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Clinical Paper

AWARE—AWAreness during REsuscitation—A prospective study[☆]

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ABSTRACT

Background: Cardiac arrest (CA) survivors experience cognitive deficits including post-traumatic stress disorder (PTSD). It is unclear whether these are related to cognitive/mental experiences and awareness during CPR. Despite anecdotal reports the broad range of cognitive/mental experiences and awareness associated with CPR has not been systematically studied.

Methods: The incidence and validity of awareness together with the range, characteristics and themes relating to memories/cognitive processes during CA was investigated through a 4 year multi-center observational study using a three stage quantitative and qualitative interview system. The feasibility of objectively testing the accuracy of claims of visual and auditory awareness was examined using specific tests. The outcome measures were (1) awareness/memories during CA and (2) objective verification of claims of awareness using specific tests.

Results: Among 2060 CA events, 140 survivors completed stage 1 interviews, while 101 of 140 patients completed stage 2 interviews. 46% had memories with 7 major cognitive themes: fear; animals/plants; bright light; violence/persecution; deja-vu; family; recalling events post-CA and 9% had NDEs, while 2% described awareness with explicit recall of 'seeing' and 'hearing' actual events related to their resuscitation. One had a verifiable period of conscious awareness during which time cerebral function was not expected.

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Conclusions: CA survivors commonly experience a broad range of cognitive themes, with 2% exhibiting full awareness. This supports other recent studies that have indicated consciousness may be present despite clinically undetectable consciousness. This together with fearful experiences may contribute to PTSD and other cognitive deficits post CA.

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1. Introduction

The observation that successful cardiac arrest (CA) resuscitation is associated with a number of psychological and cognitive outcomes including post-traumatic stress disorder, depression and memory loss as well as specific mental processes that may share some similarities with awareness during anaesthesia,^{1,2} has raised the possibility that awareness may also occur during resuscitation from CA.³ In addition to auditory perceptions, which are characteristic of awareness during anaesthesia, CA survivors have also reported experiencing vivid visual perceptions, characterized by the perceived ability to observe and recall actual events occurring around them.⁴ Although awareness during anaesthesia is associated with dream like states, the specific mental experience described in association with CA is unknown. CA patients have reported visual perceptions together with cognitive and mental activity including thought processes, reasoning and memory formation.³ Patients have also been reported to recall specific details relating to events that were occurring during resuscitation.⁴

Although there have been many anecdotal reports of this phenomenon, only a handful of studies have used rigorous research methodology to examine the mental state that is associated with CA resuscitation.^{4–7} These studies have examined the scientifically imprecise yet commonly used term of ‘near-death experiences’ (NDE).³ While NDE have been reported by 10% of CA survivors,³ the overall broader cognitive/mental experiences associated with CA, as well as awareness, and the association between actual CA events and auditory/visual recollection of events has not been studied. The primary aim of this study was to examine the incidence of awareness and the broad range of mental experiences during resuscitation. The secondary aim was to investigate the feasibility of establishing a novel methodology to test the accuracy of reports of visual and auditory perception and awareness during CA.

2. Methods

In this multicenter observational study, methods were initially pilot tested at 5 hospitals prior to study start-up (01/2007–06/2008) at which point the study team recruited 15 US, UK and Austrian hospitals (out of an original selected group of 25) to participate in data collection. Between 07/2008 and 12/2012 the first group of CA patients were enrolled in the AWARE study. These patients were identified using a local paging system that alerted staff to CA events. CA patients were eligible for study participation if they met the following inclusion criteria:

- CA as defined by cessation of heartbeat and respiration (in-hospital or out-of-hospital with on-going cardiopulmonary resuscitation (CPR) on arrival at the emergency department (ED)).
- Age > 18 years.
- Surviving patients deemed fit for interview by their physicians and caregivers.
- Surviving patients providing informed consent to participation.

When possible, interviews were completed by a research nurse or physician while the CA survivor was still an inpatient. The

interviewers all underwent dedicated training regarding the interview methodology by the study chief/principle investigator. Informed consent was obtained when patients were deemed medically fit to complete an in-person interview prior to discharge. For patients who could not be interviewed during their hospital stay, a telephone interview protocol was established to consent and interview these patients by telephone to minimize losses to follow up. Given the severity of the condition, the study provided for a large proportion of patients being unable to participate due to ill health in the sample size calculations.

