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Association between somatosensory evoked potentials and EEG in comatose patients after cardiac arrest

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HIGHLIGHTS

- Absent SSEP and suppressed or synchronous EEG on suppressed background predict poor outcome.
- SSEP is either present or absent, with no changes over the first 5 days.
- SSEP cannot be predicted by EEG patterns, except for preserved N20 in normal EEG.

ABSTRACT

Objective: To analyze the association between SSEP results and EEG results in comatose patients after cardiac arrest, including the added value of repeated SSEP measurements.
Methods: Continuous EEG was measured in 619 patients during the first 3–5 days after cardiac arrest. SSEPs were recorded daily in the first 55 patients, and on indication in later patients. EEGs were visually classified at 12, 24, 48, and 72 h after cardiac arrest, and at the time of SSEP. Outcome at 6 m was dichotomized as good (Cerebral Performance Category 1–2) or poor (CPC 3–5). SSEP and EEG results were related to outcome. Additionally, SSEP results were related to the EEG patterns at the time of SSEP.
Results: Absent SSEP responses and suppressed or synchronous EEG on suppressed background $\geq$24 h after cardiac arrest were invariably associated with poor outcome. SSEP and EEG identified different patients with poor outcome (joint sensitivity 39% at specificity 100%). N20 responses were always preserved in continuous traces at >8 Hz. Absent SSEPs did not re-emerge during the first five days.
Conclusions: SSEP and EEG results may diverge after cardiac arrest.
Significance: SSEP and EEG together identify more patients without chance of recovery than one of these alone.

1. Introduction

Comatose patients after cardiac arrest have an uncertain prognosis. Despite treatment on intensive care units (ICUs), approximately half have a poor outcome as a result of severe postanoxic encephalopathy (Zandbergen et al., 1998). Early recognition of patients with and without chances of recovery of brain functioning may prevent continuation of futile intensive care treatment and contribute to communication between doctors and families.

Somato-sensory evoked potential (SSEP) and EEG recordings hold valuable information for prediction of outcome. Absent SSEP responses after restoration of normothermia are strongly associated with a poor outcome and have been included in prognostication guidelines since the late 1990s (Nolan et al., 2015; Sandroni et al., 2014). Recent studies have shown the prognostic value of EEG patterns. An evolution towards continuous rhythms within twelve hours after arrest was strongly related to good outcome (Cloostermans et al., 2012; Hofmeijer et al., 2015; Oh et al., 2015; Sivaraju et al., 2015). Otherwise, lasting iso-electricity or

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synchronous patterns on a suppressed background invariably predicted a poor outcome (Cloostermans et al., 2012; Hofmeijer et al., 2015; Ruijter et al., 2019a; Sivaraju et al., 2015; Sondag et al., 2017; Spalletti et al., 2016).

Since previous authors have reported that EEG and SSEP are complementary for detection of patients with a poor outcome (Hofmeijer et al., 2015; Ruijter et al., 2019a), pathological EEG patterns and absent SSEPs probably reflect different manifestations of irreversible brain damage. In fact, EEG rhythms primarily reflect pyramidal cell functioning, including their synchrony, for which a sufficient number of functioning pyramidal synapses is required (Buzsaki et al., 2012). Otherwise, SSEP responses depend on intact thalamocortical projections (van Putten, 2012).

In the current study, we analyze the association between SSEP results and EEG results in comatose patients after cardiac arrest. We hypothesize that SSEP and EEG results may diverge and are complementary for reliable detection of patients with poor outcome. In addition, we analyze the added value of repeated SSEP measurements.

2. Materials and methods

2.1. Study design

This is a retrospective analysis of a prospective cohort study on continuous EEG registration of comatose patients after cardiac arrest, conducted on ICUs of two teaching hospitals in the Netherlands. In the Medisch Spectrum Twente (Enschede), patients were included from June 2010 to November 2017. In Rijnstate Hospital (Arnhem), patients were included from June 2012 to September 2017. Part of the EEG data were used in previous studies (Cloostermans et al., 2012; Hofmeijer et al., 2015, 2014; Ruijter et al., 2018, 2019a; Sondag et al., 2017; Tjepkema-Cloostermans et al., 2017, 2015).

