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Effect of sedation on quantitative electroencephalography after cardiac arrest

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ABSTRACT

Background: Electroencephalography (EEG) has clinical and prognostic importance after cardiac arrest (CA). Recently, interest in quantitative EEG (qEEG) analysis has grown. The qualitative effects of sedation on EEG are well known, but potentially confounding effects of sedatives on qEEG after anoxic injury are poorly characterized. We hypothesize that sedation increases suppression ratio (SR) and decreases alpha/delta ratio (ADR) and amplitude-integrated EEG (aEEG), and that the magnitude of sedation effects will be associated with outcome.

Methods: We routinely monitor comatose post-arrest patients with EEG for 48–72 h. We included comatose EEG-monitored patients after CA who had protocolized daily sedation interruptions. We used Persyst v12 to quantify qEEG parameters and calculated medians for 10 min immediately prior to sedation interruption and for the last 5 min of interruption. We used paired *t*-tests to determine whether qEEG parameters changed with sedation cessation, and logistic regression to determine whether these changes predicted functional recovery or survival at discharge.

Results: 78 subjects were included (median age 56, 65% male). Interruptions occurred a median duration of 34 h post-arrest and lasted a median duration of 60 min. Prior to interruption, higher aEEG predicted survival, while lower SR predicted both survival and favorable outcome. During interruption, SR decreased ($p < 0.001$), aEEG increased ($p = 0.002$), and ADR did not change. Larger decreases in SR predicted decreased survival (OR = 1.04 per percent change; 95% CI 1.00–1.09).

Conclusion: Higher aEEG and lower SR predict survival after CA. Sedation alters aEEG and SR, but importantly does not appear to affect the relationship between these parameter values and outcome.

Introduction

Cardiac arrest (CA) affects over 500,000 Americans annually [1]. Most patients with return of spontaneous circulation are comatose on hospital arrival. For these patients, sequelae of ischemic brain injury are the most common cause of morbidity and mortality [2]. Electroencephalography (EEG) has clinical and prognostic importance in this population. In addition to assessing reactivity to external stimuli, EEG is helpful to detect seizures and can guide therapeutic decision making [3–5]. EEG interpretation may be qualitative or quantitative (qEEG), but interest in qEEG analysis has recently grown. Continuous or reactive patterns predict favorable recovery, while patterns such as burst suppression and attenuation, with qEEG analogues of suppression ratio (SR) and amplitude-integrated EEG (aEEG), are known predictors of poor outcomes [5–8].

Sedation and analgesia use is almost ubiquitous in post cardiac arrest care [9–11]. In healthy individuals and non-brain injured patients, it is known that sedative and anesthetic administration can cause burst suppression and generalized slowing of EEG, however few studies describe sedation effects on EEG in patients with severe global ischemic brain injury [12]. In particular, quantitative effects of sedation and analgesia on EEG are unknown in the

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Table 1
Baseline characteristics and outcomes.

Characteristic	Overall cohort (n = 78)
Age, years	56 ± 17
Female sex	27 (35)
Out-of-hospital arrest	63 (81)
Witnessed arrest	57 (73)
Bystander CPR	30 (38)
Initial rhythm	
VT/VF	26 (33)
PEA	23 (29)
Asystole	14 (18)
Unknown	15 (19)
Pittsburgh Cardiac Arrest Category	
II	27 (35)
III	10 (13)
IV	33 (42)
Unable[a]	8 (10)
Cardiac catheterization	25 (32)
Survived	38 (49)
Favorable outcome	29 (37)

Data are presented as mean ± standard deviation or raw number with corresponding percentages.

[a] Pittsburgh Cardiac Arrest Category cannot be assigned when the neurological exam is confounded by neuromuscular blockade, overdose or severe metabolic disarray.

post-cardiac arrest population, and sedation may be an important confounder in clinical prognostication using EEG [5]. Coma after global ischemic brain injury is associated with functional reduction of thalamo-cortical connectivity [2,13,14]. In patients with some preservation of cortical function, sedation may further reduce connectivity, increasing EEG suppression and altering EEG component frequencies. Specifically, sedation would decrease EEG amplitude and alpha/delta ratio (ADR) and increase suppression ratio (SR).

In this study, we describe sedation-induced changes in qEEG of post-cardiac arrest patients, and we explore the association of response to sedation with functional recovery. We hypothesize that sedation would: 1) significantly increase SR and decrease both ADR and EEG amplitude, and 2) the magnitude of sedation effects on qEEG will be associated with outcome at hospital discharge.

