Feasibility of non-invasive neuro-monitoring during extracorporeal membrane oxygenation in children.

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ABSTRACT

INTRODUCTION: Detection of neurological complications during extracorporeal membrane oxygenation (ECMO) may be enhanced with non-invasive neuro-monitoring. We investigated the feasibility of non-invasive neuro-monitoring in a paediatric intensive care (PIC) setting.

METHODS: In a single centre, prospective cohort study we assessed feasibility of recruitment, and neuro-monitoring via somatosensory evoked potentials (SSEP), electroencephalography (EEG) and near infrared spectroscopy (NIRS) during venoarterial (VA) ECMO in paediatric patients (0-15 years). Measures were obtained within 24-hours of cannulation, during an intermediate period, and finally at decannulation or echo stress testing. SSEP/EEG/NIRS measures were correlated with neuro-radiology findings, and clinical outcome assessed via the pediatric cerebral performance category (PCPC) scale 30 days post ECMO cannulation.

RESULTS: We recruited 14/20 (70%) eligible patients (median age: 9 months; IQR:4-54, 57% male) over an 18-month period, resulting in a total of 42 possible SSEP/EEG/NIRS measurements. Of these, 32/42 (76%) were completed. Missed recordings were due to lack of access/consent within 24 hours of cannulation (5/42, 12%) or PIC death/discharge (5/42, 12%). In each patient, the majority of SSEP (8/14, 57%), EEG (8/14, 57%) and NIRS (11/14, 79%) test results were within normal limits. All patients with abnormal neuroradiology (4/10, 40%), and 6/7 (86%) with poor outcome (PCPC ≥4) developed indirect SSEP, EEG, or

NIRS measures of neurological complications prior to decannulation. No study-related adverse events or neuro-monitoring data interpreting issues were experienced.

CONCLUSIONS: Non-invasive neuro-monitoring (SSEP/EEG/NIRS) during ECMO is feasible and may provide early indication of neurological complications in this high-risk population.

KEY WORDS: Somatosensory evoked potential, Electroencephalography, Near-infrared spectroscopy, Extracorporeal membrane oxygenation, Neurological injury, Prognostication, Neuro-monitoring.

INTRODUCTION

Identification of neurological complications in critically unwell infants and children is important but extremely challenging; especially in the vulnerable patient population requiring extracorporeal membrane oxygenation (ECMO) in paediatric intensive care (PIC).

Clinical examination is the gold standard for assessing neurological status but the deep sedation and neuromuscular blockade required for patient management confounds the interpretation of neurological signs[1], which is often the situation during ECMO. Despite improving ECMO survival rates (60-70%)[2] up to 70% of patients may develop a long-term neurological disability[3,4].

Neurological complications before and during ECMO can cause hypoxic ischaemic encephalopathy (HIE). Stroke and impaired cerebral autoregulation occur in 13% of patients[5]. Non-invasive monitoring allows early detection of neurological deterioration that can be used in the management of patients where clinical exam is not feasible[6,7]. Neuro-monitoring devices that record somatosensory evoked potentials (SSEP), electroencephalography (EEG), and near-infrared spectroscopy (NIRS) measure peripheral-to-cortical evoked potential transmission, cortical electrical activity, and cerebral tissue oxygenation, respectively[8–10].

Although each can be used to detect neurological injury, there is a lack of, or conflicting evidence demonstrating SSEP/EEG/NIRS neuro-monitoring utility, particularly during ECMO. This could in part be due to limitations in the feasibility of a neuro-monitoring protocol. For example, long-term SSEP/EEG recording in the critical care environment could be limited by the need for expert acquisition and interpretation in an electrically hostile environment, and there is a lack of evidence demonstrating the utility of NIRS[11–13]. Although each non-invasive

neuro-monitoring device provides an indirect measure of possible neurological complications, the role of SSEP/EEG/NIRS monitoring in ECMO decision making is still unclear.

