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Clinical paper

AWAreness during REsuscitation - II: A multi-center study of consciousness and awareness in cardiac arrest

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Abstract

Introduction: Cognitive activity and awareness during cardiac arrest (CA) are reported but ill understood. This first of a kind study examined consciousness and its underlying electrocortical biomarkers during cardiopulmonary resuscitation (CPR).

Methods: In a prospective 25-site in-hospital study, we incorporated a) independent audiovisual testing of awareness, including explicit and implicit learning using a computer and headphones, with b) continuous real-time electroencephalography(EEG) and cerebral oxygenation(rSO_2) monitoring into CPR during in-hospital CA (IHCA). Survivors underwent interviews to examine for recall of awareness and cognitive experiences. A complementary cross-sectional community CA study provided added insights regarding survivors' experiences.

Results: Of 567 IHCA, 53(9.3%) survived, 28 of these (52.8%) completed interviews, and 11(39.3%) reported CA memories/perceptions suggestive of consciousness. Four categories of experiences emerged: 1) emergence from coma during CPR (CPR-induced consciousness [CPRIC]) 2/28 (7.1%), or 2) in the post-resuscitation period 2/28(7.1%), 3) dream-like experiences 3/28(10.7%), 4) transcendent recalled experience of death (RED) 6/28(21.4%). In the cross-sectional arm, 126 community CA survivors' experiences reinforced these categories and identified another: delusions (misattribution of medical events). Low survival limited the ability to examine for implicit learning. Nobody identified the visual image, 1/28 (3.5%) identified the auditory stimulus. Despite marked cerebral ischemia (Mean rSO_2 = 43%) normal EEG activity (delta, theta and alpha) consistent with consciousness emerged as long as 35–60 minutes into CPR.

Conclusions: Consciousness. awareness and cognitive processes may occur during CA. The emergence of normal EEG may reflect a resumption of a network-level of cognitive activity, and a biomarker of consciousness, lucidity and RED (authentic "near-death" experiences).

Keywords: Cardiac arrest, Cardiopulmonary Resuscitation (CPR), Consciousness, Recalled Experience of Death (RED), Near-Death Experiences (NDE)

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Introduction

Cardiac arrest (CA) occurs ~350–750,000/year with ~10% survival in the United States. CA related cognitive activity, consciousness and awareness, and their relationship with the quality of survivorship and psychological outcomes while of interest to the American Heart Association (AHA), remain poorly understood.[1] Some survivors report memory impairment, depression, and post-traumatic stress disorder (PTSD) (20–50%),[2] while 10–20% report positive outcomes, including transformation after a transcendent experience during CA,[2–4] lucidity with external visual awareness, and a purposeful life review without external signs of consciousness.[2–4] These contrast with cardiopulmonary resuscitation (CPR)-induced consciousness (CPRIC), where staff observe signs of consciousness, including combativeness/agitation/groaning, eye opening/rolling in ~0.9%.[5]

Although, awareness is assumed absent during CA, among 2060 CA patients; 55 of 143(39%) survivors reported perceived awareness, without recall or memories, 9% transcendent experience, and 46% diverse themes, including fear, persecution, and features suggesting emergence from coma.[3] Furthermore, reports of synchronized gamma oscillations - signifying heightened lucid consciousness - in humans and animals on electroencephalography (EEG) during cardiac standstill and death, has raised the intriguing possibility of electrocortical biomarkers of lucid/heightened consciousness during CA.[11–13]

The breadth of CA cognitive experiences and their contribution to long-term psychological outcomes remains unknown.[1] It is equally unclear, whether explicit recall reflects the entirety of awareness, or whether implicit (unconscious) learning occurs as seen with general anesthesia[6–10]? Despite reports of electrocortical biomarkers of consciousness on EEG with death,[11–13] no systematic studies have examined their occurrence during CA. Identifying consciousness and its biomarkers may assist with measuring the depth of consciousness and identifying those at risk for adverse psychological outcomes who may require sedation during CPR.[1]

The primary aim of this multiphase-multisite study was to characterize the breadth of cognitive themes and awareness by CA survivors. Secondary aims were to: i) assess the feasibility of incorporating tests of implicit learning and explicit recall of visual and auditory perceptions and awareness during CA, ii) identify EEG biomarkers of emergence of consciousness and lucid cognitive activity during CPR.

Methods

Study design and rationale

Given ~5–10% probability of CA survival with many survivors unable to undergo interviews, we combined a prospective and cross-sectional design. The prospective arm was used to: i) identify the incidence and categories of recalled cognitive themes, ii) establish sub-studies of implicit learning and explicit recall, and iii) pilot-test brain monitoring systems. The cross-sectional arm aimed to overcome the limitation of low survival, by providing a larger population of survivors with self-reported memories for qualitative analysis of the themes and breadth of CA-related experiences. This study is reported per the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline.

Prospective study

This was established in phases: 1) feasibility (04/2013–05/2015), 2) five-site pilot (05/2015–05/2017), 3) 25-site (05/2017–03/2020). Patients received CPR according to guidelines relevant at the time (2010 and 2015).[14,15] In-hospital cardiac arrest (IHCA) was identified via pager that alerted research staff. Patients were recruited consecutively during working hours (~0800–1700 weekdays). Inclusion criteria: 1) age $\geq$ 18 years, 2) IHCA lasting $\geq$ 5 minutes. Exclusion: out-of-hospital cardiac arrest (OHCA). The protocol received ethics committee approval (NYUIRB-s17-00142) from all sites prior to enrolling the first participant at each site. Written informed consent was obtained from survivors; a waiver allowed use of data from non-survivors. Survivors were followed until discharge or death.

Definitions and outcome measures

CA was defined as absent heartbeat and respiration, requiring CPR. Sustained return of spontaneous circulation (ROSC) was defined lasting $\geq$ 20 minutes. Survival and neurological outcomes were defined using the Glasgow Outcome Scale (GOS) - GOS4-5 indicates survival with favorable neurological outcomes (supplementary-methods).[16] Our primary outcome was visual or auditory consciousness/awareness. Secondary outcomes were 1) EEG biomarkers of consciousness, 2) implicit learning using audiovisual tests of awareness.

