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Single electroencephalographic patterns as specific and time-dependent indicators of good and poor outcome after cardiac arrest

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HIGHLIGHTS

- Based on standardised definitions of continuity of background activity we identified single EEG patterns with 100% specificity for good or poor outcome.
- Good outcome was predicted by continuous pattern at 12 h.
- Poor outcome was predicted by isoelectric pattern since 12 h, by burst-suppression pattern since 24 h and by suppression pattern since 48 h.

ABSTRACT

Objective: To evaluate the prognostic value of single EEG patterns recorded at various time-frames in postanoxic comatose patients.
Methods: This retrospective study included 30-min EEGs, classified according to the definitions of continuity of background activity given by the American Clinical Neurophysiology Society. Isoelectric pattern was distinguished from other suppressed activities. Epileptiform patterns were considered separately. Outcome was dichotomised based on recovery of consciousness as good (Glasgow Outcome Scale [GOS] 3–5) or poor (GOS 1–2).
Results: We analysed 211 EEGs, categorised according to time since cardiac arrest (within 12 h and around 24, 48 and 72 h). In each time-frame we observed at least one EEG pattern which was 100% specific to poor or good outcome: at 12 h continuous and nearly continuous patterns predicted good outcome and isoelectric pattern poor outcome; at 24 h isoelectric and burst-suppression predicted poor outcome; at 48 and 72 h isoelectric, burst-suppression and suppression (2–10 μV) patterns predicted poor outcome.
Conclusions: The prognostic value of single EEG patterns, defined according to continuity and voltage of background activity, changes until 48–72 h after cardiac arrest and in each time-frame there is at least one pattern which accurately predicts good or poor outcome.
Significance: Standard EEG can provide time-dependent reliable indicators of good and poor outcome throughout the first 48–72 h after cardiac arrest.

1. Introduction

For many decades EEG has been used routinely for prognostication in postanoxic comatose patients, using various classifications before therapeutic hypothermia (TH) entered clinical practice (e.g. Hockaday et al., 1965; Synek, 1988; Young et al., 1997). Despite this widespread use of EEG in clinical practice, the

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guidelines for prognostication in postanoxic patients published by the American Academy of Neurology (Wijdicks et al., 2006) did not recommend the use of EEG as its prognostic accuracy was still considered insufficient on the basis of pre-TH evidence of EEG studies.

In the following years several new prospective (Cloostermans et al., 2012; Hofmeijer et al., 2015; Rundgren et al., 2010; Sivaraju et al., 2015; Tjepkema-Cloostermans et al., 2015) and retrospective (Crepeau et al., 2013) studies gave new evidence about the prognostic role of EEG. These studies indicated that the prognostic meaning of EEG patterns varied according to the timing of recording. They also showed that early EEG recordings can reliably predict good outcome, whereas previous research had only considered predictors of poor outcome. These findings derived from continuous EEG recordings in TH-treated patients analysed combining several EEG patterns into few easily recognisable categories.

Following this renewed interest and the need of prognostic guidelines for TH-treated patients, a European advisory statement (Sandroni et al., 2014) suggested that the presence of certain EEG patterns (absence of reactivity, burst-suppression) at 72 h after cardiac arrest (CA) predicted poor outcome. However the authors noted that definitions were inconsistent among the studies (especially for burst-suppression) and that the overall quality of evidence was low. No mention was made of prognostication in the first 24 h after CA because of insufficient evidence.

There was clearly a need for standardised definitions in this field and the recent guide to terminology for EEG in critical care (Hirsch et al., 2013) published by the American Clinical Neurophysiology Society (ACNS) represents an important advance in this respect.

Two studies have used this terminology for prognostic grading of EEGs in postanoxic patients (Sivaraju et al., 2015; Søholm et al., 2014) and have proposed EEG categories consisting of several patterns with unfavourable or favourable prognostic significance, finding a strong specificity for poor outcome and a somewhat lower specificity for good outcome.

In the present study we used the ACNS terminology to describe single EEG patterns in postanoxic patients in terms of the continuity parameter. Our aim was to evaluate retrospectively the prognostic significance of single EEG patterns defined according to ACNS terminology, and to analyse how their predictive value changed during the first 12–72 h after CA.

