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EEG reactivity evaluation practices for adult and pediatric hypoxic-ischemic coma prognostication in North America

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Abstract

Introduction: We aimed to assess the variability in EEG reactivity evaluation practices during cardiac arrest prognostication.

Methods: We conducted a survey of institutional representatives from North American academic hospitals participating in the Critical Care EEG Monitoring Research Consortium to assess practice patterns involving EEG reactivity evaluation. This 10-question multiple choice survey evaluated metrics related to technical, interpretation, personnel, and procedural aspects of bedside EEG reactivity testing and interpretation specific to cardiac arrest prognostication. We obtained one response per hospital.

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Author Contributions

E.A., J.W.L, N.G., S.S.C. and M.B.W. conceptualized and designed the study. E.A., N.S.A., C.D.H., L.J.H., and M.B.W. acquired and analyzed the data. E.A., E.J.G., N.S.A., C.D.H., N.G., S.T.H., L.J.H., J.W.L., S.S.C., and M.B.W. drafted a significant part of the manuscript or figures. All authors approved the final version of the manuscript.

Results: We received responses from 25 hospitals including seven pediatric hospitals. A standardized EEG reactivity protocol was available in 44% of centers. Sixty percent of respondents felt that reactivity interpretation was subjective. Reactivity bedside testing always (100%) started during hypothermia and was performed daily during monitoring in the majority (71%) of hospitals. Stimulation was performed primarily by neurodiagnostic technologists (76%). The mean number of activation procedures modalities tested was 4.5 (standard deviation 2.1). The most commonly used activation procedures were auditory (83.3%), nail bed pressure (63%), and light tactile stimuli (63%). Changes in EEG amplitude alone were not considered consistent with EEG reactivity in 21% of centers.

Conclusions: There is substantial variability in EEG reactivity evaluation practices during cardiac arrest prognostication among North American academic hospitals. Efforts are needed to standardize protocols and nomenclature according with national guidelines and promote best practices in EEG reactivity evaluation.

Keywords

electroencephalogram; heart arrest; prognosis; EEG reactivity

Introduction

Severe neurological injury is the most common reason for withdrawal of life-sustaining therapies in patients successfully resuscitated after cardiac arrest.(1) Most literature in cardiac arrest prognostication has focused on identifying predictors of unfavorable outcomes, however few recent studies have investigated biomarkers of functional recovery.(2–5) This approach is of particular relevance in the context of the current high rates of early withdrawal of life-sustaining therapies due to perceived poor neurological prognosis despite guideline recommendations to postpone prognostication to at least 72 hours from resuscitation.(6, 7)

Electroencephalography is the most commonly used ancillary test in cardiac arrest prognostication.(8) Specifically, EEG reactivity is a strong predictor of coma recovery.(7) EEG reactivity refers to a change in the EEG background activity in response to external stimulation, which can be observed despite the use of therapeutic hypothermia and sedative mediations. (9–11) However, recent studies have shown that interpretation of EEG reactivity is unreliable, with inter-rater agreement as low as 26–55%.(12, 13) Although best practices for EEG reactivity evaluation have been defined by the American Clinical Neurophysiology Society (ACNS), the actual current state of practice involving EEG reactivity evaluation in cardiac arrest prognostication is not known.(13–15) Therefore, in this study, we aimed to assess the current practice of EEG reactivity bedside testing and interpretation in cardiac arrest prognostication across academic hospitals in North America. In addition, we evaluated expert opinions about the utility and objectivity of EEG reactivity interpretation in prognostication.

Methods

Survey Development and Distribution

The final questionnaire used in this survey was reviewed by a group of members of the Critical Care EEG Monitoring Research Consortium. We distributed a paper copy of the survey to representatives of academic hospitals affiliated with the Critical Care EEG Monitoring Research Consortium during the ACNS annual meeting in Phoenix, AZ on February, 2017 (Supplementary material 1). We obtained one response per hospital. This study was considered an exempt activity by the Partners Healthcare Institutional Review Board.