2.2. Standard protocol approvals, registrations, and patient consents

EEG registration is part of current care in the two participating hospitals. The Medical Ethical Committee Twente approved the protocol and waived the need for informed consent for EEG registration. Oral informed consent was obtained at follow up.

2.3. Patients

Consecutive, adult, comatose patients after cardiac arrest (Glasgow Coma Scale score ≤ 8), admitted to the ICU, were included in our prospective cohort study. Exclusion criteria were concomitant acute stroke, traumatic brain injury, hanging/choking, auto intoxication, anaphylactic shock, drowning, preexisting dependency, severe spinal cord injury, or progressive neurodegenerative disease.

2.4. Treatment

"Patients were treated according to standard protocols for comatose patients after cardiac arrest. This included targeted temperature management at 33 °C or 36 °C. In Rijnstate Hospital, since February 2014, the target temperature was set from 33 °C to 36 °C. In Medisch Spectrum Twente, there was a gradual shift from 33 °C to 36 °C in 2017. Target temperature was induced as soon as possible after arrival at the emergency room or ICU and maintained for 24 h. After 24 h, passive re-warming was controlled to a speed of 0.25 °C or 0.5 °C per hour. In case of $T > 38$ °C and a Glascow Coma Scale score ≤ 8, targeted temperature management was restarted at 36.5–37.5 °C for another 48 h. In Medisch Spectrum Twente, propofol and fentanyl or remifentanil were used for sedation. In Rijnstate Hospital, patients received a combination of propofol, midazolam, and/or morphine. Mostly, analgo-sedation was discontinued at a body temperature of 36.5 °C. In both hospitals, a non-depolarizing muscle relaxant (rocuronium or atracurium) was occasionally added in case of severe compensatory shivering." (Hofmeijer et al., 2015).

2.5. Decisions on withdrawal of treatment

"Withdrawal of treatment was considered $\geq$72 h after cardiac arrest, during normothermia, and off sedation. Decisions on treatment withdrawal were based on international guidelines including bilateral absence of evoked SSEPs, absent or extensor motor responses, incomplete return of brainstem reflexes and treatment resistant myoclonus (Sandroni et al., 2014; Wijdicks et al., 2006). Discontinuation of life sustaining treatment was sporadically initiated between 48 h and 72 h in case of absent SSEP responses. EEG data were not used for decisions regarding treatment withdrawal. However, physicians were not blinded to the EEG and treatment of electrographic seizures was left to the discretion of the treating physician." (Ruijter et al., 2018).

2.6. Outcome

"The primary outcome measure was neurological outcome expressed as the score on the five-point Glasgow-Pittsburgh Cerebral Performance Category (CPC) at six months (Cummins et al., 1991). Outcome was dichotomized as "good" (CPC 1–2) or "poor" (CPC 3–5). CPC scores were obtained by telephone follow-up at 6 months by one of the investigators (MTC, BR, or HK), blinded for EEG patterns and SSEP recordings. Scoring was based on a Dutch translation of the EuroQol-6D questionnaire." (Hofmeijer et al., 2015).

2.7. EEG registrations and analyses

"Continuous EEG registrations were started as soon as possible in all patients after arrival at the ICU. Twenty-one silver-silverchloride cup electrodes were placed on the scalp according to the international 10–20 system. A Neurocenter EEG recording system (Clinical Science Systems, Leiden, The Netherlands) or a Nihon Kohden system (VCM Medical, Leusden, The Netherlands) were used to make EEG registrations.

All EEG analyses were prespecified and performed offline, after the registrations. Epochs of 5 min were automatically selected by a computer algorithm at 12, 24, 48, and 72 h after cardiac arrest (Tjepkema-Cloostermans et al., 2013)" (Hofmeijer et al., 2015). Additionally, five-minute epochs were selected at the time of SSEP recording ±10 h, preferably within 1 h from the SSEP recording.