Our aim was to investigate the feasibility of SSEP, EEG and NIRS neuro-monitoring during ECMO in critically unwell infants and children in a PIC environment. We present exploratory SSEP/EEG/NIRS indices of possible neurological complications during ECMO and report whether these predict neurodevelopmental outcome at 30 days post ECMO cannulation.

METHOD

Design and recruitment

We conducted a prospective feasibility cohort study in the Birmingham Children's Hospital (BCH) PIC, United Kingdom. Between April 2017 and October 2018, we included all patients aged 0-15 years who required venoarterial (VA) ECMO following 1) cardiac arrest and extracorporeal cardiopulmonary resuscitation (ECPR); 2) post-surgical failure to separate from cardiopulmonary bypass (CPB); and 3) development of cardiomyopathy or myocarditis and subsequent refractory low cardiac output state.

Exclusion criteria were lack of informed consent; the inability to apply recording electrodes; peripheral neuropathy (PN), spinal cord injury (SCI) or traumatic brain injury (TBI) as these interfere with SSEP recording[14].

A discussion between the study team and consultant Intensivist looking after the child took place before approaching the family for informed consent. At this point, the child's clinical

team could exclude the participant from the study if the family were too emotionally distressed. In other cases, the study team would approach the parent/guardian and would exclude the participant if the family were thought to be under too much emotional distress to consider their child's participation.

We also excluded those with severe jaundice, which interferes with NIRS monitoring[15], and patients requiring ECMO primarily for respiratory support regardless of whether cannulation type was VA or venovenous (VV). A neuropathy was considered absent if peripheral evoked potentials (described in method subsection neuro-monitoring measurements) were present. The absence of a SCI, TBI or jaundice was confirmed by the patient's Intensivist. If patients required re-cannulation after unsuccessful ECMO weaning, this data was considered for inclusion.

Written informed consent for the neuro-monitoring protocol was obtained within 24 hours of cannulation from the patient's parent/guardian. To maximise recruitment and coordinate an approach for consent, all members of the research and ECMO team received communication via a Smartphone messenger app and monthly meetings. The study was approved by the UK Coventry & Warwickshire Research Ethic Committee (REF: 17/WM/0029).

ECMO management

Extracorporeal blood flow was managed using the Levitronix centrifugal pump system. Patients were anaesthetised using ketamine and received morphine and midazolam analgesia and sedation. Neuromuscular blockade was maintained with Rocuronium for the first 24 hours of therapy. Open chest transthoracic cannulation of the right atrium and the

aortic arch was performed in patients who could not wean from intraoperative bypass or ECPR in PIC. Cannulation via the right side of the neck using the carotid artery and internal jugular vein was performed in those requiring VA support that did not have an open chest. Correct cannula position was confirmed via chest X-ray and echocardiogram. A continuous heparin infusion was titrated according to activated clotting time. Ventilation was pressure regulated and volume controlled with standard settings: respiratory rate 10 breaths per minute, with an inspired oxygen concentration of 30%. Chest physiotherapy was delivered as indicated by the child's condition and >70% venous saturations.

Neuro-monitoring protocol.

All patients received continuous SSEP and EEG monitoring at a minimum of three time points, each for 4-hour duration during high-risk periods (within 24 hours of ECMO initiation; during and soon after decannulation; and/or during ECHO stress testing). An intermediate period in-between these was also recorded. NIRS was monitored continuously throughout the patient's care, but only time-locked cerebral tissue oxygen saturations ($SctO_2$) recorded during SSEP and EEG intervention were analysed. This study was not blinded and clinical staff had access to SSEP/EEG/NIRS data for clinical decision making.

We collected feasibility data including rate of recruitment, rate of complete monitoring implementation and any barriers associated with these. Each neuro-monitoring intervention was classified as technically successful if the data was interpretable with no significant external electrical artefact.

Demographic (age, gender), clinical (indication, duration and type of ECMO), and imaging (US, CT, MRI) data was collected and adverse events/reactions related to study

interventions (pressure sores, skin adhesions, or other serious unexpected adverse events) was recorded. Survival status and paediatric cerebral performance category (PCPC)[16] score was collected at 30 days post ECMO cannulation. Good neurodevelopmental outcome was defined as PCPC score 1-3 (normal, mild or moderate disability) and poor 4-6 (severe disability, coma/vegetative state, or death).