Methods

The University of Pittsburgh Institutional Review Board approved all aspects of this observational study with a waiver of informed consent for a minimal risk intervention.

Prior to performing this observational cohort study, we implemented a quality improvement (QI) project to systematically interrupt sedation at least daily in all comatose post-arrest patients. This intervention is consistent with institutional sedation practice for general intensive care [10,11]. Clinical contraindications to sedation interruptions included cases using sedation to suppress seizure activity, patients with significant hemodynamic instability or severe hypoxia, or patients with ongoing neuromuscular blockade. Treating clinicians determined the duration of sedation interruptions, restarting sedation for agitation, ventilator dyssynchrony, or worsening hemodynamic instability.

We included comatose patients being monitored with EEG after cardiac arrest. We excluded subjects who had a clinical contraindication to sedation interruption, a traumatic etiology of arrest, were pregnant, a prisoner or had comfort measures only as their goal of care. We also excluded sedation interruptions lasting less than 10 min. We prospectively screened and enrolled subjects from June 2015 and February 2017 (Fig. 1). To increase our sample size, we also generated a retrospective cohort including sedation interruptions performed between February 2015 and January 2016 by retrospectively examining electronic medical records to include any interruptions which were not formally recorded as the QI was being implemented. Bedside nurses recorded sedation interruption start and stop times in the electronic medical record. We collected data for up to 5 days following cardiac arrest, but only included data from each patient's first sedation interruption in our analysis.

Our institution routinely monitors EEG continuously after cardiac arrest for 2–3 days (during active targeted temperature management) or until death or awakening, whichever occurs first. We archive all continuous EEG recordings as part of the electronic medical record. We applied 22 gold-plated cup electrodes to the scalp in the standard 10–20 International System of Electrode Placement. Data was recorded using XLTech Natus Neuroworks digital video/EEG systems (Natus Medical, Pleasanton, CA). We used Persyst v12 (Persyst Development Co., Prescott, AZ) to generate qEEG data including SR, amplitude-integrated EEG (aEEG), and ADR. The software calculates SR by dividing each lead's data into 10 s epochs and determines the percentage of the total duration of each epoch that is "suppressed" (defined as ≥0.5 s of <3 μV amplitude) [15–18]. aEEG is a summary measure of the amplitude characteristics of a filtered, rectified peak-to-peak measure of the EEG signal in 1 s epochs. ADR is calculated by dividing the band-pass filtered spectral power in the alpha frequency range (8–13 Hz) by the band-pass filtered spectral in the delta frequency range (1–4 Hz) within a 2-min running average [15–18]. We used Persyst's algorithm for automated artifact reduction to reduce the contribution of physiological and electrode artifact. For each parameter, we averaged data across all leads of the standard 10–20 monitoring montage.

We calculated the median value of each parameter for the 10 min immediately prior to sedation interruption (this was termed "pre" data) and for the last 5 min of interruption (termed "post" data). We then calculated the difference between these two values to determine the change pre to post. If sedation was not restarted, we calculated post values 12 h after sedation discontinuation. In addition to qEEG measures, our other outcomes of interest were survival to hospital discharge and functionally favorable recovery at discharge, which we determined based on discharge disposition. Patients discharged home or to acute rehabilitation were considered to have a functionally favorable outcome at discharge, while functionally unfavorable recoveries were discharged to a skilled nursing facility, long-term acute care facility, hospice or death. This method of determination was used because we have previously demonstrated that this correlates with long-term outcome [19,20].

We summarized population characteristics and outcomes using descriptive statistics. We used paired *t*-tests to determine whether qEEG parameters changed from pre to post, and used unadjusted logistic regression to determine whether pre, post or the difference from pre to post in any qEEG parameter predicted neurological outcome at hospital discharge. Because of our small sample size, we did build adjusted models. We performed a post hoc analysis to test for significant difference between data collected prospectively and retrospectively. We performed all analyses using STATA v 14.2 (StataCorp, College Station, TX). We considered a P value <0.05 to be statistically significant for all analyses.

Results

Of 316 prospectively screened patients, 44 met inclusion and exclusion criteria, while 34 of 260 patients screened retrospectively met criteria, providing 78 total records for analysis (Fig. 1). Reasons for exclusions in the prospective cohort were primarily contraindications to sedation interruption (52% of exclusions: comfort measures only care (14% of exclusions), hemodynamically instability (11% of exclusions), no sedation administered (10% of exclusions), sedation used for seizure control (10% of exclusions),

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