The study received ethical approval at each participating site prior to the start of data collection. Following advice from the ethics committee, a protocol was implemented to avoid contacting individuals not interviewed during their hospital stay who died after hospital discharge. Death registries and letters to the patients’ doctors requesting permission to contact their patients were implemented to identify patients who either died or should not be contacted. If no objections or concerns were raised and patients were still alive after discharge, a member of the original clinical team sent an introductory letter together with a stamped addressed envelope requesting permission to contact patients for the study who were missed while in hospital. For these patients who agreed to be contacted, a member of the research team, obtained informed consent, and completed data collection via the telephone. However due to the severity of the medical condition (and in particular the differing levels of physical impairment) combined with the requirements set forth by the ethics committee for contacting patients (outlined above), the time to telephone interviews following hospital discharge was between 3 months and 1 year. All in-hospital interviews were carried out prior to discharge. These took place between 3 days and 4 weeks after cardiac arrest depending on the severity of the patients’ critical illness.

To assess the accuracy of claims of visual awareness (VA) during CA, each hospital installed between 50 and 100 shelves in areas where CA resuscitation was deemed likely to occur (e.g. emergency department, acute medical wards). Each shelf contained one image only visible from above the shelf (these were different and included a combination of nationalistic and religious symbols, people, animals, and major newspaper headlines). These images were installed to permit evaluation of VA claims described in prior accounts.⁴ These include the perception of being able to observe their own CA resuscitation from a vantage point above. It was postulated that should a large proportion of patients describe VA combined with the perception of being able to observe events from a vantage point above, the shelves could be used to potentially test the validity of such claims (as the images were only visible if looking down from the ceiling).¹ Considering these perceptions may be occurring after brain function has returned following resuscitation, we

¹ Some researchers have proposed such recollections and perceptions are likely illusory. This method was proposed as a tool to test this particular hypothesis. We considered this to be important as despite widespread interest no studies had objectively tested this claim. It was considered that should a large group of patients with VA and the ability to observe events from above consistently fail to identify the images, this could support the hypothesis that the experiences had occurred through a different mechanism (such as illusions) to that perceived by the patients themselves.

also installed a different image (triangle) on the underside of each shelf to test the accuracy of VA based on the possibility that patients could have looked upwards after CA recovery or had their eyes open during CA.

Using a three stage interview process, patients were asked general and focused questions about their remembrances during cardiac arrest. Stage 1 of the interviews included demographic questions as well as general questions on the perception of awareness and memories during CA. Stage 2 interviews probed further into the nature of the experiences using scripted open ended questions and the 16 item Greyson NDE scale.⁸ This validated NDE scale was used to define NDE's in this study. For each of the 16 items in the NDE scale, responses were scored 0 (not present), 1 (weakly present) or 2 (strongly present). Out of a possible maximum score of 32, a NDE was considered present with a score of ≥ 7 , while experiences < 7 are not compatible with NDE.⁸ Patients with detailed auditory and visual recollections relating to their period of cardiac arrest were flagged for a further in-depth interview (stage 3) to obtain details of their experience. This later interview was conducted by the study principal investigator (PI).

Using both the qualitative and quantitative data, patients' memories and experiences were initially classified into 2 broad categories:

- (1) No perception of awareness and/or memories.
- (2) Perception of awareness and/or memories.
Based on patient's responses to the NDE scale the second category was subdivided into three further categories.
- (3) Detailed non-NDE memories without recall and awareness of CA events.
- (4) Detailed NDE memories without recall and awareness of CA events.
- (5) Detailed NDE memories with detailed auditory and/or VA with recall of CA events.

In order to evaluate auditory recollections we proposed a protocol to introduce "auditory stimuli" during CA similar to those used in studies of implicit learning during anaesthesia.⁹ During the pilot testing phase, staff were asked to mention the names of three specific cities or colors and evaluate the survivors' ability to recall these through explicit or implicit memory recall, however unlike the relatively controlled environment of anesthesia, staff found it impractical to administer these stimuli and this was therefore not carried forward to the main study. Patients who claimed to have had visual and auditory awareness (category 5 above) whether identified in hospital or during the telephone interview were invited to complete an in-depth interview conducted by the study principal investigator to obtain more details of their experiences.