Qualitative analysis of survivors' cognitive recollections

Survivors underwent three-stage interviews in-hospital, including the Abbreviated Mental Test Score (AMTS) to assess cognitive impairment. Those with AMTS $\leq$ 6 were not interviewed. Those with AMTS > 6[17–19] underwent stage-1 interviews regarding their perceptions of awareness and memories during CPR. Stage-2 interviews probed the nature of experiences using scripted open-ended questions and the 16-item near-death scale,[20,21] a tool to detect transcendent experiences of death (score $\geq$ 7). Patients with auditory and visual recollections were flagged for in-depth interview (stage-3) to corroborate their testimonies with documented events. Summaries of scripted interviews were clustered into themes. Depending on recovery, survivors were interviewed ~2–4 weeks after CA.

Cross-sectional study of cardiac arrest survivors' cognitive recollections

Community CA survivors, sent their narratives/experiences by mail, or, were identified based on a history of CPR/defibrillation from a public database.[2] Inclusion criteria: 1) age $\geq$ 18 years, 2) CA self-reported cognitive experiences. We applied the principles of Grounded Theory[22,23] and 1) created a database from narratives, 2) line-by-line coding, 3) grouping codes into categories, and 4) constant comparison of the codes. As more data were analyzed, additional codes emerged and were clustered into categories based on how they described aspects of the experience. A subset was re-coded to confirm the coding standard and ensure methodological rigor. Summaries of these data were clustered into themes and subthemes.

[2] Near-death-experience research foundation (NDERF).

Establishing tests of visual and auditory awareness during CPR

A tablet-computer with an application containing independent audio-visual stimuli connected via Bluetooth headphone was taken to IHCA (supplementary-methods) and clamped above the patient's head, away from chest compressions (Figs. S2A, S2B). The headphones were placed over the ears during CPR. One minute after being switched on, the tablet randomly projected one of 10 stored images onto its screen, and after five minutes (derived from implicit learning protocols during anesthesia).[6–10] audio cues (three fruits: apple-pear-banana) were delivered to the headphones every minute for five minutes. For analysis of explicit recall, survivors were asked to recall memories, including audiovisual stimuli during CPR. To test for implicit learning, survivors were asked to randomly select one image (from 10) and randomly state the names of any three fruits they thought were present during CPR (supplementary-methods).

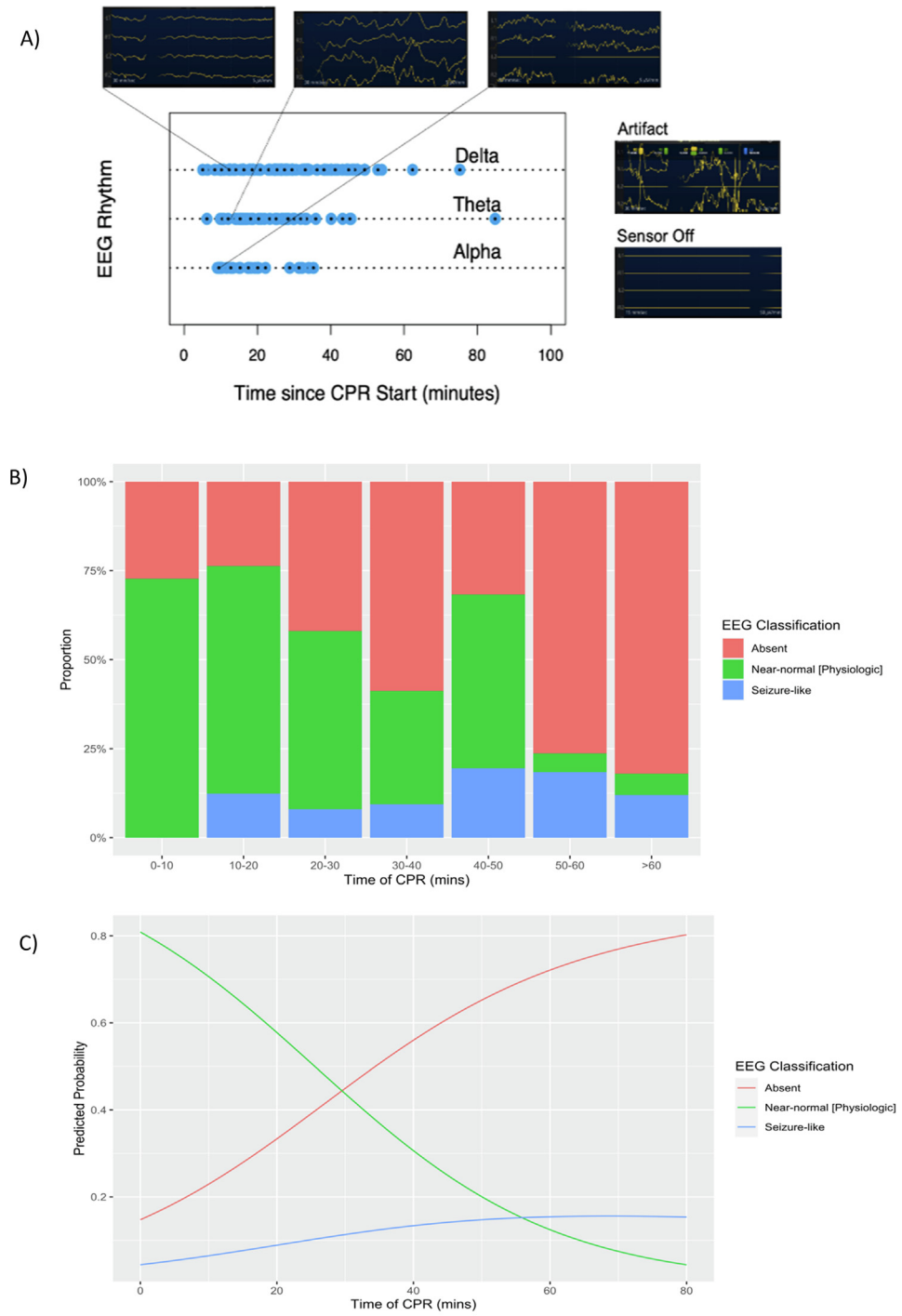
Pilot-Substudy: Real-time cerebral oximetry and electroencephalography