Anonymized epochs with raw EEG data were presented to a reviewer (MvP, JH, BR, MTC, HK or AG) by the computer, in random order, blinded to the point in time of the epoch, the patient's clinical status during the recording, medication, and outcome. EEG epochs were visually classified by two reviewers, independently. "Upon disagreement, consensus was determined. If necessary, a third reviewer was consulted" (Hofmeijer et al., 2015).

Epochs were classified as suppressed (<10 μV), low-voltage (<20 μV), synchronous patterns on suppressed background ($\geq$50%) (burst suppression with identical bursts, generalized periodic discharges (GPD) on a suppressed background, or burst-suppression with generalized abrupt onset bursts with suppressed background), other burst-suppression patterns, GPDs with other background, other epileptiform patterns and continuous patterns (dominant frequencies <4 Hz, 4–8 Hz, >8 Hz) (Hofmeijer et al., 2014; Ruijter et al., 2019a, 2015). "Burst-suppression" was defined

as clear increases in amplitude (bursts) with interburst intervals of at least one second with low-voltage or absent activity (suppressions, <10 μV) (Hofmeijer et al., 2015). Subsequently, burst suppression with identical bursts (Hofmeijer et al., 2014) and highly epileptiform bursts typically meet the criteria of "synchronous burst-suppression" (Ruijter et al., 2019a). GPD patterns were subdivided into GPDs on a suppressed background and GPDs with other background activity (Ruijter et al., 2015). Continuous patterns were subdivided according to their dominant frequency (delta, theta, or ≥alpha).

2.8. SSEP recordings and analyses

In the first 55 patients, repeated SSEP recordings during the first 5 days of the ICU stay, or until discharge from the ICU, were intended. For later patients, SSEP recordings were done at the discretion of the treating physician. Generally, SSEPs were recorded between 48 and 72 h in patients who remained comatose after restoration of normothermia, off-sedation. "The SSEP was measured after stimulation of the right and left median nerve using a bipolar surface electrode at the wrist. Stimulus duration was set at 0.3 ms and stimulus amplitude was adjusted until a visible twitch of the thumb was produced. Two sets of >200–1000 responses were averaged, band pass filtered between 0.1 Hz and 2.5 kHz, and notch filtered around 50 Hz. Stimulus frequency was set at 1.7 or 2.3 Hz. Silver-silver chloride cup electrodes were placed at Erb's point, cervical spine (C5), and 2 cm posterior to C3 and C4 (C3′ and C4′). Fz was used as a reference." (Cloostermans et al., 2012). Peripheral N9 and N13 responses, and cortical N20 responses were recorded. SSEP results were categorized as present or absent based on the presence or absence of N20 responses. Unilateral present N20 responses were considered as present SSEP. SSEP recordings were classified as inconclusive if noise level was higher than signal or in the absence of peripheral responses. SSEP recordings were made using a Nicolet Bravo system (Viasys, Houten, The Netherlands).

2.9. Statistical analyses

Demographic, baseline, EEG, and SSEP data are presented in a descriptive way. Differences between groups of patients were tested by a chi-square test for categorical variables and Student's *t*-test for continuous variables, given a normal distribution. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for (groups of) predictors of poor or good outcome, including corresponding 95% confidence intervals. Association between SSEP and EEG is expressed as risk ratio (RR). Interobserver agreement of the EEG classification was analyzed with Cohen's Kappa. Analysis was performed with SPSS-22 (IBM).

2.10. Data availability statement

Raw EEG and outcome data used for this article will be kept for at least 15 years and made available upon request, for verification of results or new relevant research questions, conditionally. Conditions include optimal data safety, adequate methodology, mutual appointments on collaboration, and approval of all collaborators.