Both quantitative and qualitative data were analyzed in a descriptive manner. Potential confounders such as age, gender and time to interview were evaluated. Summaries of the scripted interviews were reviewed and responses grouped based upon themes identified. Potential differences in demographic characteristics between reporting groups was evaluated. Age was compared using two sample t-test or Wilcoxon's rank sum test when sample sizes were small. Gender was compared using chi-square test or Fisher's exact test when sample sizes were small. Statistical analysis was carried out using StatXact-9 (Cytel Inc., Cambridge, MA) and SAS 9.3 (SAS Institute Inc., Cary, NC).

3. Results

A total of 2060 CA events were recorded with an average 16% ($n=330$) overall survival to hospital discharge. Of the 330 survivors, 140 patients were found eligible, provided informed

consent, and were interviewed. Fifty-two interviews were completed in-hospital and 90 after discharge. Two patients refused interview and the remaining 188 patients either did not meet inclusion criteria, died after hospital discharge, were not deemed suitable for further follow up by their physicians, or did not respond to the invitation letters for a telephone follow up. A summary of study participation and outcomes is reported in Fig. 1. From the 140 patients completing stage 1 of the interview process, 101 patients (72%) went on to complete stage 2 interviews. The 39 patients unable to complete both stages did so predominantly due to fatigue.

Among those interviewed 67% ($n=95$) were men. The mean age (\pm SD) was 64 ± 13 years (range 21–94). After stage 1 interview 61% (85/140) of patients reported no perception of awareness or memories (category 1). Although no patient demonstrated clinical signs of consciousness during CPR as assessed by the absence of eye opening response, motor response, verbal response whether spontaneously or in response to pain (chest compressions) with a resultant Glasgow Coma Scale Score of 3/15, nonetheless 39% (55/140) (category 2) responded positively to the question "Do you remember anything from the time during your unconsciousness". There were no significant differences with respect to age or gender between these two groups.

Among the 101 patients who completed stage 2 interviews, no differences existed by age or gender. Responses to the NDE scale are summarized in Table 1 and 46 (46%) confirmed having had no recall, awareness or memories. The remaining 55 of 101 patients with perceived awareness or memories (category 2) were subdivided further. Forty-six described memories incompatible with a NDE

Table 1
Responses to the Greyson NDE Scale^a (number and percent responding positively to each of the 16 scale questions^b).

Question	n	%
(1) Did you have the impression that everything happened faster or slower than usual?	27	27
(2) Were your thoughts speeded up?	7	7
(3) Did scenes from your past come back to you?	5	5
(4) Did you suddenly seem to understand everything?	6	6
(5) Did you have a feeling of peace or pleasantness?	22	22
(6) Did you have a feeling of joy?	9	9
(7) Did you feel a sense of harmony or unity with the universe?	5	5
(8) Did you see, or feel surrounded by, a brilliant light?	7	7
(9) Were your senses more vivid than usual?	13	13
(10) Did you seem to be aware of things going on that normally should have been out of sight from your actual point of view as if by extrasensory perception?	7	7
(11) Did scenes from the future come to you?	0	0
(12) Did you feel separated from your body?	13	13
(13) Did you seem to enter some other, unearthly world?	7	7
(14) Did you seem to encounter a mystical being or presence, or hear an unidentifiable voice?	8	8
(15) Did you see deceased or religious spirits?	3	3
(16) Did you come to a border or point of no return?	8	8

$n=101$. Mean Greyson score \pm SD = 2.02 ± 3.71 . Score range = 0–22.

^a The total is based upon individuals completing the instrument (101/142, 72%).

^b A positive response was defined as responses of either weakly or strongly present for each item.