Within the parent-prospective study, a substudy of brain monitoring of EEG combined with a marker of ischemic depth using regional cerebral oximetry (rSO_2) during CPR was established. The feasibility of EEG and rSO_2 during CPR was tested at one-site (04/2013–05/2015),[24] then rSO_2 alone was extended to five-sites (05/2015), and eventually all sites (05/2017–03/2020). From these, nine demonstrated the infrastructure to add real-time portable EEG monitoring during CPR. rSO_2 was measured by near-infrared spectroscopy (NIRS) (Equanox 7600, Nonin, MN).[25] EEG was collected using a portable, 4-lead frontotemporal EEG (SedLine, Masimo, CA). To

Table 1 – Demographic and clinical characteristics of cardiac arrest patients.

	Non-Interviewed patients **N = 539**	Interviewed patients **N = 28**	p
Sex (%)			0.03
Male	346 (64.2)	24 (85.7)	
Female	193(35.8)	4(14.3)	
Age (mean ± SD)	69.37 ± 15.96	63.57 ± 13.65	0.06
Race (%)			0.12
African Descent	34 (6.3)	2 (7.1)	
Asian	24 (4.5)	0 (0.0)	
Caucasian	372 (69.0)	18 (64.3)	
Other	24 (4.5)	1 (3.6)	
South Asian	40 (7.4)	6 (21.4)	
NA	45 (8.3)	1 (3.6)	
Initial Rhythm (%)			0.001
Shockable Rhythm	79 (14.7)	11 (39.3)	
Non-shockable rhythm	460 (85.3)	17 (60.7)	
Clinical Site (%)			0.80
Stony Brook University Hospital	73 (13.5)	3 (10.7)	
Southampton General Hospital	49 (9.1)	7 (25.0)	
Royal London Hospital	95 (17.6)	6 (21.4)	
Newham General Hospital	2 (0.4)	0 (0.0)	
Whips Cross University Hospital	21 (3.9)	2 (7.1)	
Birmingham Heartlands Hospital	95 (17.6)	2 (7.1)	
Watford General Hospital	54 (10.0)	3 (10.7)	
Queen Elizabeth Hospital King's Lynn	21 (3.9)	1 (3.6)	
James Cook University Hospital	1 (0.2)	0 (0.0)	
Basingstoke and North Hampshire Hospital	3 (0.6)	0 (0.0)	
Basildon and Thurrock University Hospitals	2 (0.4)	0 (0.0)	
NYU Langone Health	25 (4.6)	1 (3.6)	
University Hospital Bristol	8 (1.5)	0 (0.0)	
St. George's University Hospital	31 (5.8)	3 (10.7)	
Kingston Hospital	4 (0.7)	0 (0.0)	
Bellevue Hospital	11 (2.0)	0 (0.0)	
University of Arizona	3 (0.6)	0 (0.0)	
University Hospital St. Anna	15 (2.8)	0 (0.0)	
University of Texas Southwestern Medical Center	14 (2.6)	0 (0.0)	
University of Iowa	7 (1.3)	0 (0.0)	
University of Texas San Antonio	5 (0.9)	0 (0.0)	
APACHE II Score (pre-cardiac arrest) (mean ± SD)	23.30 ± 9.02	24.50 ± 6.53	0.50
Charlson Comorbidity Score (mean ± SD)	2.58 ± 2.34	2.81 ± 2.17	0.60
Hemoglobin (g/dL) (mean ± SD)	10.90 ± 2.68	11.44 ± 3.11	0.40
$PaCO_2$ (mmHg) (mean ± SD)	64.39 ± 29.03	51.00 ± 17.24	0.10
PaO_2 (mmHg) (mean ± SD)	99.26 ± 109.37	119.62 ± 114.68	0.51
CPR Duration (min) (mean ± SD)	33.95 ± 67.82	15.17 ± 12.55	0.18

minimize CPR motion artifact, EEG was captured during 3–5 sec pauses in compressions for pulse checks, as consecutive images using a screenshot (1-image/sec) (Fig. 2). The pulse was absent throughout. Staff marked time of ROSC, or end of CPR using event-marking buttons (supplementary-methods). Data were stored automatically and uploaded to an online database (REDCap).[24] EEG was analyzed by a board certified neurophysiologist (RS) using definitions adapted from the American Clinical Neurophysiology



A. Actual EEG screen shot images/data Showing i) Near-Normal/Physiological EEG (Delta, Theta, Alpha), ii) Artifact and iii) Lead Error. B. Progression of EEG States Over Time Throughout CPR, C. Modeling the Probability of the Emergence of Different EEG States Over Time During CPR

Fig. 1 – Electroencephalography (EEG) Activity during Cardiac Arrest. A. Actual EEG screen shot images/data Showing i) Near-Normal/Physiological EEG (Delta, Theta, Alpha), ii) Artifact and iii) Lead Error. B. Progression of EEG States Over Time Throughout CPR, C. Modeling the Probability of the Emergence of Different EEG States Over Time During CPR.

Table 2 – Categories of cognitive experiences in relation to cardiac arrest.

Table 2A Categories of Cognitive Experiences in Relation to Cardiac Arrest Derived From the Prospective Study

1) Recalled Experience of Death
- "I remember seeing my dad."
- "I could see what was going on [. . .] I stood next to the bed, it was very odd."
- "I thought I heard my grandma [who is passed] saying 'you need to go back.'"