The survey consisted of 10 multiple-choice questions (Supplementary material 2). The questionnaire was divided into three sections: a) respondent training background; b) respondent opinion about EEG reactivity usefulness and objectiveness in prognostication; and c) institution-specific metrics related to technical, personnel, and procedural aspects of bedside EEG reactivity testing, abbreviated as “bedside testing”, and reactivity interpretation by the electroencephalographer, abbreviated as “interpretation”, in cardiac arrest prognostication. The institution representatives participating in the survey were instructed to provide the institution’s practice and not their own. Representatives of pediatric hospitals provided information regarding EEG reactivity testing and interpretation practices for pediatric patients only while non-pediatric hospitals provided information about those practices for adults only. The EEG activation procedures modalities included in the survey were auditory, light tactile stimulus, shaking shoulder, nostril tickle, sternal rub, nail bed or skin pressure, trapezius pressure, nipple pressure, tracheal suction, and passive eye opening. Electroencephalogram background attenuation was considered indicative of EEG reactivity under the category change in amplitude. After the survey was completed, we contacted participants who provided their contact information (92%) to inquire how many cardiac arrest patients were monitored with EEG every year.

Statistics

All analyses were performed using MATLAB 2017 (Natick, MA, USA) and GraphPad Prism 7 (La Jolla, CA, USA).

Results

Representatives from 25 academic hospitals from the United States (92%) and Canada (8%) completed the survey (Fig. 1). The survey response rate was 100%, of which 30.4% (n= 7) were from pediatric hospitals. All respondents were physicians. Twenty-four respondents (96%) had fellowship training in clinical neurophysiology or epilepsy whereas one respondent was a neurologist with neurocritical care fellowship training. The estimated average number of patients monitored with EEG for cardiac arrest per year in pediatric hospitals was 33 and 61 in non-pediatric hospitals.

The majority (56%) of the centers did not have a standardized EEG reactivity protocol for cardiac arrest prognostication (Fig. 2A). Most participants (76%) considered EEG reactivity often or always useful in cardiac arrest prognostication, (Fig. 2B). More than half of

respondents (60%) considered EEG reactivity interpretation subjective while none considered it very objective (Fig. 2C).

EEG Reactivity Bedside Testing

Three centers, including two pediatric hospitals, did not routinely provide targeted temperature management. All other hospitals started to test EEG reactivity during hypothermia (Fig. 3). EEG reactivity was tested less than daily in seven centers (29%), once daily in 11 centers (46%), and 2–3 times per day in four centers (17%). The mean number of activation procedures modalities was 4.5 (standard deviation 2.1). Auditory stimulation was the most common activation procedure used to test EEG reactivity (83%, Fig. 4). Nail bed pressure was the most common method of noxious stimulation (62%), followed by sternal rub (46%) and nostril tickle (42%); only one center utilized nipple pressure (4%). Among the pediatric hospitals, six (86%) utilized auditory stimulation, four (57%) nail bed pressure, and two (29%) utilized tracheal suction. EEG reactivity bedside testing was most commonly performed by neurodiagnostic technologists (76%, Fig. 2D).

EEG Reactivity Interpretation

Most hospitals (92%) utilized retrospective video-EEG review to assess for EEG reactivity. Five centers (20%) also evaluated EEG reactivity at the bedside. Two centers did not have video-EEG review available and one center routinely utilized quantitative EEG (compressed spectral array displays) in addition to review of the unprocessed EEG data. All centers considered an EEG reactive if a change in the frequency of EEG background activity in response to external stimulation was present. Five centers (21%) did not consider changes in EEG amplitude alone as evidence of reactivity (one pediatric hospital). Stimulus-induced (SI) rhythmic, periodic, or ictal discharges and other changes in EEG patterns were considered indicative of EEG reactivity in 11 (46%) and 15 (63%) centers, respectively. Muscle artifact was considered consistent with EEG reactivity by one (4%) respondent.

Discussion

We identified wide variability in EEG reactivity bedside testing and interpretation practices in cardiac arrest prognostication at adult and pediatric North American academic hospitals. Most participating hospitals did not have a standardized EEG reactivity evaluation protocol. Additionally, while most respondents considered EEG reactivity useful in prognostication, nearly half considered its interpretation subjective.

