid out in the publication "Statistical Methods for Assessing Agreement between two Methods of Clinical Measurement", an alternate way of investigating the extent of the agreement between the two methods was pursued (Bland, 1986). The results of this analysis are well illustrated in figure 10. While the mean difference between the two methods was 5.4 seconds, the range in which 95% of the differences fell was quite broad. When compared to the observed motor response, one would expect the corresponding EEG response to be anywhere from 33 seconds longer to 23 seconds shorter 95% of the time. Considering that the generally accepted cut off for deeming a seizure response adequate is only 15 seconds this disparity was too large to accept.

5.2 Addressing the Scientific Question

The original scientific question posed at the outset of this study was, what is the relationship between estimated seizure duration when comparing observed motor response and EEG interpretation?

5.2.1 Statistical Analysis of the Raw Continuous Variable Time
Neither the traditional methods, nor the alternative method employed to quantify the relationship between the seizure estimation methods identified a consistent predictable relationship between the two.

### 5.2.2 Statistical Analysis Following Conversion to Categorical Data

As mentioned, a strong, consistent, predictable relationship was not established between the methods of seizure estimation. The decision was then made, post hoc, to convert the continuous variables of estimated seizure time via EEG and observed motor response to categorical variables. The two categories were adequate seizure response (15 seconds or more) or inadequate seizure response (less than 15 seconds). The results of the conversion to categories were depicted in the histogram of figure 11 and the scatterplot of figure 12.

The conversion to categories allowed for considering the amount of agreement regarding the clinically important purpose of these measures, which is identifying adequate seizure responses. Of the 102 procedures, both methods agreed for 79 cases, or 77% of the time. Of these 79 cases of agreement, 6 seizure responses were deemed inadequate and 73 were deemed adequate. Had the seizure estimation been carried out using only observed motor response 86 of the responses would have been deemed adequate. Taking this approach would simplify the procedure and save time, but the results would obviously have been different. Time would have been saved in that for 102
procedures it would not have been necessary to identify appropriate locations for EEG lead placement, prepare the patients scalp for EEG placement, or to interpret EEG print outs and record the results in charts. Excluding EEG measurement would have resulted in 13 more seizures being identified as adequate. This would have resulted in an altered course for those patients in that subsequent stimulation immediately following the procedure would not have been required, nor would an alteration in the stimulus delivery parameters. Given that the two methods of seizure estimation differ, the next logical question is which one is a better measure of adequate response? This study was not designed to address this question, but simply to attempt to quantify the relationship between the two methods.

5.3 Comparison to Similar Studies

Benbow et al determined that EEG seizure estimation was longer than observed motor response estimation based on retrospective analysis of 95 courses of ECT in 67 patients (Benbow, 2003). Mayur et al came to similar conclusions in their prospective case series; however, excluding any case which failed to have at least a 25 seconds response on EEG may have contributed to their findings (Mayur, 1999). The results of this study did not support the findings of these other publications. Average seizure duration estimation based on EEG exceeded estimates based on observed motor response. However, there were many cases where observed motor response exceeded EEG
response. The findings of this study suggest that the two measures differ, and that there is not a strong, consistent, predictable relationship between them.

Swartz presented two case reports which demonstrated that the two seizure duration estimation methods do not always agree (Swartz, 1996). His findings are in keeping with the results of this study in that the two methods are different. The findings of this study support his statement that it is not known which measurements are necessary or sufficient to assure ECT quality, and that further research is needed to clarify this.

It remains unclear as to which of the two methods of seizure duration estimation is the most accurate, or more importantly most indicative of clinical efficacy. Identifying which of these methods is the most appropriate could potentially decrease the cost associated with this treatment. If observing the motor response is deemed to be at least as effective as EEG interpretation, time would be saved by removing the task of applying EEG leads and interpreting print outs. This time saved could result in cost savings. Review of the literature did not identify any work in the area that has been published since 2003. In the absence of knowledge of active research aimed at solving this problem, one could consider that the complexity and cost of answering such a question may out weigh the potential savings.
Chapter 6. Conclusions

6.1 Summary

This study was carried out in an attempt to quantify the relationship between two indirect measures of ECT stimulus response. The original hypothesis was not supported, and a strong positive correlation between seizure estimation via EEG interpretation and observed motor response was not identified.