2) Emergence from Coma during CPR (CPRIC)
- "I remember when I came back and they were putting those two electrodes to my chest, and I remember the shock."
- "I could feel someone doing something on my chest. I couldn't feel the actual compressions, but I could feel someone rubbing quite hard. It was quite painful."

3) Emergence from Coma in the Post-Resuscitation Period
- "I remember looking at the nurse asking for help to breathe, then waking up in the ICU."
- "I heard my partner saying [patient's name] and my son saying 'mom.'"

4) Dreams and Dream-like Experiences:
- "I [went to a house where I shouldn't have been]. [The police] caught me. . . [I was thinking how to explain what I was doing in the house]. Then, I walked into a puddle. . . When I got out of the puddle, I was not wet and I sort of melded into the pavement. . . There was a fisherman singing a sea shanty over me and it was raining."
- "[I] felt as though someone was holding my hand. It was very black, I couldn't see anything."

Table 2B. Categories of Cognitive Experiences Derived From Self-Reported Memories by Community Cardiac Arrest Survivors

1) Recalled Experience of Death:
   a) Perception of separation from the body
- "I was no longer in my body. I floated without weight or physicality. I was above my body and directly below the ceiling of the intensive therapy room. I observed the scene that was taking place below me ... I, who no longer was the body that had belonged to me just a moment prior, found myself in a position which was . . . more elevated. It was a place that had nothing to do with any kind of . . . material experience."

   b) Perception of heading towards a destination
- "I remember entering a . . . tunnel. The feelings I experienced . . . were much more intense than [usual]. The first feeling was a feeling of intense peace. It was so calm and serene with an incredible amount of tranquility. All of my . . . worries, thoughts, fears, and opinions were gone. The intensity of the tranquility was so incredible and overwhelming that there was no fear in what I was experiencing. I had no fear about where I was going and what to expect when I arrived there. Then I felt warmth . . . Then there was the desire to be home."

   c) Undergoing a purposeful, meaningful and educational re-evaluation of life
- "I do remember a being of light . . . standing near me. It was looming over me like a great tower of strength, yet radiating only warmth and love . . . I caught glimpses of my life and felt pride, love, joy, and sadness, all pouring into me. Each images was of me, but from the standpoint of a being standing with me or looking on. . . I was shown the consequences of my life, thousands of people that I'd interacted with and felt what they felt about me, saw their life and how I had impacted them. Next I saw the consequences of my life and the influence of my actions."

   d) Returning to a place that felt like home
- "I went directly to a place of light. It was calm and immediate . . . The place where I was I perceived to be analogous in a way to the exterior of an entry way. . .There was one major being of love and many other beings of love . . . There was nothing but love, goodness, truth, and all things to do with love. There was no room for fear or evil or anything but this love. It was more wonderful than any of my best hopes or experiences [in this place]. It was beyond perfect and loving, as we in our human state know it. There are no words to describe it. I was so happy to be there."

   e) Returning again
- "I was asked if I wanted to come home (meaning there) or wanted to come back here. I told them that my two sons needed me and I had to go back. I was suddenly in my body again feeling my achy joints flaring in pain. I really don't remember what was going on around me at that point, just that I hurt."

2) Emergence from Coma during CPR (CPRIC)
- "As they tried to revive me and get my heart started again I could feel them using the paddles to get my heart started. I could feel my body moving up and down"
- "I felt as if someone was pushing hard on my chest. I was trying to push them off but my hands felt tied."

3) Emergence from Coma in the Post-Resuscitation Period
- "Then I. . . woke up on an Intensive Care Unit bed with all IV's, Electrocardiogram machines and a number of doctors around me who said, 'Welcome back, Peter, we thought we had lost you. You were gone for 20 minute."
- "I woke up in the hospital bed. The hives were like bunches of grapes on my body and I was on oxygen mixed with medication. I was hooked up to tubes. There were many doctors around me."

4) Delusion"I heard my name, over and over again. All around me were things like demons and monsters. It felt like they were trying to tear off my body parts. At the upper right corner of wherever I was at, I could see someone. There was no face, but it was a male figure. He screamed my name and grabbed my hand before it was too late. I reached out and felt someone pulling me in their direction. I heard, 'Is she breathing? Is she breathing?'"

5) Dreams and Dream-like Experiences:
- "I do remember being in a vast field with gray tents spread everywhere. There were faceless figures. I remember walking away through a canyon. On either side of the canyon were men in white robes with hoods hiding their faces. The last thing I remember was all of them pointing to me. Then the world was swallowed by gray."
- "A man came into my view and walked about 2 to 3 feet in front of me at a 30-degree angle, from a starting point of maybe 10 feet away. He looked like a 1940's gangland character. His nose was long and pointed. He had a white-wall haircut, and a face, as they say; only his mother could love . . .He was scared, angry, and hostile."

Table 2.A represents examples of the results from survivors' interviews. The thematic analysis of these experiences resulted in four categories of experiences: 1) emergence from coma during CPR, 2) emergence from coma in the post-resuscitation period, 3) dream/dream-like experiences, and 4) recalled experience of death. **Table 2.B** represents data from the retrospective qualitative study of experiences in relation to CA. The analysis of these experiences resulted in five categories of experiences including 1) emergence from coma during CPR, 2) emergence from coma in the post-resuscitation period, 3) dream/dream-like experiences, 4) delusional mis-attribution of ongoing medical events, 5) recalled experience of death. This table provides an exemplary quote for the first four categories for illustrative purposes. The category of recalled experience of death is further categorized into five sub-categories of 1) perception of separation from the body, 2) perception of heading towards a destination, 3) undergoing a purposeful, meaningful and educational re-evaluation of life, 4) returning to a place that felt like home, 5) returning again. An exemplary quote from each subcategory has been provided here. Please refer to the Excel supplementary document for the more illustrative examples.