3. Results

EEG registrations were started in 647 patients. Twenty-eight patients were excluded from this analysis because they met one of the exclusion criteria: relevant traumatic brain injury, hanging/-choking, preexisting dependency, auto intoxication, anaphylactic shock, drowning, recent ischemic stroke, severe spinal cord injury, or progressive neurodegenerative disease (Fig. 1). 619 consecutive patients were included, 352 in MST and 267 in Rijnstate Hospital. Baseline characteristics are summarized in Table 1. Seventeen subjects (2.7%) were lost to follow up, leaving 602 inclusions for analysis (Fig. 1). Of 14 patients, the CPC score at three months was used. Poor neurological outcome occurred in 314 patients (52%), of whom 287 died. The EEG pattern could be classified in 356 patients at 12 h, in 525 patients at 24 h, in 398 patients at 48 h and in 241 patients at 72 h. EEG classification was missing in case of abundant artifacts, at 12 h if EEG was started later than 12 h after cardiac arrest, and at ≥24 h if the patient had already died or woken up.

3.1. Prediction of poor outcome

Description of EEG and SSEP findings: At 12, 24, 48, and 72 h after cardiac arrest, a suppressed or synchronous pattern on suppressed background was observed in 87, 84, 36, and 16 patients,

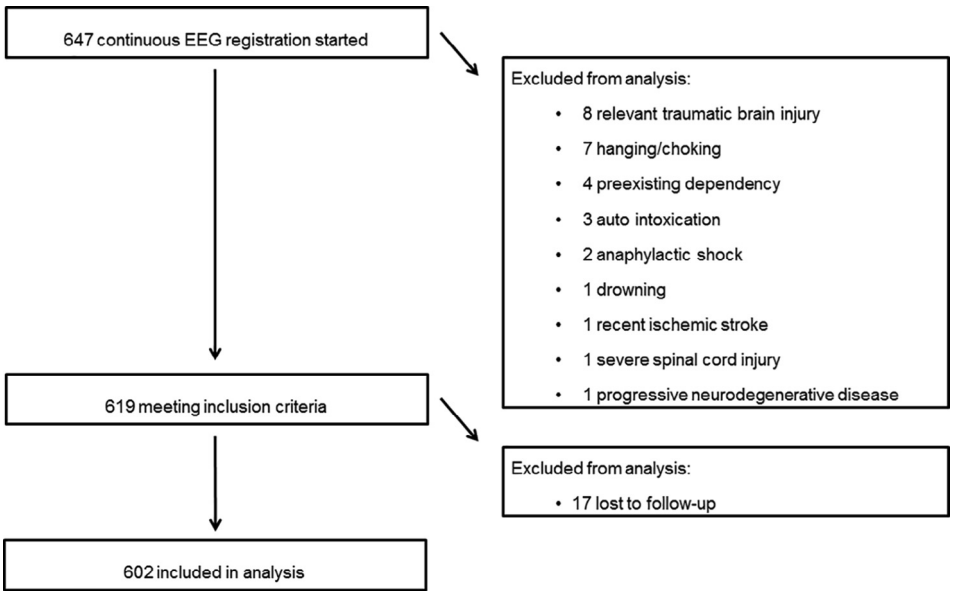

Fig. 1. Flow of patients through this study.

Table 1
Patient characteristics and differences between patients with good and poor neurological outcome.

	Good outcome N = 288	Poor outcome N = 314	p-value
Female sex	68 (24%)	74 (24%)	1
Mean age (±SD)	59 ± 12	66 ± 12	<0.001
OHCA	265/288 (92%)	279/314 (89%)	0.1
Cardiac etiology	256/269 (95%)	228/284 (80%)	<0.001
VF rhythm	254/288 (88%)	176/314 (56%)	<0.001
Mild therapeutic hypothermia (33 °C)	172/240 (72%)	201/263 (76%)	0.2
Propofol in first 24 h	269/281 (96%)	274/305 (90%)	0.005
Max propofol dose in first 24 h (mg/kg/h)	2.93 ± 1.16	2.63 ± 1.03	0.002
Midazolam in first 24 h	89/281 (32%)	108/305 (35%)	0.2
Max midazolam dose in first 24 h (μg/kg/h)	117.7 ± 73.0	129.8 ± 92.7	0.3
Suppressed or synchronized EEG with suppressed background EEG at 12 h	0/181 (0%)	87/175 (50%)	<0.001
Suppressed or synchronized EEG with suppressed background at 24 h	0/274 (0%)	84/251 (34%)	<0.001
Suppressed or synchronized EEG with suppressed background at 48 h	0/191 (0%)	36/207 (17%)	<0.001
Suppressed or synchronized EEG with suppressed background at 72 h	0/108 (0%)	16/133 (12%)	<0.001
Bilaterally absent SSEP	0/40 (0%)	87/204 (43%)	<0.001
Continuous EEG at 12 h	83/181 (46%)	17/175 (10%)	<0.001