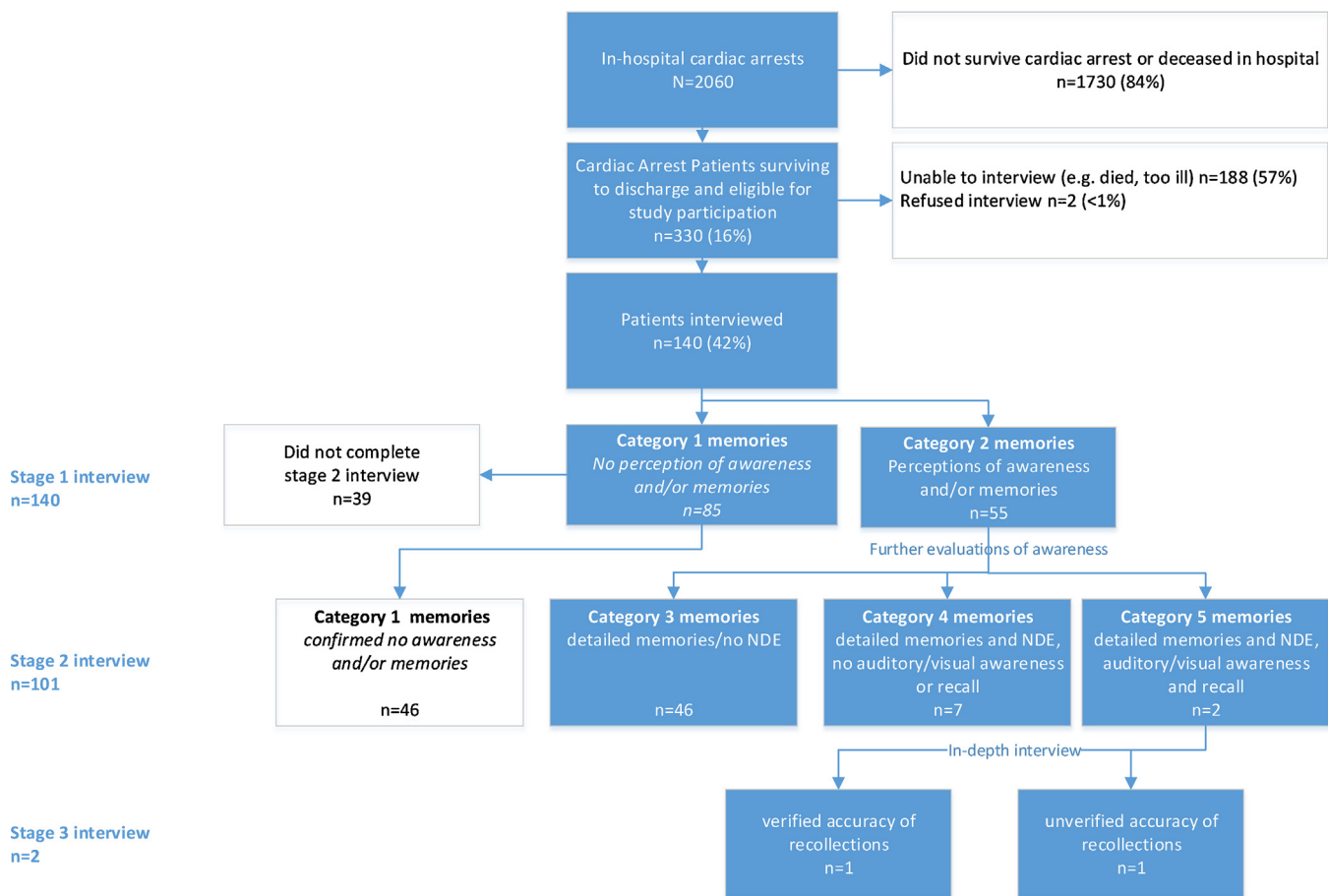


Fig. 1. Summary of study enrollment and outcomes.

and without recall of CA events (median NDE score = 2) (IQR = 3) (category 3). The remaining 9 of 101 patients (9%) had experiences compatible with NDE's. Seven (7%) had no auditory or visual recall of CA events (median NDE scale score = 10 (IQR = 4), highest NDE score 22) (category 4). The detailed NDE account from one patient in this group is summarized in Table 2. The other two patients (2%) experienced specific auditory/visual awareness (category 5). Both patients had suffered ventricular fibrillation (VF) in non-acute areas where shelves had not been placed. Their descriptions are summarized in Table 2. Both were contacted for further in-depth interviews to verify their experiences against documented CA events. One was unable to follow up due to ill health. The other, a 57 year old man described the perception of observing events from the top corner of the room and continued to experience a sensation of looking down from above. He accurately described people, sounds, and activities from his resuscitation (Table 2 provides quotes from this interview). His medical records corroborated his accounts and specifically supported his descriptions and the use of an automated external defibrillator (AED). Based on current AED algorithms, this likely corresponded with up to 3 min of conscious awareness during CA and CPR.² As both CA events had occurred in non-acute areas without shelves further analysis of the accuracy of VA based on the ability to visualize the images above or below the shelf was not possible. Despite the installation of approximately