Society (ACNS) Standardized Critical Care EEG terminology (2021) (supplementary-methods).[26]

Statistical analysis

Data were sent to a Data Coordinating Center-Stony Brook University(05/15–03/17), NYU(04/17–11/21). Two statisticians (blinded to patient histories) analyzed rSO_2 and EEG data. The distribution of EEG rhythms over time and rSO2 were summarized by means/standard deviations. Comparisons between interviewed survivors and non-survivors were analyzed using 2-sample t-tests. The predicted probability of EEG changes over time was calculated by multinomial logistic regression with a Likelihood Ratio Test (2-degrees freedom). Continuous data were summarized using means, medians, and standard deviations and compared between different groups using two-sample t-tests or Wilcoxon's rank sum tests for small samples. Categorical variables were summarized using counts and percentages and compared using chi-square or Fisher's exact test for small samples. Analyses were carried out using R (version 4.0.5) and Atlas.ti software for qualitative data (SP,TKS).

Results

Part one: thematic recollections of awareness and cognitive activity

Prospective study

Of 567 subjects, 213(37.6%) achieved sustained ROSC, 53(9.3%) survived to discharge, and 44(7.8%) achieved GOS 4–5. Due to poor health, 28/53 completed interviews (Table 1, Fig. 1). Average CPR duration was 26 ± 23 mins. During stage 1–2 interviews, 11/28 (39%), reported memories and/or perceptions from CA. Using the near-death scale, 6/28(21%) had a transcendent experience (median = 7, high = 18). There were no reports of external signs of consciousness (groaning, moving, rolling).

Thematically, four categories of experiences emerged: 1) emergence from coma during CPR (CPRIC) 2/28(7%), or 2) in the post-resuscitation period 2/28(7%), 3) dreams/dream like experiences 3/28(11%), 4) recalled experience of death 6/28(21%) (Fig. 1, Table 2A). Some described more than one category.

Regarding explicit recall, 2/28(7%) one described "they were putting two electrodes to my chest, and I remember the shock." Another, "heard people talking. . ." and drugs given but without specifics. The same person (1/28 [3.5%]) perceived visual awareness of doctors. He felt like he could see what was going on, including hearing/seeing doctors getting organized and a doctor with a "surgical hat and blue scrubs". He said he "could feel someone rubbing the bony bit" on his chest. During stage-3, the claim of being shocked was verified by chart review. No other information for further independent corroboration was provided.

Cross-sectional study

Among 126 community CA survivors with self-reported testimonies, four themes consistent with the prospective study plus a fifth: delusions (misattributing medical events) were identified. This complemented the prospective study by providing greater detail regarding the breadth of survivors' recollections. The characteristics of these five themes are summarized. For more examples, analyses and subthemes see supplementary-results (Table 2B, Fig. 3).

Theme-1) emergence from coma during CPR (CPRIC)

Subjects described the impact of CPR on their bodies, including feeling electrodes, pain, pressure, bouncing from chest compressions, and hearing conversations by clinicians during resuscitation (Table 2B, Fig. 3A).

Theme-2) emergence from coma in the post-resuscitation period

These were distinguished from CPRIC based on the absence of CPR-related activities, while referring to intensive care unit (ICU) clinical activities (Table 2B, Fig. 3B).

Theme-3) delusional misattribution of ongoing medical events

Characterized by negative, persecutory or frightening misinterpretations of actual medical events. For example, misinterpreting the burning of a "tissued" potassium intravenous line, as burning in hell. (Table 2B).

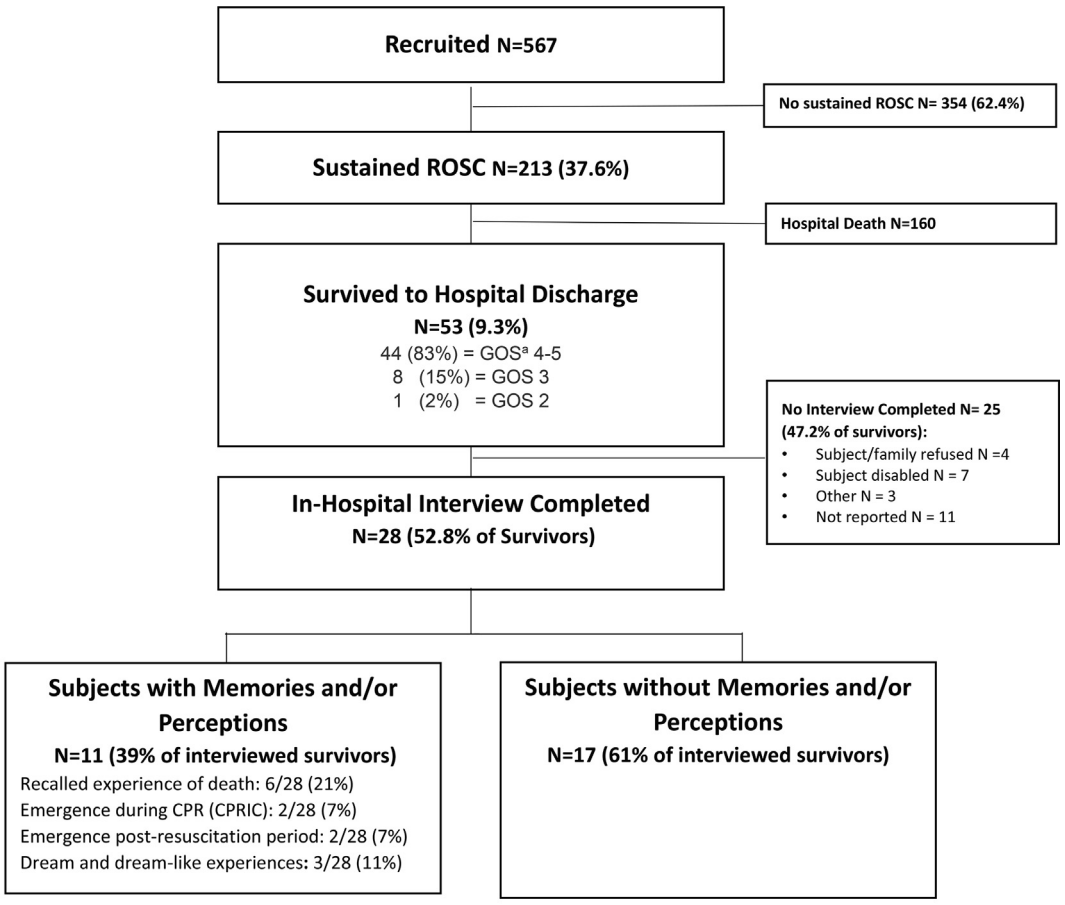
Theme-4) recalled experience of death (RED)