Neuro-monitoring measurements

SSEPs and EEG were recorded in synchrony using the Matrix acquisition system (Micromed, Woking, UK). SSEPs were obtained following stimulation of either the median or ulnar nerve at the wrist or elbow. Peripheral evoked potentials were recorded bilaterally from Erb's point to ensure absent or low amplitude cortical responses were not the result of inadequate stimulation.

Cortical recording electrodes were placed on the scalp 2cm posterior to C3/4 international 10-20 electrode sites and a range of recording montages were used in line with recognised guidelines[14]. Stimulation was interleaved with a 500ms delay between left-then-right wrist stimulation at a rate of 1Hz and intensity >1.5 times above motor threshold for a duration of 500µS. If neuromuscular junction blockade prevented a visible hand twitch (which is used to gauge supramaximal sensory stimulation), up to 50mA stimulation intensity was used.

Left limb stimulation was marked in the EEG using a digital trigger and averaging was performed off-line (meaning analysis occurred after data capture) using NPX lab software suite[17]. A greater than 50% decrease in SSEP amplitude is used as an indicator of cerebral ischaemia intraoperatively[18]. In the PIC setting, absent SSEPs suggest severe HIE[19], therefore

SSEP absence/presence, and whether there was significant asymmetry (>50%) between left and right hemispheres was recorded for each patient.

EEG was recorded from 4 scalp electrodes secured with a collodion adhesive 2cm posterior to international 10-20 system locations. This was because quantitative EEG (qEEG) electrodes used as part of routine clinical care were in F3, C3, F4, C4 positions. The EEG was recorded in a reduced bipolar montage (F3'-C3', F4'-C4') and digitally filtered with low and high frequency filters of 0.53Hz and 70Hz, respectively.

Background EEG was interpreted by neurophysiology study team members as benign (normal, nonspecific abnormalities) or malignant (discontinuous/burst-suppression or suppressed), including the presence/absence of electrographic seizures[20–22]. Features of cerebral ischaemia include hemispheric asymmetry in the frequency or amplitude of EEG activity[23]. We considered a >50% difference in total EEG power (uV^2/Hz) between left and right cortical hemispheres as a measure of possible neurological injury.

NIRS

NIRS was recorded continuously using the FORE-SIGHT ELITE® (CAS Medical Systems, Branford, CT, USA) tissue oximeter. Left and right sensors were placed equidistant between the patient's eyebrow and hair line, and the midpoint of the sensor was aligned with the patients' pupils. Each sensor had a light source and 2 detectors which continuously emitted and received 5 near-infrared wavelengths (690, 730, 770, 810, 870nm) that penetrated a depth of 1.25cm & 2cm in a curvilinear fashion.

The device calculated $SctO_2$ by dividing the concentration of oxyhaemoglobin (HbO_2) by the sum of HbO_2 and concentration of deoxyhaemoglobin (HHb) and multiplying by 100[24]. This

gave left and right cortical hemisphere $SctO_2$ (%) every two seconds. Asymmetries >20% between left and right hemispheric $SctO_2$, and a mean $SctO_2$ <56% were defined as indices of possible neurological injury[25–27]. This device was synchronised (in date and time) to the EEG/SSEP recording.

Primary outcome was neuro-monitoring feasibility assessed via patient recruitment rate, the rate of missed study interventions, incomplete data collection and adverse reactions to study interventions (SSEP/EEG). A secondary outcome was morbidity, assessed using the PCPC scale 30 days post cannulation.

Data analysis

Descriptive data were reported as percentages for categorical variables and either means with standard deviations (SD) or medians with interquartile ranges (IQR) for continuous variables. Visual inspection of a scatter graph identified asymmetries in NIRS $SctO_2$, SSEP amplitude (μV) and EEG power ($\mu V^2/Hz$). This was dichotomised (asymmetry vs. no asymmetry), as was outcome (Good: PCPC 1-3 vs. Poor: PCPC 4-6), EEG background (benign vs. malignant) and seizures (present/absent).

