EEG Cap for Identification of Non-Convulsive Status Epilepticus

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RESEARCH PROTOCOL OUTLINE

Title: EEG Cap Placement for Expedited Identification of Non-Convulsive Status Epilepticus

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Abstract

Altered mental status (AMS) is one of the most common reasons for inpatient neurology consultation. Non-convulsive status epilepticus (NCSE) is frequently a differential diagnosis of the patient with AMS. NCSE becomes more refractory to treatment after one hour of seizure activity, making rapid identification and treatment of NCSE of great clinical importance. Currently, an EEG technician must be called in from home during non-workday hours in order to obtain a stat EEG. We propose the time required for diagnosis of NCSE in our institution can be significantly decreased with rapid placement of an EEG cap by the onsite neurology residents.

A. Specific Aims

1. Utilize EEG cap for rapid assessment of seizure activity in 20 patients with suspected NCSE
2. Rapid EEG review by on-call resident & attending physicians
3. Employ existing standard of care for NCSE evaluation with standard electrodes as soon as technician can apply them (cap to not delay standard of care)
4. Evaluate endpoints for cap vs. standard electrodes of time from consultation to:
    a. completed EEG
    b. Diagnosis or exclusion of NCSE

B. Background and Significance

Status epilepticus is operationally defined as a seizure greater than five minutes in duration or more than one seizure within a five minute period without return to normal baseline mental status. Convulsive status epilepticus is a medical emergency. Status epilepticus is more likely to become refractory to medical therapy when treatment is delayed for over 1 hour (DeLorenzo et al). NCSE is a persistent change in behavior and processes from baseline associated with continuous epileptiform EEG changes, but without major motor signs. Nonconvulsive status epilepticus (NCSE) in a comatose patient cannot be diagnosed without electroencephalography (EEG). A previous study has demonstrated the urgency of rapid identification and treatment of NCSE (Meierkord et al). Hospital neurology programs frequently rely on EEG technologists who are on-call but not onsite to place EEG electrodes that are used for assessment of NCSE. EEG caps allow for more rapid electrode placement and EEG analysis, but there exists ambiguity whether rapidly placed caps are sufficiently accurate to reliably identify NCSE for clinical decision-making. Use of EEG cap (also referred to as EEG headsets) in the inpatient setting by onsite neurology providers, if sufficiently reliable versus standard of care electrode-placement, may allow for more rapid identification of NCSE and associated expedited pharmacological treatment.

C. Study Design, Methods, & Statistics

Study will be of prospective design involving 20 patients evaluated at the Mayo Clinic emergency department or hospital that are referred to neurology for evaluation of mental status changes or suspected seizures.

Review type: minimal risk
Is this an interventional study? Yes **No**

At the completion of neurology evaluation, if NCSE is in the differential diagnosis according to institution best practice, then consented participants will undergo placement of a large size, 20-channel EEG cap from Eectro-Cap International with a Natus E-2-2520-26 electrode board adapter with initiation of recording. The placement of the EEG cap will be restricted to residents formally trained in its placement by an EEG tech. The EEG-cap is already owned by the Mayo Clinic Neurology department, and therefore we will not require further funds to obtain equipment for this study. This study will only be performed during times when EEG techs are not available onsite for rapid placement of standard 21-channel EEG electrodes, such as during night-call shifts. We will not bill for the EEG cap placement, only the subsequent standard EEG protocol which will be followed after the EEG-cap placement.

Prior to placement of EEG cap, evaluating staff member will request stat standard-electrode EEG. We will record time from neurology consultation request to placement of EEG cap as well as time from consultation request to obtaining a standard EEG. We will also record time to confirmation or exclusion of NCSE. Initial diagnosis or exclusion of NCSE will be performed by on call resident, if they received prior training regarding EEG cap placement, and attending. Secondary quality assessment will be performed by two independent EEG interpreters blinded to clinical history. Secondary assessment will be qualified as acceptable or inacceptable interpretation based on whether greater or less than 50% of the recording is judged interpretable. Secondary assessment will also include interpretation of NCSE by a third independent reader if there is disagreement between first two. The number of patients excluded from the study will also be recorded, including the reason for exclusion.

Specific data points for statistical analysis include:

- Time of consultation
- Time of standard-electrode EEG order
- Time that 10 minutes of EEG have been completed (for both cap & standard-electrodes)
- Time that 20 minutes of EEG have been completed (for both cap & standard-electrodes)
- Time of diagnosis or exclusion of NCSE

Primary outcome measure: time from stat EEG order to diagnosis or exclusion of NCSE

Secondary outcome measures include:

- Overall quality of cap recordings as operationalized by:
    - Aforementioned >50% interpretability
    - Concordance between cap & standard-electrode diagnostic assessments
- comparison of diagnostic assessments/concordance between 10 and 20 minute captures

Statistical methodology: chi-square and Student T-test will be employed to compare categorical variables.