SD = standard deviation; OHCA = out of hospital cardiac arrest; VF = ventricular fibrillation; SSEP = somatosensory evoked potential.

Table 2
Predictive values of (combinations of) EEG and SSEP parameters.

Predictor	Predicted outcome	Specificity (95% CI)	Sensitivity (95% CI)	PPV (95% CI)	NPV (95% CI)
Continuous EEG pattern at 12 h	Good	90% (84–94)	46% (38–53)	83% (74–90)	62% (55–68)
Suppressed or synchronized EEG with suppressed background at 24 h	Poor	100% (98–100)	27% (22–32)	100% (95–100)	56% (51–60)
Absent SSEP, typically 48–72 h after resuscitation	Poor	100% (98–100)	28% (23–33)	100% (95–100)	56% (52–60)
Suppressed or synchronized EEG with suppressed background at 24 h or absent SSEP	Poor	100% (98–100)	39% (33–44)	100% (96–100)	60% (55–64)

CI = confidence interval; SSEP = somatosensory evoked potential.

and invariably associated with a poor outcome. Bilaterally absent SSEP responses were observed in 87 patients and also invariably associated with a poor outcome. Fifty patients with a poor outcome had a suppressed or synchronized EEG on suppressed background at 24 h after cardiac arrest and an absent SSEP.

Predictive values: Sensitivity, specificity, PPV and NPV of (a combination of) EEG and SSEP factors associated with a poor outcome are summarized in Table 2. Thirty-four patients with a poor outcome could be identified based on EEG pattern (suppressed or synchronous pattern on suppressed background) at 24 h after cardiac arrest, but had a present SSEP response. Thirty-seven patients with a poor outcome had an absent SSEP, but continuous or other EEG pattern at 24 h after cardiac arrest.

3.2. Prediction of good outcome

Description of EEG and SSEP findings: Continuous EEG patterns at 12 h after cardiac arrest were observed in 83 patients with a good outcome vs. 17 with a poor outcome. Predictive values: Specificity, sensitivity, PPV and NPV are summarized in Table 2. Beyond 12 h, the observed incidence of continuous patterns among patients with a poor outcome grew. Consequently, the specificity of continuous patterns for prediction of good outcome decreased after 12 h (data not shown).

3.3. Repeated SSEP

In 55 patients, daily SSEP recordings during the first five days after cardiac arrest were planned. All were treated with mild therapeutic hypothermia. One of these patients had no SSEP recording and seven had only one, because of death within 32 h after cardiac arrest. Eight patients had two SSEP recordings, fourteen patients had three SSEP recordings on day 1–3, eleven patients had four SSEP recordings on day 1–4, fifteen had five SSEP recordings on day 1–5. In one patient, the first SSEP was considered inconclusive, whereas it was present on the following recording. One patient had present responses in the first four recordings and absent responses in the fifth SSEP recording. In all other patients with repeated SSEP recordings, N20 responses were either present ($n = 40$), or absent in all recordings ($n = 5$).

3.4. Association of SSEP and EEG pattern

A total of 360 SSEP recordings were done in 244 patients. Three hundred twenty-six of the according EEG epochs (91%) were obtained at the time of SSEP recording ± 1 h. The remaining epochs were collected at a mean of 3 h before or after SSEP recording. SSEP results in relation to the EEG background pattern at the moment of the SSEP recording are summarized in Table 3. All patients with continuous, normal voltage (>20 μV) EEG patterns with a dominant frequency > 8 Hz had preserved N20 responses. However, none of the other EEG patterns was invariably associated with a preserved N20 response, and none of the EEG patterns was invariably associated with an absent N20 response. If EEG and SSEP results were stratified to time since cardiac arrest, these results were essentially the same (see Appendix A: supplementary material).