A post hoc analysis consisted of having the continuous variable Time converted to the categorical variables of adequate (seizure of 15 seconds or more) and inadequate (seizure of less than 15 seconds) response. This allowed for considering the agreement of the two measures in relation to their clinically important role of identifying adequate responses. The measures were found to agree for approximately three quarters of the cases included.

This study supports the case reports published by Schwartz, indicating that the two measures are simply different (Swartz, 1996).

6.2 Clinical Implications

Had this study identified a strong, consistent, predictable relationship between the two measures, it would have had a significant impact on the ECT procedure. If the
measures had been shown to be strongly related, it would be reasonable to simplify the procedure, and rely on observed motor response alone. Unfortunately, this was not the case.

It is not possible to make any recommendations on which of the two methods is superior based on the findings of this study. The relationship between the two was all that was considered, at no stage was accuracy, appropriateness, or indication of efficacy examined. This study reflects the lack of general consensus as to which method is preferred, simply demonstrating that they differ.

Based on the findings of this study, as well as findings from others, further research is required to determine which of these methods is the best indicator of seizure response, and more importantly ECT efficacy. Research of this nature would be more complicated. Establishing superiority would be best achieved by double blinded, randomized, controlled clinical trials.

Until such a time that a preferred method can be identified it would be prudent to use both methods simultaneously. Ideally, the team administering ECT would collaborate with the patient’s attending physician. This would allow both parties to consider clinical response as well as estimated seizure duration when making decisions regarding management.
6.3 Limitations

6.3.1 Two Indirect Measures

A major limitation of this study design was that it was focused on comparing two separate indirect measures. ECT is not administered because it causes a motor response, or EEG changes. ECT is administered because it is an effective treatment for multiple forms of mental illness. Estimated seizure duration in response to ECT is used to guide changes in the stimulus administered in future treatments. A randomized double blind trial comparing treatment outcome when motor response is used versus EEG interpretation would be the ideal way to investigate which is the superior method. Unfortunately, there are several obstacles to attempting such a trial. ECT is used to treat a myriad of mental illnesses, and patients often have comorbid psychiatric conditions. ECT is sometimes used as a diagnostic trial. Patients often have medical comorbidities, which may include epileptiform conditions. There are often various medications involved, these can include antiepileptic drugs, or drugs that have antiepileptic properties. This study was simply focused on quantifying the relationship between the two methods, no inferences can be made based on the results regarding either method and treatment response.
6.3.2 Study Design

Another limitation of this study is its design. A case series is not the most robust form of research, but as previously mentioned it is the most appropriate choice to answer the research question posed. Without an established gold standard, the best that can be done is analysis for correlation and agreement of measures.

6.3.3 Statistical Analysis

A single ECT machine was used for all of the procedures included in the data collection. It did not begin the EEG recording until after the stimulus had been administered. However, when the treating physician was timing the motor response, they began timing when the stimulus was initiated. For the vast majority of the cases the stimulus was administered over 6 seconds. This difference would not have affected the estimation of the relationship between the two measures. While the treating physicians at the site where the data was collected did not alter the length of time over which the stimulus is delivered, treating physicians at another site sometimes decreased the duration to 3 seconds. It is possible, though unlikely, that a small number of the procedures may have had the stimulus delivered over 3 seconds. This would only have happened if the patient had their ECT initiated at the alternate site and were then transferred to the study site. If this had happened, and the physicians at the alternate site had decreased the stimulus duration, the physicians at the study site would have simply continued the decreased duration as documented. Unfortunately, this information was discovered after
the data had been collected. Given that no identifying data had been recorded along with the seizure duration estimations there was no way to determine if this had occurred. This may represent another limitation and may have made a small contribution to the statistical analysis.

6.3.4 Interrater Variability

The observed motor response seizure estimates were carried out by the four different psychiatrists that administered the ECT procedures. It is possible that there may have been some interrater variability which was not accounted for in this study.
Bibliography