The ACNS consensus statement on continuous EEG in critically-ill adults and children advocates that EEG reactivity should follow a protocol and that neurodiagnostic technologists should perform the bedside stimulation protocol at least daily.(14) Despite these recommendations, a standardized protocol was not available in most hospitals surveyed and nearly a third of participants did not perform EEG reactivity bedside testing daily. Repeated evaluation of EEG reactivity is important because reactivity might emerge during or after rewarming.(11) The consensus statement also suggests that visual, auditory, tactile, and painful stimulation should be performed to test EEG reactivity despite stating that there are no data regarding the optimal method for doing so. While most centers

surveyed included auditory, tactile, and painful stimulation as part of their activation procedures, visual stimulation was less frequently performed. There is conflicting evidence in literature about which type of stimulation is more sensitive and more reproducible.(13, 16, 17)

Interpretation of EEG reactivity was frequently done retrospectively using video-EEG monitoring. Retrospective review of the raw EEG signal allows modification in the EEG recording settings and video reproduction rates that may facilitate determination of EEG reactivity in some cases.(16) Quantitative EEG (QEEG) tools were only used by one of the participating centers, though their usefulness in reactivity evaluation is suggested by the American Academy of Neurology and ACNS report on digital EEG, QEEG, and brain mapping.(18) A few recent studies concluded that QEEG methods for EEG reactivity evaluation may be at least equivalent and even superior to visual interpretation by experts. (12, 19–22)

A surprising finding in this survey was the fact that 21% of respondents did not consider change in amplitude alone consistent with EEG reactivity, despite the fact that EEG amplitude is part of the definition of EEG reactivity in the ACNS guidelines.(15) In addition, nearly half of survey respondents considered stimulus-induced changes in the ictal- interictal continuum as a sign of reactivity. Stimulus-induced rhythmic, periodic, or ictal discharges are commonly seen in cardiac arrest patients. In one small series using an univariate analysis, stimulus-induced changes in the ictal- interictal continuum were associated with poor outcome in cardiac arrest patients when seen during hypothermia (not during rewarming) and when associated with an otherwise unreactive EEG background.(23) In contrast, a study involving a mixed population of critically-ill patients that included cardiac arrest subjects concluded that the presence of stimulus-induced changes in the ictal-interictal continuum was not an independent predictor of poor outcome, but an unreactive EEG was.(24) The mixed survey responses related to EEG reactivity definition and stimulus-induced changes in the ictal- interictal continuum may be a nomenclature artifact, however. The 2013 ACNS standardized critical care EEG terminology guideline points out that if the only form of EEG reactivity observed is a stimulus induced response such as rhythmic delta activity, periodic discharges, or seizures, the EEG should be reported as “reactive, SI only.” This specific nomenclature describing the EEG background was devised to clearly differentiate ictal or interictal stimulus-induced responses from the more favorable type of EEG reactivity.

This variability in EEG evaluation practices and nomenclature is also evident in cardiac arrest prognostication literature.(5, 9, 10, 25–29) Details about inter-rater agreement and reactivity bedside testing protocol were often omitted, and the definition of a reactive or unreactive EEG also varied between studies. For prognostication purposes, most studies did not consider an EEG reactive if the only response to stimulation was stimulus-induced changes in the ictal- interictal continuum , while some studies did not specify if that was taken into consideration. (5, 9, 10, 27, 28) Despite the inconsistency in EEG reactivity evaluation practices among these studies, the absence, or presence, of EEG reactivity was always considered one of the most important predictors of outcome. While this observation underscores the importance of routinely test EEG reactivity, it does not answer what type of

activation procedures are needed nor which are more sensitive or specific in outcome prediction.

This study has several limitations. An important potential source of variability not assessed in our study is standardization of training of clinical neurophysiologists, neurodiagnostic technologists, and other intensive care unit providers involved in determining EEG reactivity; previous studies have shown that EEG responses to stimulation are variable and are dependent on stimulation intensity, sequence, and activation procedure, and are often subject to artifacts that could confound EEG interpretation.(16, 17) Although most reactivity testing is performed by EEG technologists, a detailed description of reactivity testing methods are not included in the best practices competencies for neurodiagnostic technologists performing continuous EEG in the ICU.(30) Incorporation of EEG technologists input on EEG reactivity evaluation would be very valuable in designing testing protocols. Our survey included only 25 hospitals, and the institutions involved were primarily academic hospitals, limiting the generalizability of our findings. In addition, the responses received may be influenced by individual opinions and may not reflect the broad clinical care practice of the respondent's hospital. Many of the centers surveyed use continuous EEG monitoring for cardiac arrest prognostication, a practice mainly limited to major academic hospitals. This survey also only included physicians, and primarily expert clinical neurophysiologists. Contributions from other providers such as intensivists, nurses, and neurodiagnostic technologists could enhance the evaluation of current practices involving use of EEG in cardiac arrest prognostication.