RESULTS

Feasibility

Over the study period, 20/35 (57%) patients requiring ECMO fulfilled the inclusion criteria and 14/20 (70%) were successfully enrolled. Of the six eligible patients who were not enrolled, four were not approached due to parent/guardian emotional distress; one due to

a lack of staff with SSEP/EEG acquisition expertise and one due to a failure in study team communication which prevented patient identification before decannulation (Figure 1). Sixty-seven percent (4/6) of failed recruitment occurred within the first five months of study initiation. All SSEP/EEG/NIRS recordings were considered technically successful and were interpreted without significant contribution of external artefact.

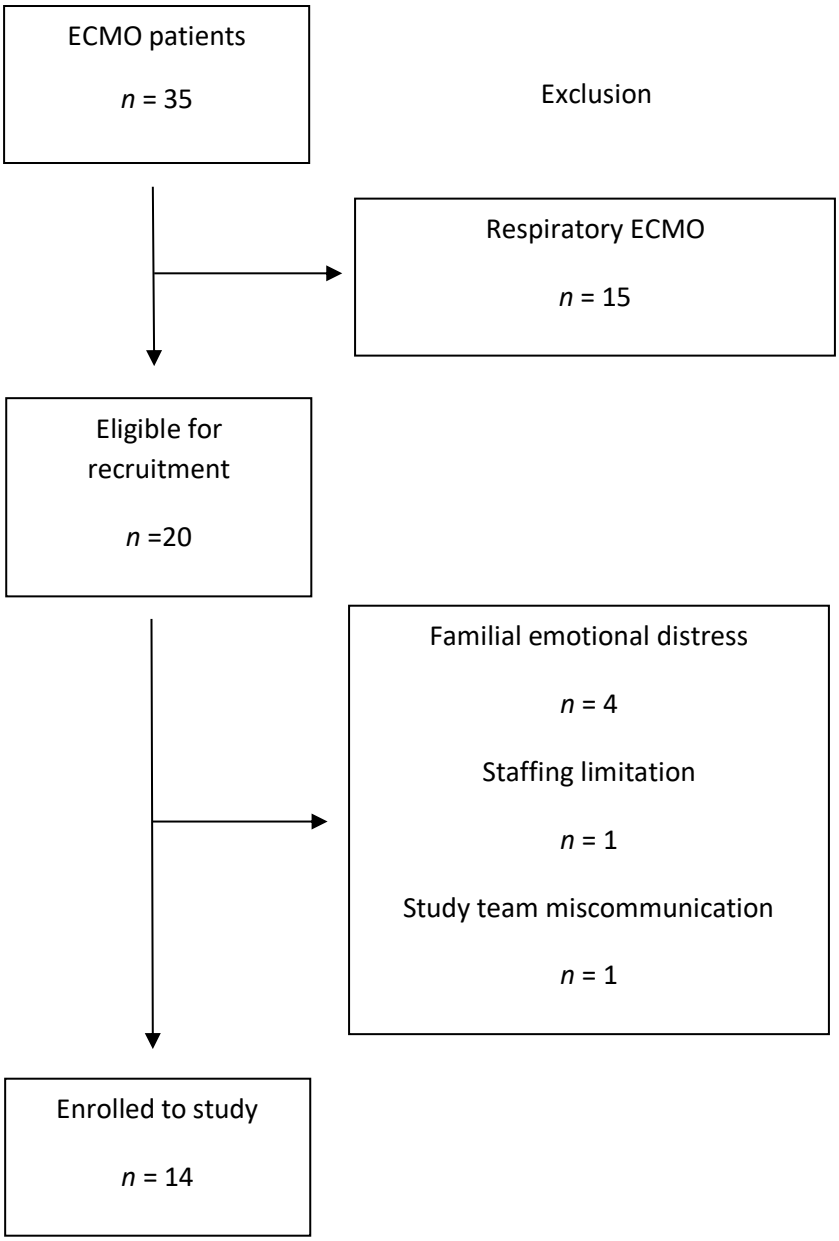

Figure 1: Study flow chart: Recruitment and exclusion of patients due to respiratory indication for ECMO, including familial emotional distress, staffing limitation and study team miscommunication.