A consistent category of memories were identified with a specific narrative arc (Table 2B, Figs. 3D, S1):

1) perception of separation from the body, often with a recognition of having died, paradoxical lucidity (lucid thoughts, with reasoning and memory of ongoing events) and external visual awareness, without distress, while seemingly unconscious from the perspective of people resuscitating them (unlike CPRIC, this didn't involve perceptions of pain from compressions or other senses); 2) perception of heading towards a destination; 3) a purposeful, meaningful and educational re-evaluation of life (moral quality of a person's intentions, thoughts, actions in relation to others); 4) returning to a place like home. The arc was completed through a decision to 5) return. For each theme, subthemes (totaling 42) were identified (summarized Fig. S1, Table S1A).

Theme-5) dream-like experiences

We identified 14-themes, including visions of rainbows, fish, elevator, igloo, humanoid beings, wooden houses. (Table 2B). These diverse, apparently random, unrelated themes could not be readily clustered and did not follow the narrative arc of RED (Fig. 3C). They did not reflect recollections of medical events during emergence (CPRIC, post-resuscitation), or misinterpretations of medical events.



[a]Glasgow Outcome Scale (GOS): The five GOS categories are 1: death, 2: vegetative state, 3: severe cerebral disability (neurological damage and dependence on others but preserved consciousness) 4: moderate cerebral disability (but with independent activities of daily life), 5: good cerebral performance (normal life with possible minor psychological and/or neurological deficits). Unfavorable outcomes are typically defined as GOS1-3 and survival with a favorable neurological outcome is defined as a GOS score 4-5.
Two of 28 interviewed subjects had EEG data, but, weren't among those with explicit cognitive recall.

Fig. 2 – Summary of Prospective Study Enrollment and Outcomes. * No staff refers to instances where research staff were unable to attend the scene of CA within the required 10 mins timeframe, due to other research commitments. + Futile refers to when resuscitation attempts were started but CPR was deemed futile and the clinical team decided to stop CPR. ++ Others refers to reasons other than the options provided, including rooms being overly crowded, cardiac arrest event occurring outside of the recruitment areas approved by institutional review board (IRB), research staff attending another cardiac arrest event at the same time, clinical team not finding recruitment appropriate under specific circumstances such as opening the patient's chest, cardiac arrest happening in isolation hospital rooms, false cardiac arrest alerts, and late arrival of research team members to the cardiac arrest event. Glasgow Outcome Scale (GOS): The five GOS categories are 1: death, 2: vegetative state, 3: severe cerebral disability (neurological damage and dependence on others but preserved consciousness) 4: moderate cerebral disability (but with independent activities of daily life), 5: good cerebral performance (normal life with possible minor psychological and/or neurological deficits). Unfavorable outcomes are typically defined as GOS1-3 and survival with a favorable neurological outcome is defined as a GOS score 4-5. Two of 28 interviewed subjects had EEG data, but, weren't among those with explicit cognitive recall.

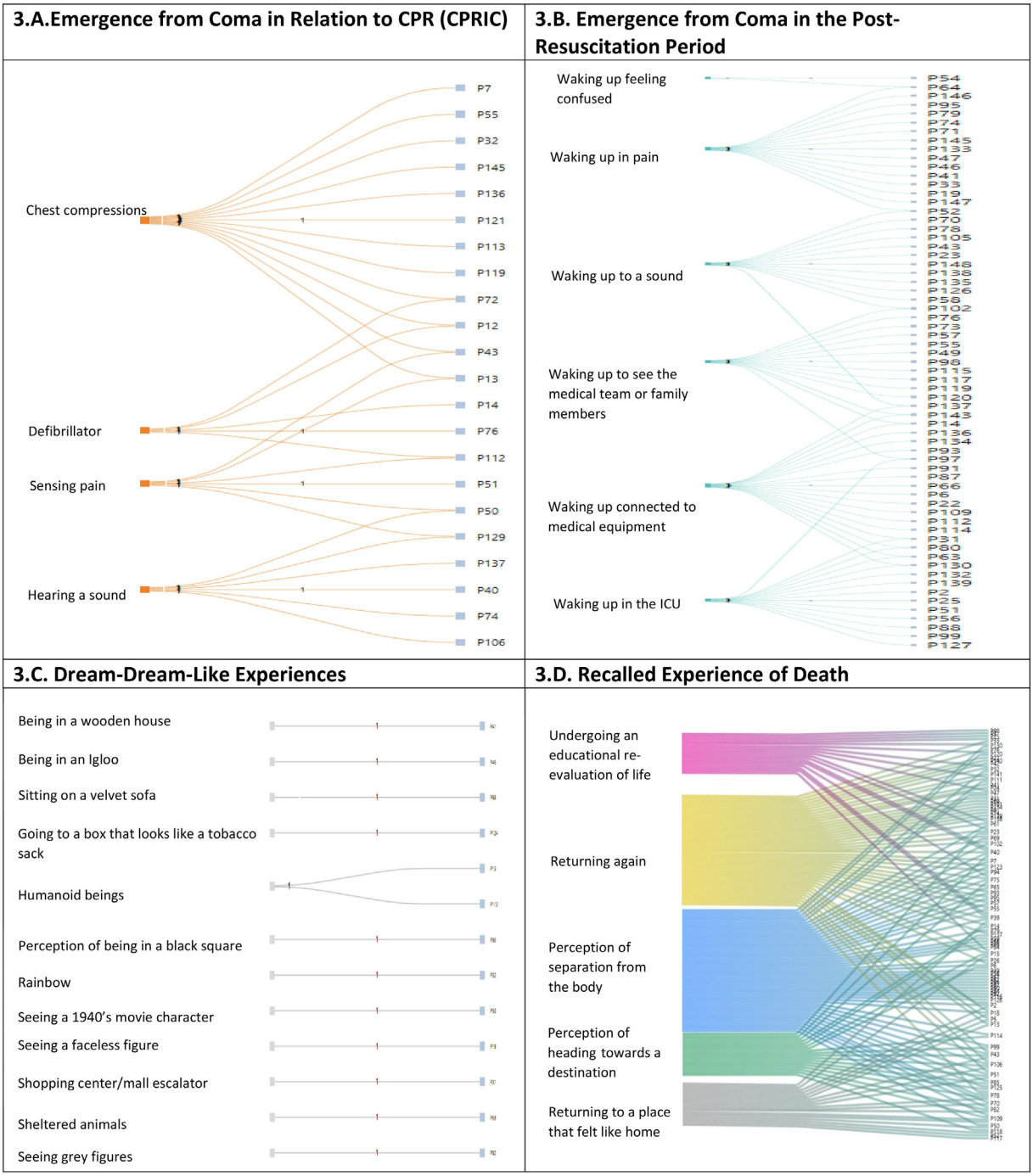
Part two: Pilot sub-studies of implicit learning and brain monitoring