Conclusion

EEG reactivity bedside testing and interpretation practices in cardiac arrest prognostication vary substantially between North American centers. Limited standardization of testing protocols in concert with inconsistency of interpretation parameters and qualitative review of EEG responses could contribute to subjectivity and inaccuracy in EEG reactivity interpretation. Prognostic decisions in cardiac arrest have high-stakes and ensuring that best practices are followed is of great relevance. Future work should evaluate the impact of standardized protocols and interpretation of EEG reactivity in neurological prognostication and evaluate the role of QEEG analysis in limiting variability on reactivity evaluation.

Acknowledgments

Disclosures:

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Figure 1.
Participating academic hospitals in the United States and Canada

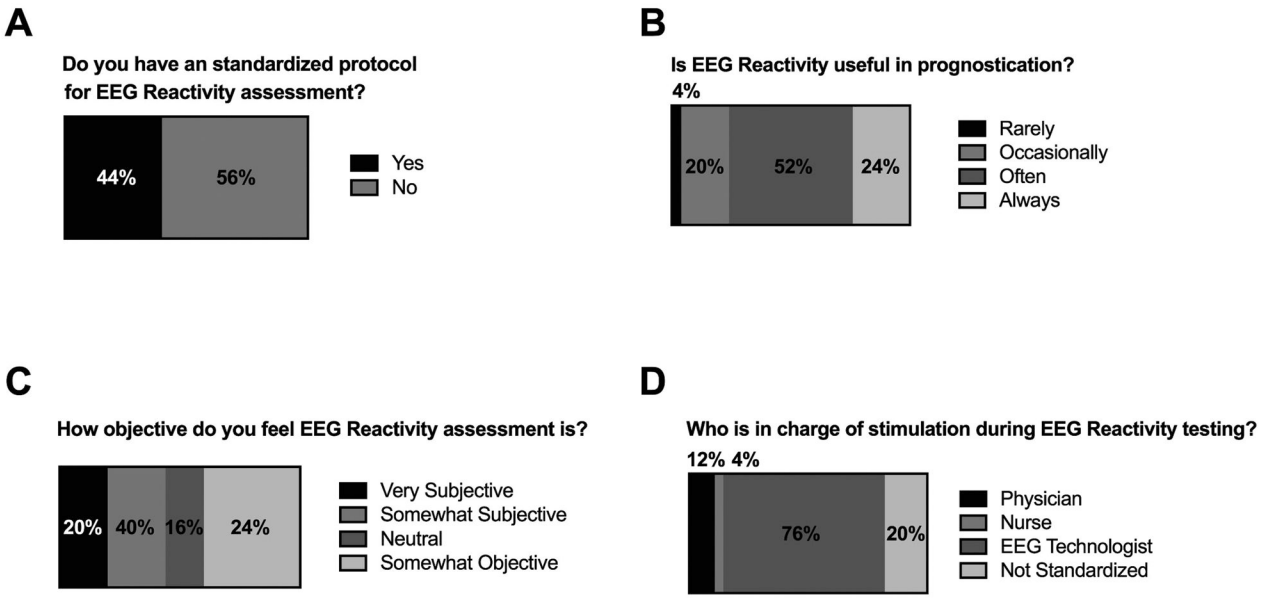

Figure 2.

EEG reactivity practices and expert opinion: A. Presence of an EEG reactivity protocol; B. EEG reactivity usefulness in prognostication; C. EEG reactivity objectiveness; D. Practitioners in charge of EEG reactivity testing.