² After the recognition of a first shockable rhythm, the built in AED algorithms require at least 2 min of CPR before a further rhythm check is followed by a second defibrillation attempt if advised. Adding in time for analysis of the rhythm and defibrillation it is likely the period of CA would have been at least 3 min.

1000 shelves across the participating hospitals only 22% of CA events actually took place in the critical and acute medical wards where the shelves had been installed and consequently over 78% of CA events took place in rooms without a shelf.

While NDE's provided a quantifiable measure of a patients' cognitive recollections in relation to CA, using our CA survivor interview transcripts as part of stage 2 interviews, we evaluated the narratives of patients' memory's without NDE's (NDE scale < 7). Although prior studies had by enlarge focused on the occurrence of NDE's in CA only, however our observation that other cognitive themes aside from NDE's also exist in CA led to an evaluation of the narratives for other specific themes. Narratives were categorized into 7 themes: (1) fear; (2) animals and plants; (3) a bright light; (4) violence or a feeling of being persecuted; (5) deja vu experiences; (6) seeing family; (7) recalling events that likely occurred after recovery from CA. Narratives are presented in Table 3 by theme.

4. Discussion

Our data suggest that CA patients may experience a range of cognitive processes that relate both to the CA and post-resuscitation periods. Although, the relatively high proportion of patients who perceived having memories and awareness was unexpected and should be confirmed through future research, the fact that the observed frequency of NDE (9%) in our study was consistent with reports from prior studies (approximately 10%),^{4–7} may provide some measure of internal validity for this observation.

The finding that conscious awareness may be present during CA is intriguing and supports other recent studies that have indicated consciousness may be present in patients despite clinically

Table 2
Categories 4 and 5 recollections from structured interviews.

Category 4 recollections

"I have come back from the other side of life. . . God sent (me) back, it was not (my) time—(I) had many things to do. . . (I traveled) through a tunnel toward a very strong light, which didn't dazzle or hurt (my) eyes. . . there were other people in the tunnel whom (I) did not recognize. When (I) emerged (I) described a very beautiful crystal city. . . there was a river that ran through the middle of the city (with) the most crystal clear waters. There were many people, without faces, who were washing in the waters. . . the people were very beautiful. . . there was the most beautiful singing. . . (and I was) moved to tears. (My) next recollection was looking up at a doctor doing chest compressions".

Category 5 recollections

Recollection # 1

(Before the cardiac arrest) "I was answering (the nurse), but I could also feel a real hard pressure on my groin. I could feel the pressure, couldn't feel the pain or anything like that, just real hard pressure, like someone was really pushing down on me. And I was still talking to (the nurse) and then all of a sudden, I wasn't. I must have (blacked out). . . but then I can remember vividly an automated voice saying, "shock the patient, shock the patient," and with that, up in (the) corner of the room there was a (woman) beckoning me. . . I can remember thinking to myself, "I can't get up there". . . she beckoned me. . . I felt that she knew me, I felt that I could trust her, and I felt she was there for a reason and I didn't know what that was. . . and the next second, I was up there, looking down at me, the nurse, and another man who had a bald head. . . I couldn't see his face but I could see the back of his body. He was quite a chunky fella. . . He had blue scrubs on, and he had a blue hat, but I could tell he didn't have any hair, because of where the hat was.

The next thing I remember is waking up on (the) bed. And (the nurse) said to me: "Oh you nodded off. . . you are back with us now." Whether she said those words, whether that automated voice really happened, I don't know. . . I can remember feeling quite euphoric. . .

I know who (the man with the blue had was). . . I (didn't) know his full name, but. . . he was the man that. . . (I saw) the next day. . . I saw this man [come to visit me] and I knew who I had seen the day before."