Data storage and PHI: Initial data collection will be to a password-protected Excel spreadsheet that is only accessible by the study authors. No PHI will be collected, but a unique identifying number will be used to initially distinguish between patients. Data will then be aggregated for statistical analysis. The final paper will only include patient data in aggregate form.

D. Preliminary Studies/Progress Report

EEG is the only definitive way to diagnose NCSE. Although useful, standard surface EEG can be a cumbersome, complex and time-consuming process, all of which can limit its applicability in emergent time-sensitive clinical situations and rural areas without available technology, financial resources or neurophysiologic expertise. EEG headsets, caps or "dry EEG" have been developed and have become commercially available over the past few decades and have been used in multiple brain computer interface (BCI) studies, evoked potentials and biofeedback (Halford, et al, Slater et al). This novel technology does not require measurement of relative electrode differences by EEG technologists or pose increased risk for skin abrasions. Disadvantages EEG caps do exist which may affect its clinical suitability, including movement artifact, sweat artifact and increased weight of the system (Halford, et al).

Some studies have investigated the time differences and validity of EEG headsets versus standard EEG recordings in various clinical scenarios. For instance, a study demonstrated that application of an EEG caps in comparison to a standard EEG was performed over 15 minutes faster, with 87% of the EEG being interpreted as technically adequate. In addition, patients preferred the EEG caps over the standard EEG (Halford, et al). The EEG headset recordings were also felt to be adequate in identifying status epilepticus and were significantly faster to set up (Slater et al). "Light" EEG has also been shown to be comparable to standard EEG in detecting findings suggestive of hepatic encephalopathy, but with higher proportion of light EEG samples being discarded due to artifact (Schiff et al).

Data in identifying epileptiform activity or NCSE utilizing EEG caps is lacking. Disposable forehead electrodes have also been shown to identified status epilepticus, although studies have included a limited number of patients with NCSE and the results have been variable (Myllymaa et al) (Muraja-Murro, et al). In one study, only two out of four patients with status epilepticus were identified with forehead electrodes due to EEG abnormalities being restricted to the posterior regions of the brain (Muraja-Murro, et al).

Due to the small sample sizes, limited number of patients with NCSE and variable electrode placements in prior studies, it remains unclear the applicability of EEG caps in the identification of NCSE, which our study seeks to investigate further. In addition, we plan to readdress the quality and interpretability, as well as the time taken from ordering to interpretation of the EEG cap compared to standard EEG.

E. Gender/Minority/Pediatric Inclusion for Research

Gender and ethnicity will not be used as exclusion criteria when selecting patients. The study will include both men and women. Pediatric patients under the age of 18 will be excluded from our study to permit use of adult size EEG cap for all participants.

F. Human Participants

Inclusion:

1. Patients with suspected NCSE in the Mayo Clinic Florida hospital, emergency room or intensive care unit.
2. Age: Patients of 18 years or older will be included in this study

3. Education: All education levels will be included

Exclusion:

1. Patients younger than 18 years of age.
2. Patients with open head trauma.
3. Patients with anatomy that would preclude EEG cap placement.
4. Patients excluded for anatomical or age-related reasons will be tracked to determine applicability of the EEG cap to the patient population at Mayo Clinic.
5. Pregnant females
6. Large head size not amenable to cap placement
7. Scalp infection
8. Inability to obtain informed consent

Informed Consent:

Patients will lack the capacity to consent, as by definition patients in NCSE have very impaired mental status. NCSE is an emergency, and our protocol is an emergency evaluation. The procedure we are following is minimal risk, and we will still provide the typical standard of care for patients with suspected NCSE. Therefore we will obtain prior verbal consent from a healthcare proxy. If patients regain ability to interact and accurately answer questions while the study is being performed, the study will be stopped, as they would be unlikely to be in NCSE.

Standard of care will be followed in context of emergent intervention. Consent from HCPOA or next of kin or will be obtained, per Florida hierarchy. If the legally authorized representative (LAR) is not available at bedside, an attempt will be made to contact them by way of phone. Given the treatment of NCSE is an emergency, if the first LAR is not available, the Florida hierarchy of consent will be followed with regard to an alternate source of consent.