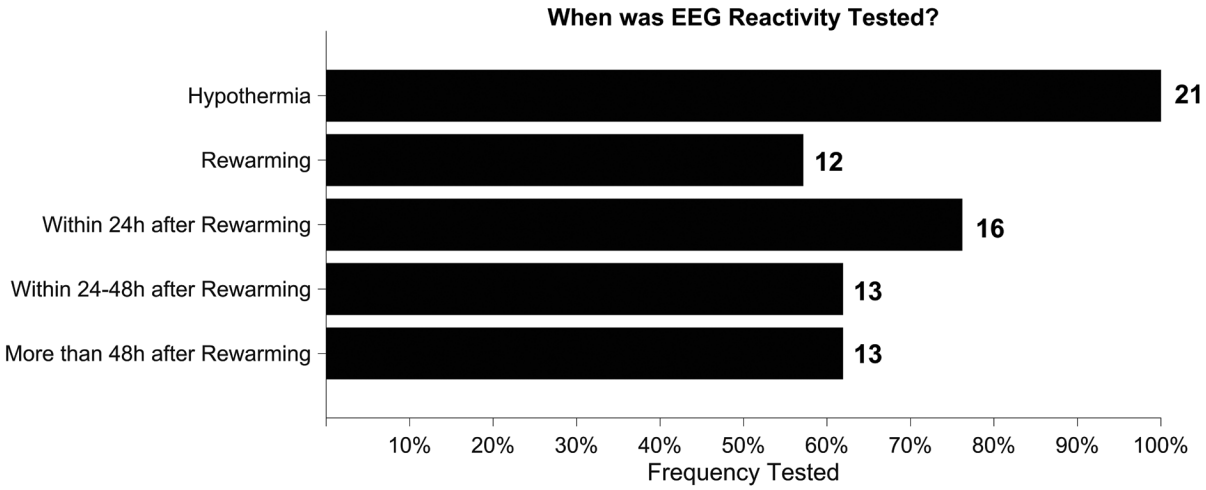

Figure 3.
EEG reactivity testing in relation to hypothermia management timing

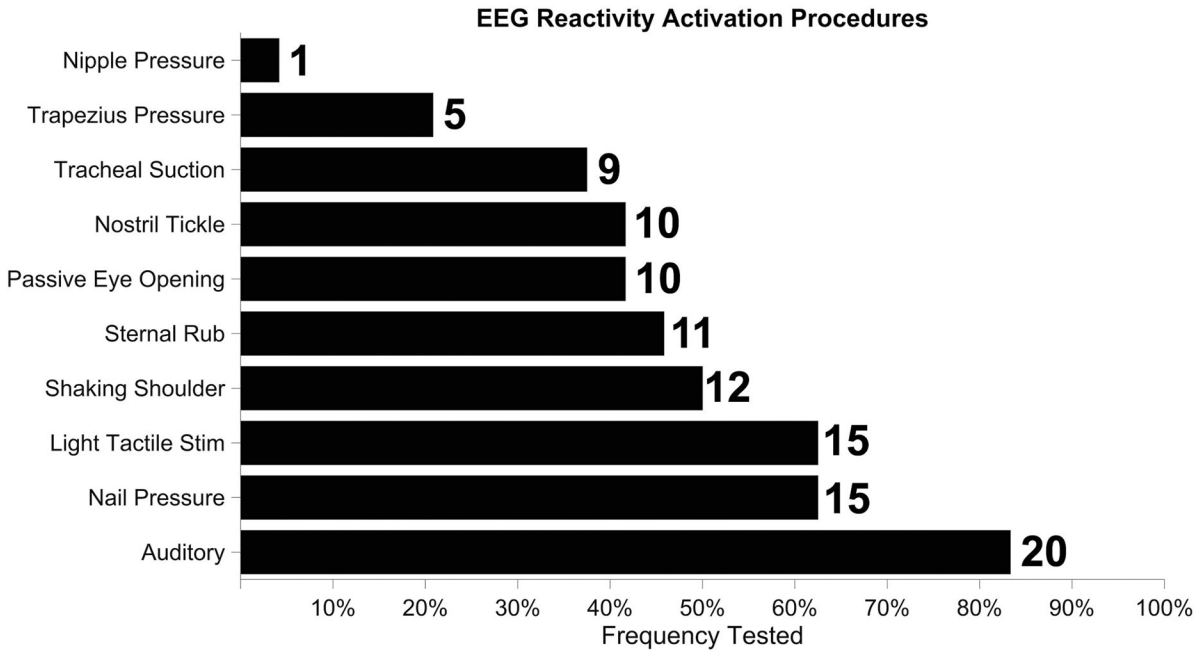

Figure 4.
EEG reactivity activation procedures routinely tested at participating centers