2. Materials and methods

2.1. Patients

From our EEG database we retrospectively identified all adult (>16 years old) comatose patients who underwent EEG study after CA of presumed cardiac origin, treated with TH and admitted to the Emergency Department of Careggi Teaching Hospital (Florence, Italy) between January 2007 and June 2014. EEGs were performed on request by ICU physicians. Exclusion criteria were: absence of EEG recordings taken within 72 h from CA; CA of non-cardiac origin; TH not performed or interrupted within 24 h from CA; intra-operative CA; presence of other severe neurological injury (such as intracranial haemorrhage, traumatic brain injury, intoxication due to drugs or carbon monoxide); presence of severe extra-neurological pathology implying a life expectancy of less than six months.

Approval for the study was obtained from the local Institutional Review Board with a waiver on the requirement for informed consent as EEG recordings were part of the current standard clinical management.

2.2. Treatment protocol

Mild endovascular TH was started as soon as possible and maintained for 24 h. The CoolGard Icy Catheter (Alsius Corp., Irvine, California, U.S.A.; 8.5fr) was positioned in the right femoral vein. Patients' core temperature was maintained at 32–34 °C (tympanic temperature). Strict glucose homeostasis was maintained in accordance with the post-resuscitation support protocol. Clinical parameters were monitored continuously and an arterial blood gas analysis was performed every 2 h. At the end of the cooling period patients were allowed to return passively to normothermia. The sedation protocol consisted of a bolus of IV midazolam at 0.03 mg/kg followed by an infusion of 1 mg/h, or propofol 1–2 mg/kg/h. Neuromuscular paralysis was induced with a bolus of 0.4 mg/kg atracurium, followed by an initial infusion of 4 μg/kg/min if was required to facilitate ventilation or to abolish shivering. Venous districts were monitored frequently using ultrasound to detect deep venous thrombosis. No complications occurred during or after the cooling procedure.

2.3. EEG recordings

Standard 30-min EEG recordings were initiated as soon as possible after patients arrived in the ICU using a portable digital machine (EBN GalNT, Florence, Italy). Ten needle to 21 silver-silver chloride electrodes were placed according to the international 10–20 system. When reduced montage was applied a bipolar longitudinal montage with Fp2, F4, C4, P4, O2, Fp3, F3, C3, P3, O1 was used. Recordings were acquired with a sampling rate of 128 Hz. During reviewing digital filters (low-pass filter = 30 to 70 Hz; time constant = 0.1 or 0.3 s; notch filter = 50 Hz) and sensitivity gain (2 to 10 μV/mm with a standard gain of 7 μV/mm) were adjusted according to interpretation needs. When more than one recording was available for a patient, we included the first EEG in the study. Recordings were retrospectively organised into four time-frames relative to the CA: 12 h (range: 6–13 h post-CA), 24 h (range: 14–30 h post-CA), 48 h (range: 33–62 h post-CA), 72 h (range: 67–96 h post-CA).

2.4. EEG classification

All EEGs were classified retrospectively according to the most recent terminology for EEGs recorded in ICU (Hirsch et al., 2013). The main parameter used to classify background activity was 'continuity', but 'voltage' and 'reactivity' were also considered. Reactivity was defined as a clear, reproducible change in background frequency and/or amplitude following auditory (clapping and calling patient's name loudly) and/or noxious stimulations (nail bed and supraorbital notch pressure). *Isoelectric* (voltage < 2 μV) recordings were also identified although the original classification did not distinguish them from suppressed activity (voltage < 10 μV).

All recordings with ictal or periodic epileptiform activity were assigned to a separate category (*Epileptiform discharges*) independent of background activity. EEGs showing sporadic (i.e. non-periodic) epileptiform activity were also included in this category if the epileptiform activity was classified as "abundant" according to above-mentioned ACNS terminology (Hirsch et al., 2013). Thus, the main patterns identified were: *continuous*; *nearly continuous*; *discontinuous*; *burst-suppression*; *burst-suppression with highly epileptiform bursts*; *suppression*; *isoelectric*; *epileptiform discharges*.

2.5. Burst-suppression with identical bursts

In addition to ACNS classification, the EEGs with *burst-suppression* (including those *with highly epileptiform bursts*) at 12