3.5. Interobserver agreement

Interobserver agreement for designation of a suppressed or synchronized EEG on suppressed background was 0.72–0.80, depending on the timing of the EEG classification.

Table 3
SSEP results per EEG pattern.

EEG pattern	N20 not bilaterally absent $N = 247$	N20 bilaterally absent $N = 92$	*P*-value	RR	95% CI
Suppressed ($A \leq 10$ μV)	2 (1%)	6 (6%)	0.007	2.9	1.9–4.5
Low-voltage (10 μV < $A \leq 20$ μV)	12 (5%)	11 (11%)	0.04	1.9	1.2–3.0
Burst suppression with identical bursts	4 (2%)	8 (8%)	0.005	2.6	1.7–4.0
Burst-suppression with generalized, abrupt onset bursts, with suppressed background	1 (<1%)	5 (5%)	0.008	3.2	2.1–4.8
Other burst suppression	82 (32%)	19 (20%)	0.03	0.6	0.4–1.0
Continuous < 4 Hz	33 (13%)	7 (7%)	0.2	0.6	0.3–1.2
Continuous 4–8 Hz	55 (22%)	11 (11%)	0.05	0.6	0.3–1.0
Continuous > 8 Hz	20 (8%)	0 (0%)	0.01	0.0	0.0–0.0
GPDs with suppressed background	13 (5%)	15 (15%)	0.002	2.2	1.5–3.2
GPDs with other background	22 (9%)	8 (8%)	0.9	1.0	0.5–1.8
Other epileptiform patterns	3 (1%)	2 (2%)	0.9	1.5	0.5–4.4

SSEP = somatosensory evoked potential; RR = Risk Ratio for absent SSEP; CI = confidence interval; GPD = generalized periodic discharges.

4. Discussion

We confirm that absent SSEP and suppressed or synchronized EEG on suppressed background are reliable predictors of poor outcome of comatose patients after cardiac arrest, and complementary with regard to identification of patients with a poor outcome. Furthermore, for the first time, we demonstrate that the EEG background pattern at the time of SSEP testing does not reliably predict presence or absence of the SSEP response. This is with the exception of continuous, normal voltage traces with a >8 Hz frequency content, where N20 responses were always preserved. There was no relevant additional value of daily SSEP testing over single SSEP testing, since SSEP responses were either present or absent every day in the vast majority of patients.

Complementarity of SSEP and EEG for prediction of poor outcome is in line with previous publications on outcome prediction after cardiac arrest using multimodal approaches (Cloostermans et al., 2012; Grippo et al., 2017; Hofmeijer et al., 2015; Nolan et al., 2015; Oddo and Rossetti, 2014; Sivaraju et al., 2015; Tsetsou et al., 2018). Apparently, SSEP and EEG partly identify different patients with severe encephalopathy and a subsequent poor outcome. Continuous EEG patterns at 12 h after cardiac arrest are strongly associated with a good neurological recovery (Hofmeijer et al., 2015; Tjepkema-Cloostermans et al., 2015). However, preserved SSEP responses are not specific for good outcome (Zandbergen et al., 2006). In these patients, the EEG may differentiate between patients with good and poor prognosis (Rossetti et al., 2009; Rothstein et al., 2010). Specific SSEP characteristics, such as N20 amplitude <0.62 μV, may contribute to prediction of poor neurological outcome (Endisch et al., 2015), but have not been studied with regard to prediction of good outcome.

To further study the association between SSEP and EEG, we analyzed the N20 response in relation to the EEG pattern at the time of SSEP testing. Suppressed EEG and synchronous patterns on suppressed background were associated with absent SSEPs, but not invariably so. Even with suppressed or synchronous EEG on a suppressed background, N20 responses could be evoked in some patients. Otherwise, with continuous, traces, SSEPs could be absent.