The use of EEG caps is acceptable for assessment of epilepsy, and, additionally, we will still provide our typical standard of care. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. Therefore, verbal consent following the Florida Hierarchy of Consent with documentation of the individual consenting in the chart is appropriate.

The consent will be obtained through a discussion with the patient's healthcare proxy at bedside if possible. If no healthcare proxy is available at bedside, a call will be placed to the appropriate healthcare proxy. As the placement of the EEG cap for detection of NCSE if an emergency, the time dedicated to discussion is anticipated to be 2-3 minutes in order to present the risks and benefits of the procedure. The healthcare proxy will be clearly described the risks and benefits of the procedure. They will be offered a waiting period between discussion and decision, and they will be explicitly told that the patient's overall care, outside of the context of the study, will not change based on their decision. Residents responsible for consenting patients in the study will formally complete the consent training in the Mayo Clinic Simulation Center regarding proper technique. Informed verbal consent will be documented on the neurology consult note.

Given the nature of the project aimed at expeditiously identifying NCSE the following details will be verbally provided to health care proxies prior to placement of the EEG cap:

- The study involves assessing patient brain waves with an experimental EEG cap to attempt to diagnose and treat seizures that do not produce convulsive movements, but can alter mental status.

- The cap could identify seizures before the normal method of analyzing brain waves will be performed, which could potentially allow for earlier treatment.
- There is minimal risk, with main risk being that cap may be inaccurate and might be misinterpreted. The risk of misdiagnoses, leading to inappropriate diagnosis and treatment is likely small, but exact data is not available.
- The normal method of analyzing brain waves will be used either way as fast as possible
- Do not feel obligated to consent if you prefer for our typical protocol to be followed. The patient's overall care, outside of the context of this study, will not change based on your decision.
- If you would like some time to think about this decision, I will attempt to return at a time of your choosing.

G. Risks and benefits:

This study is considered minimal risk given the only deviation from standard of care involves application of EEG cap prior to standard of electrodes. To the extent that cap electrodes might be misinterpreted due to theoretically poorer quality risks include:

- Misinterpretation of EEG so as to miss seizure activity, which would not affect time to treatment, given we will still be following and giving priority to our standard protocol.
- Misinterpretation of EEG so as to diagnose non-seizure activity as epileptiform, which his unlikely as attendings will avoid diagnosing NCSE if there is any uncertainty in the EEG.

1. Procedures protecting against or minimizing potential risks:
    a. Patients will be evaluated by neurology residents or faculty members
    b. EEG cap will be applied by neurology staff and cleaned between each use
    c. Electronic data will be stored in a password-protected Excel spreadsheet that contains no PHI
    d. Regular EEG protocol will be followed in addition to EEG cap placement. Standard electrode placement will be given priority in the event EEG technician is available before EEG cap is placed. There will be no deviation from the current standard of care.
2. Future benefits and importance to the participants and others:
    a. Use of EEG cap technology can expedite diagnosis of or exclusion of NCSE.
    b. Rapid identification of NCSE can reduce time to treatment, which may improve patient outcomes
5. Justification of risks in relation to benefits: Since this study adds use of an EEG cap to existing NCSE protocol without modification of existing method of diagnosis and treatment, risk to patients is minimal and consists of incorrect diagnosis of NCSE and administration of medications that would not otherwise be indicated. However, we believe that verification of EEG findings by a faculty member experienced in EEG interpretation will minimize this risk. Further, misdiagnosis is an existing risk under the current NCSE protocol. If seizure activity is missed on cap electrodes, this would have been missed anyways prior to standard electrode application

H. Data and Safety Monitoring

1. Data and Safety Monitoring Board

a. Patient charts will only be accessed at the Mayo Clinic by neurology residents and faculty members. This study will involve review of the medical chart only as in required for treatment of the patient in the hospital setting.
b. All study data will be electronically stored in a password-protected Excel spreadsheet. No PHI will be recorded. Study results will be presented in aggregate form only.
c. Adverse events will be limited to misdiagnosis of NCSE and administration of anti-seizure medication to a patient with an alternate diagnosis. However, this is an existing risk with current NCSE protocol.
d. In the event of an unexpected disclosure, the IRB will be notified. The affected patients and their care providers will be informed about the disclosure.

2. Data and Safety Monitoring Plan: Dr. Tatum will supervise the research and data collection process. All procedures will be recorded as a part of video EEG monitoring. In the unlikely event that unforeseen safety concerns arise, the study will be brought back to the IRB for further review or terminated.

I. Literature Cited

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