Explicit recall and implicit learning

Overall, 365/567(64%) had combined tablet/headphones. However, low survival (sample size) limited testing. Nonetheless, among 28 survivors, nobody described explicit recall of seeing the independent image on the tablet, nor hearing the auditory stimuli. Regarding implicit learning, nobody identified the displayed visual image (from 10 candidate-images) and 1/28(3.5%) chose the correct three fruits (apple, pear, banana).

Real-time brain monitoring: rSO2 and EEG

The median time between CA and research team arrival was four mins, with ~five mins to set up equipment (Fig. S2A,B). EEG data were obtained from n = 85 subjects with 851 total EEG images captured, but due to electrical interference, electrode malfunction, motion artifact, only n = 53/85 subjects had interpretable EEG data with 466/851(55%) images (Fig. 2A). Among these 53 subjects, n = 49 also had rSO_2 with mean ± SD rSO_2 43.49 (±12.75), consistent with significant ischemia (normal ~70%). Those not-interviewed had a similar rSO_2 to those interviewed (43.29 ± 12.61 vs. 48.54 ± 1



These Sankey diagrams represent the flow of themes and categories for each type of experience. Each line represents individual participants from the analysis. The themes/categories are on the (left) and individual participants (abbreviated as P followed by a number) on the right).

Fig. 3 – Sankey Diagram: Visualization of Emergence from Coma in Relation to CPR, in the Post-Resuscitation Period, Dream like Experiences and Recalled Experience of Death. Figure 3 These Sankey diagrams represent the flow of themes and categories for each type of experience. Each line represents individual participants from the analysis. The themes/categories are on the (left) and individual participants (abbreviated as P followed by a number) on the right).

5.64, p = 0.18). Among 28 interviewed survivors, mean rSO_2 was similar between those with and without memories (53.45 ± 2.72 vs. 46.70 ± 18.25, p = 0.55). Although, absence of cortical brain activity (suppressed EEG) was dominant (47% of data/images), seizure-like (epileptiform) activity also emerged (5%) (Fig. 2B). Importantly, near-normal/physiological EEG consistent with consciousness also

emerged: delta, theta activity in 22% and 12% respectively (up to CPR 60 minutes), alpha 6% of data/images (up to CPR 35 minutes) and beta 1% (Fig. 2B). The relative frequency of near-normal EEG patterns declined over time, especially after 50 minutes of CPR. In parallel, there was a relative increase in suppressed (absent) EEG. Seizure-like activity occurred after 10 mins of CPR but remained steady throughout (~12–24% of all EEG recordings) (Fig. 2B). Modeling the likelihood of emergence of the EEG patterns identified a significant difference in the predicted probability of emergence of the three categories of EEG (normal-near normal, seizure like, absence) with prolonged CPR duration ($p < 0.001$) (Fig. 2C)[3].

Discussion

While unrecognized, people undergoing CA may have consciousness, awareness and cognitive experiences despite absent visible signs of consciousness. In the prospective arm, we identified a spectrum of cognitive activity and explicit recall: ~39% reported broad perceptions/memories, ~20% transcendent experience, ~7% auditory, 3.5% visual perceptions, and 7% experiences compatible with CPRIC. Notwithstanding predominantly absent EEG, and seizure-like (epileptiform) activity, consistent with cerebral ischemia (rSO2~40%), near-normal/physiological EEG activity (delta, theta, alpha, beta rhythms) consistent with consciousness and a possible resumption of a network-level of cognitive and neuronal activity emerged up to 35–60 minutes into CPR. This is the first report of biomarkers of consciousness during CA/CPR. Other novel findings include the discovery of ~42 new cognitive themes and subthemes in relation to the unique, yet, little studied recalled experience of death.