The origin of pathological EEG and SSEP traces cannot be derived from the data. Previous studies to clarify mechanisms used divergent experimental models. Still, the pathophysiology of (pathological) EEG patterns is only partly known and many explanations are, at least partly, speculative. In a previous mathematical study we hypothesized that somatosensory evoked responses, which reflect extracellular currents generated by excitatory postsynaptic potentials, depend on a preserved thalamocortical synaptic transmission to somatosensory cortical neurons (van Putten, 2012). Otherwise, some pathological EEG patterns that we typically observe after cardiac arrest seemed to be associated with disturbed synaptic transmission between pyramidal cells (Ruijter et al., 2017; Tjepkema-Cloostermans et al., 2014). In a postmortem study, where EEG and SSEP findings were related to results from histological analyses from the brains of non-survivors after cardiac arrest, we observed that absent SSEP responses were always accompanied with severe thalamic damage. Burst-suppression patterns with identical bursts were associated with damage to cortex and cerebellum (van Putten et al., 2019). Others have shown that diffuse slowing of the EEG may be associated with disturbed thalamocortical interactions, which in turn may result from subcortical or cortical ischemic damage (Guillery, 1995; van Wijngaarden et al., 2016). Apparently, hypoxic-ischemic brain damage may selectively affect particular systems or networks in the brain, each leading to particular EEG or SSEP patterns. However, details remain unknown.

For prediction of outcome, we followed previous reports and analyzed SSEP at 3 ± 1 days after cardiac arrest and EEG within the first 24 h. This indicates that these SSEPs were generally obtained at normothermia and off sedation, whereas EEG was analyzed during treatment with targeted temperature management and sedation. Studies relating absent N20 responses to poor outcome report on a small number of false positives, if SSEP testing was done during hypothermia and sedation (Sandroni et al., 2014). Therefore, guidelines recommend to use SSEP at normothermia (Sandroni et al., 2014). Otherwise, with EEG, the largest differences between patients with good and poor outcome are observed within 24 h and predictive values are high despite hypothermia and sedation (Tjepkema-Cloostermans et al., 2015, 2013). Patients precluding cerebral recovery display most specific patterns predicting poor outcome within the first 24 h after cardiac arrest. In later phases, the EEG tends to change to less specific patterns (Hofmeijer et al., 2015). Although the EEG during treatment with sedative drugs or hypothermia is generally deemed as " not interpretable" we emphasize that suppressed, and synchronous patterns with suppressed background cannot be induced solely by midazolam or propofol in the dosages that are generally used in the ICU. This assumption is supported by recent research (Ruijter et al., 2019b).

Our study has certain limitations. First, as in almost all unblinded studies on diagnostic accuracy the self-fulling prophecy is a potential problem. In this study, international guidelines on treatment continuation were strictly followed. Life sustaining treatment was mostly interrupted with an absent SSEP response. Otherwise, the EEG was not used for decisions on discontinuation of life sustaining treatment. Second, although EEG registrations were performed in all patients, SSEP was only done systematically

in the first 55 patients that were included. In later patients, SSEP was done on indication, which indicates that SSEPs were tested in the subgroup of patients with sustained unresponsiveness after weaning from targeted temperature management, introducing selection bias. Third, both SSEP and EEG were visually analyzed, which is subjective to personal preferences. While EEGs were classified off line, blinded for patients' clinical status, treatment, and outcome, SSEP classification was done at the bedside.

5. Conclusion

SSEP and EEG are complementary for prediction of poor outcome of comatose patients after cardiac arrest. SSEP response cannot be predicted from the EEG pattern. Differences between SSEP and EEG patterns probably reflect selective damage of either thalamocortical or inter-pyramidal synapses.

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Declaration of Competing Interest

M.J.A.M. van Putten is co-founder of Clinical Science Systems, which is a supplier of EEG systems for one of the participating sites (Medisch Spectrum Twente). Clinical Science Systems did not provide funding and was not involved in the design, execution, analysis, interpretation or publication of the study. The other authors do not report any conflicts of interest.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinph.2019.08.022.

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