Post-script – Medical record review confirmed the use of the AED, the medical team present during the cardiac arrest and the role the identified "man" played in responding to the cardiac arrest.

Recollection # 2

"At the beginning, I think, I heard the nurse say 'dial 444 cardiac arrest'. I felt scared. I was on the ceiling looking down. I saw a nurse that I did not know beforehand who I saw after the event. I could see my body and saw everything at once. I saw my blood pressure being taken whilst the doctor was putting something down my throat. I saw a nurse pumping on my chest. . . I saw blood gases and blood sugar levels being taken."

undetectable consciousness.^{9–15} For instance, implicit learning with the absence of explicit recall has been demonstrated in patients with undetectable consciousness,^{9–13} while others have demonstrated conscious awareness during persistent vegetative states (PVS).^{14,15} As the relative contribution of implicit learning and memory in CA is unknown it remains unclear whether the recalled experiences reflect the totality of patients' experiences or simply the tip of a deeper iceberg of experiences not recalled through explicit memory. It is intriguing to consider whether patients may have greater conscious activity during CA (and whether this and fearful experiences may impact the occurrence of PTSD) than is evident through explicit recall, perhaps due to the impact of post-resuscitation global cerebral inflammation and/or sedatives on memory consolidation and recall. However, the results of this and other studies (outlined above) raise the possibility that additional assessments may be needed to complement currently used clinical tests of consciousness and awareness.

Although the etiology of awareness during CA is unknown, the results of our study and in particular our verified case of VA suggest it may be dissimilar to awareness during anesthesia. While some investigators have hypothesized there may be a brief surge of electrical activity after cardiac standstill,¹⁶ in contrast to anesthesia typically there is no measurable brain function within seconds after cardiac standstill.^{17–21} This 'flatlined' isoelectric brain state

Table 3
Major non-NDE cognitive themes recalled by patients following cardiac arrest.

Fear

"I was terrified. I was told I was going to die and the quickest way was to say the last short word I could remember"
"Being dragged through deep water with a big ring and I hate swimming—it was horrid".
"I felt scared"

Animals and plants

"All plants, no flowers".
"Saw lions and tigers".

Bright light

"The sun was shining"
"Recalled seeing a golden flash of light"

Family

"Family talking 10 or so. Not being able to talk to them"
"My family (son, daughter, son-in-law and wife) came"

Being persecuted or experiencing violence

"Being dragged through deep water"
"This whole event seemed full of violence and I am not a violent man, it was out of character".
"I had to go through a ceremony and . . . the ceremony was to get burned. There were 4 men with me, whichever lied would die. . . I saw men in coffins being buried upright.

Deja vu experiences

". . . experienced a sense of De-ja vu and felt like knew what people were going to do before they did it after the arrest. This lasted about 3 days"

Events occurring after initial recovery from cardiac arrest

Experienced . . . "a tooth coming out when tube was removed from my mouth"

which occurs with CA onset usually continues throughout CPR since insufficient cerebral blood flow (CBF) is achieved²² to meet cerebral metabolic requirements during conventional CPR.^{23–25} However it was estimated our patient maintained awareness for a number of minutes into CA. While certain deep coma states may lead to a selective absence of cortical electrical activity in the presence of deeper brain activity,²⁶ this seems unlikely during CA as this condition is associated with global rather than selective cortical hypoperfusion as evidenced by the loss of brain stem function. Thus, within a model that assumes a causative relationship between cortical activity and consciousness the occurrence of mental processes and the ability to accurately describe events during CA as occurred in our verified case of VA when cerebral function is ordinarily absent or at best severely impaired is perplexing.²⁷ This is particularly the case as reductions in CBF typically lead to delirium followed by coma, rather than an accurate and lucid mental state.²⁸

