Despite standardization of stimulation and of definition of reactivity, its inter-rater reliability is only moderate to good (Gwet's AC1:58–69%)

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Abstract

Hypothermia does not limit the predictive value of reactivity testing. A combination of loud noise, shaking and trapezius muscle squeezing had the best sensitivity for favorable outcome

Keywords: Hypothermia • EEG • Post-anoxic coma

Objective

Reactivity assessment during EEG might provide important prognostic information in post-anoxic coma. It is still unclear how best to perform reactivity testing and how it might be affected by hypothermia. Our primary aim was to determine and compare the effectiveness, inter-rater reliability and prognostic value of different types of stimulus for EEG reactivity testing, using a standardized stimulation protocol and standardized definitions. Our secondary aims were to assess the effect of hypothermia on these measures, and to determine the prognostic value of a simplified sequence with the three most efficient stimuli.

Methods

Prospective single-center cohort of post-anoxic comatose patients admitted to the intensive care unit of an academic medical center between January 1, 2016 and December 31, 2018 and receiving continuous EEG monitoring (CEEG). Reactivity was assessed using standardized definitions and standardized sequence of stimuli: auditory (mild noise and loud noise), tactile (shaking), nociceptive (nostril tickling, trapezius muscle squeezing, endotracheal tube suctioning), and visual (passive eye opening). Gwet's AC1 and percent agreement (PA) were used to measure inter-rater agreement (IRA). Ability to predict favorable neurological outcome (defined as a Cerebral Performance Category of 1 to 2: no disability to moderate disability) was measured with sensitivity (Se), specificity (Sp), accuracy, and odds ratio [OR]. These were calculated for each stimulus type and at the level of the entire sequence comprising all the stimuli.

Results

One-hundred and fifteen patients were included and 242 EEG epochs were analyzed. Loud noise, shaking and trapezius muscle squeezing most frequently elicited EEG reactivity (42%, 38% and 38%, respectively) but were all inferior to the entire sequence, which elicited reactivity in 58% cases. The IRA for reactivity to individual stimuli varied from moderate to good (AC1:58–69%; PA:56–68%) and was the highest for loud noise (AC1:69%; PA:68%), trapezius muscle squeezing (AC1:67%; PA:65%) and passive eye opening (AC1:68%; PA:64%). Mild (odds ratio [OR]:11.0; Se:70% and Sp:86%) and loud noises (OR:27.0; Se:73% and Sp:75%), and trapezius muscle squeezing (OR:15.3; Se:76% and Sp:83%) during hypothermia had the best predictive value for favorable neurological outcome, although each was inferior to the whole sequence (OR:60.2; Se:91% and Sp:73%). A simplified sequence of loud noise, shaking and trapezius muscle squeezing had the same performance for predicting neurological outcome as the entire sequence. Hypothermia did not significantly affect the effectiveness of stimulation, but IRA was slightly better during hypothermia, for all stimuli. Similarly, the predictive value was higher during hypothermia than during normothermia.

Conclusions

Despite a standardized stimulation protocol and standardized definitions, the IRA of EEG reactivity testing in post-anoxic comatose patients was only good at best (AC1 < 70%), and its predictive value for neurological outcome remained imperfect, in particular with Sp values < 90%. While no single stimulus appeared superior to others, a full sequence using all stimuli or a simplified sequence comprising loud noise, shaking and trapezius muscle squeezing had the best combination of IRA and predictive value.

Significance

This study stresses the necessity to use multiple stimulus types to improve the predictive value of reactivity testing in post-anoxic coma and confirms that it is not affected by hypothermia.

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