Our data supports studies that indicate consciousness may be present despite clinically undetectable consciousness. This includes under anesthesia where implicit learning may occur without explicit recall,[6–10] and in patients assumed to be in persistent vegetative states (PVS).[27,28] Building on studies of CPRIC, and so-called "near-death experiences" [NDE] in CA,[3–5,29–31] our data suggests while seemingly unconscious, CA patients form phenomenologically different experiences, which are dividable into two categories: 1) emergence from coma (during CPR [CPRIC] or post-resuscitation), 2) inner experiences unrelated to medical events. The first reflects the correct recollection of medical events, or the misattribution of medical events (possibly due to less emergence), manifesting as frightening delusional experiences (e.g. persecuted/attacked). Although, until now CPRIC has been reported from the perspective of observing staff i.e. external signs of consciousness in ~1%,[5] our data suggests when considered from the perspective of patients, the incidence is ~7% and may occur without external visible signs. The second category includes a unique transcendent recalled experience of death (RED), that is different to delusions, with multiple newly discovered themes within a distinctive narrative arc. This reflects a heightened sense of consciousness with paradoxical lucidity- a meaningful, purposeful review and moral re-evaluation of thoughts, intentions and actions towards others, perceptions of death and a different, ineffable reality. Although, the scientifically undefined, yet popular term of NDE is commonly used, a recent guideline identified its limitations and recommended the term RED.[32] Unlike RED, dream like experiences exhibit unrelated, haphazard themes.

Recent reports of a surge of gamma and other physiological electrical activity (ordinarily seen with lucid consciousness) during and after cardiac standstill and death, led to speculation that biomarker (s) of lucidity at death may exist,[11–13] which our findings support. Taken together, these studies and ours provide a novel understanding of how lucid experiences in relation to cardiac standstill/death may arise. Ischemic depolarization may initiate brain disinhibition - leading to activation of dormant pathways - observed as transient electrocortical biomarkers of lucidity. Although of unknown evolutionary benefit, instead of being hallucinatory, illusory or delusional, this appears to facilitate lucid understanding of new dimensions of reality – including people's deeper consciousness - all memories, thoughts, intentions and actions towards others from a moral and ethical perspective. The mechanism of consciousness and its relationship with brain resuscitation and function remain undiscovered. "Bottom-up" or "top-down" mechanisms are proposed for the emergence of consciousness.[33] The former considers consciousness as an epiphenomenon from brain activities[34]; the latter, as a separate undiscovered entity not produced by understood brain mechanisms, which can independently modulate brain activity.[33,35] The identification of potential electrocortical biomarkers of consciousness doesn't resolve this conundrum, as an association doesn't imply causation.[36] However, the paradoxical finding of lucidity and heightened reality when brain function is severely disordered, or has ceased raises the need to consider alternatives to the epiphenomenon theory.[33,35,37]

Our study reinforces the need to study CA psychological outcomes as part of the broader post-intensive care syndrome.[38] It supports the possibility that PTSD and other negative psychological outcomes after CA may relate to emergence from consciousness. Those with delusional misinterpretations, or pain and distress may be more susceptible. This adds to debates by the AHA regarding sedation during CPR.[1]

While, this is the first study to test implicit learning in comatose patients during CPR, our small sample of survivors precluded testing for implicit learning. This also limited our ability to interview CA survivors prospectively. We overcame this using a cross-sectional design. Differences in time from CA onset to recall may introduce bias. Another limitation is that some patients may have knowledge about aspects of CA, such as defibrillation, yet we could not examine how this may influence their recollections. The challenge of attaching brain monitoring during CPR, limited our ability to obtain EEG and rSO2 on everyone. These may be overcome by studying awareness during deep hypothermic circulatory arrest (DHCA), which mimics CA with reported similar cognitive outcomes.[39] Finally, we could not determine whether alpha waves were physiological, or representative of alpha coma seen in brain injury. A future study with full EEG is needed to address this question.

Although systematic studies have not been able to absolutely prove the reality or meaning of patients' experiences and claims of awareness in relation to death, it has been impossible to disclaim them either. The recalled experience surrounding death now merits further genuine empirical investigation without prejudice.

[3] Further detailed analysis of the EEG/rSO2 datasets to evaluate alternative research questions, including their relationship with ROSC and survival are presented as separate studies/manuscripts.

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Take Home Message

People undergoing CPR may have consciousness despite the absence of visible external signs of consciousness. In this multisite study of 567 in-hospital cardiac arrest with portable electroencephalography monitoring during active CPR, a spectrum of cognitive activity including awareness and recalled experience of death were identified, together with near-normal/physiological EEG activity (delta, theta, alpha, beta rhythms) suggestive of the emergence of consciousness and resumption of a network-level of cognitive activity.

Tweet

People with cardiac arrest experience recalled experiences of death, including a lucid purposeful review of their lives, which may be tracked for the first time using brain monitors.

CRediT authorship contribution statement

Sam Parnia: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing. **Tara Keshavarz Shirazi:** Investigation, Formal analysis, Visualization. **Jignesh Patel:** Formal analysis. **Linh Tran:** Data curation, Formal analysis, Methodology. **Niraj Sinha:** Data curation, Investigation, Methodology. **Caitlin O'Neill:** Project administration. **Emma Roellke:** Data curation, Methodology, Project administration. **Amanda Mengotto:** Formal analysis, Methodology, Project administration. **Shannon Findlay:** . **Michael McBrine:** . **Rebecca Spiegel:** Data curation. **Thaddeus Tarpey:** Data curation. **Elise Huppert:** Data curation, Project administration. **Ian Jaffe:** Project administration. **Anelly M. Gonzales:** Project administration. **Jing Xu:** Data curation. **Emmeline Koopman:** Data curation. **Gavin D Perkins:** Project administration, Writing – review & editing. **Alain Vuylsteke:** . **Benjamin M. Bloom:** Data curation, Project administration, Writing – review & editing. **Heather Jarman:** Project administration. **Hiu Nam Tong:** Investigation. **Louisa Chan:** . **Michael Lyaker:** . **Matthew Thomas:** . **Veselin Velchev:** Project administration. **Charles B. Cairns:** . **Rahul Sharm:** Project administration. **Erik Kulstad:** Project administration. **Elizabeth Scherer:** Project administration. **Terence O'Keeffe:** Project administration. **Mahtab Foroozesh:** Project administration. **Olumayowa Abe:** Project administration. **Chinwe Ogedegbe:** Project administration, Writing – review & editing. **Amira Girgis:** Project administration. **Deepak Pradhan:** Writing – review & editing. **Charles D. Deakin:** .

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resuscitation.2023.109903.

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