Despite many anecdotal reports and recent studies supporting the occurrence of NDE's and possible VA during CA, this was the first large-scale study to investigate the frequency of awareness, while attempting to correlate patients' claims of VA with events that occurred during cardiac arrest. While the low incidence (2%) of explicit recall of VA impaired our ability to use images to objectively examine the validity of specific claims associated with VA, nonetheless our verified case of VA suggests conscious awareness may occur beyond the first 20–30 s after CA (when some residual brain electrical activity may occur)¹⁶ while providing a quantifiable time period of awareness after the brain ordinarily reaches an isoelectric state.^{17–21} The case indicates the experience likely occurred during CA rather than after recovery from CA or before CA. No CBF would be expected since unlike ventricular tachycardia, VF is incompatible with cardiac contractility particularly after CPR has stopped during a rhythm check.²⁹ Although, similar experiences have been categorized using the scientifically undefined and imprecise term of out of body experiences (OBE's), and further categorized as autoscapy and optical illusions,^{30–32} our study suggests that VA and veridical

perception during CA are dissimilar to autoscapy since patients did not describe seeing their own double.^{4–7} Furthermore as hallucinations refer to experiences that do not correspond with objective reality, our findings do not suggest that VA in CA is likely to be hallucinatory or illusory since the recollections corresponded with actual verified events. Our results also highlight limitations with the categorization of experiences in relation to CA as hallucinatory,³³ particularly as the reality of human experience is not determined neurologically.^{34,35} Although alterations in specific neuro modulators involved with every day “real” experiences can also lead to illusions or hallucinations, however this does not prove or disprove the reality of any specific experience whether it be love, NDE’s or otherwise.^{34,35} In fact the reality of any experience and the meaning associated with it is determined socially (rather than neurologically) through a social process whereby humans determine and ascribe meaning to phenomenon and experience within any given culture or society (including scientific groups and societies).^{34–35}

Our results provide further understanding of the broad mental experience that likely accompanies death after circulatory standstill. As most patients’ experiences were incompatible with a NDE, the term NDE while commonly used may be insufficient to describe the experience that is associated with the biological processes of death after circulatory standstill. Future research should focus on the mental state of CA and its impact on the lives of survivors as well as its relationship with cognitive deficits including PTSD. Our data also suggest, the experience of CA may be distinguished from the term NDE, which has many scientific limitations including a lack of a universally accepted physiological definition of being ‘near death’.^{34–36} This imprecision may contribute to ongoing conflicting views within the scientific community regarding the subject.^{36–39}

Our study had a number of limitations including the fact that we were unable to ascertain whether patients’ response to the question of having memories during CA (in category 1) truly reflected a perception of having memories or possibly difficulties with understanding the question. An additional limitation was the limited number of patients with explicit recall of CA events whose memories could have been further analyzed. Furthermore owing to the acuity and severity of the critical illness associated with CA, the time to interview for patients was invariably not exactly the same for every patient, which may have introduced biases (such as recall bias and confabulation) in the recollections. While pre-placement of visual targets in resuscitation areas aimed at testing VA was feasible from a practical viewpoint (there were no reported adverse incidents), the observation that 78% of CA events took place in areas without shelves illustrates the challenge in objectively testing the claims of VA in CA using our proposed methodology. It also suggests that a different and more refined methodology may be needed to provide an objective visual target to examine the mechanism of VA and the perceived ability to observe events during CA. Although in this study the potential role of cofounders such as age, gender and time to interview were evaluated, our results indicated a wide variation in these variables. Consequently a larger study would be warranted to further explore the relationship between these variables with VA. Such a study should also explore the impact of variables that may impact the quality of cerebral blood flow and cerebral recovery such as the duration of CA, quality of CPR during CA, location of CA (in-hospital versus out-of hospital), underlying rhythm, use of hypothermia during CA and after ROSC.

5. Conclusions

CA survivors experience a broad range of memories following CPR including fearful and persecutory experiences as well as awareness. While explicit recall of VA is rare, it is unclear whether these experiences contribute to later PTSD. Studies are also needed to

delineate the role of explicit and implicit memory following CA and the impact of this phenomenon on the occurrence of PTSD and other life adjustments among CA survivors.

Conflict of interest statement

None of the authors have any conflicts of interest to declare.

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Ethical approval

This study obtained ethics approvals from each participating center prior to the start of recruitment and data collection. Each surviving patient gave informed consent prior to their being interviewed.

Data sharing

All authors either had access to all the data or the opportunity to review all data.

Transparency declaration

I Sam Parnia as lead author affirm that the manuscript is an honest, accurate, and transparent account of the study being reported and that no important aspects of the study have been omitted and that any discrepancies from the study as planned have been explained.

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