Demographics

Of the 14 patients, median age was 9 months (IQR: 4-54), 4/14 (29%) were neonates and the majority were male with a congenital heart defect (CHD) primary diagnosis. Cannulation sites were neck (7/14, 50%) and transthoracic (7/14, 50%). The median duration of ECMO was 119 hours (IQR: 64-166) and 7/14 (50%) were cannulated following ECPR. SSEP, EEG and NIRS monitoring was performed in all (14/14, 100%) recruited patients and the majority (9/14, 64%) of initial interventions were performed within 24 hours (median: 11 hours; IQR: 10-19) of cannulation (Table 1).

Reasons for missed study interventions included 1) inability to access patient/parent/guardian within 24 hours (5/10, 50%); 2) patient death before SSEP/EEG measurement (2/10, 20%); 3) patient transferred to another hospital prior to decannulation (2/10, 20%); 4) decannulation occurred in theatre where monitoring access was not possible (1/10, 10%). Inability to access the patient within 24 hours was primarily due to the additional time requested by families to consider their child's participation. No serious adverse events related to study protocol/intervention were reported.

Patient	Age, Months	Gender	Primary diagnosis	ECMO			Time from cannulation to intervention, hours			Neuro-monitoring			Imaging modality, findings	PCPC	
				Type	Duration, hours	Cannulation site / Type	1st	2nd	3rd	SSEP Present/Absent, Asymmetry	EEG Background, Seizures, Asymmetry	NIRS Mean/Lowest $SctO_2$, asymmetry		Pre-PICU admission	Post-PICU admission
Good outcome															
1	<1	F	CHD	VA	134	A – RA / CHEST	16	57	106	Present, No asymmetry	Benign, no seizures, No asymmetry	72/63%, L<R asymmetry	US+CT, Normal	1	1
2	7	M	CHD	VA	63	A – RA /CHEST	Mis	34	Mis	Present, No asymmetry	Benign, no seizures, L<R asymmetry,	68/63%, No asymmetry	US, Normal	1	1
3	8	M	MC-> CM	ECPR	210	A – RA+LA / CHEST	4	64	Mis	Present, L<R asymmetry	Benign, no seizures, No asymmetry	78/69%, No asymmetry	CT+MRI, Scattered foci of haemosiderin	1	1
4	12	F	CHD	ECPR	60	A – RA+LA / CHEST	11	31	58	Present, No asymmetry	Benign, no seizures, No asymmetry	81/70%, No asymmetry	US, Normal	1	1
5	12	M	MC	ECPR	432	A – IJ / NECK	Mis	91	230	Present, No asymmetry	Benign, no seizures, No asymmetry	79/72%, No asymmetry	CT, Normal	1	3
6	72	M	MC	VA	272	A – RA+LA / NECK	11	55	149*	Present, No asymmetry	Benign, no seizures, No asymmetry	85/80%, No asymmetry	N/A	1	1
7	156	F	MC	VA	73	A – RA / NECK	Mis	57	78*	Present, No asymmetry	Benign, no seizures, No asymmetry	90/89%, No asymmetry	N/A	1	1
Poor outcome															
8	<1	M	CHD	VA	26 + 140	A – RA / CHEST	9	52*	21	Present -> absent, No asymmetry	Malignant, no seizures, No asymmetry	80/65%, R<L asymmetry	US, Normal	2	6
9	<1	F	CHD	ECPR	64	A – RA / CHEST	19	Mis	Mis	Absent, No asymmetry	Benign, no seizures, R<L asymmetry	80/78%, No asymmetry	US, Normal	1	6
10	<1	M	CHD	ECPR	166	A – RA / CHEST	21	36	132	Present, R<L asymmetry	Malignant, no seizures, R<L asymmetry	69/55%, R<L asymmetry	US, Right IVH	2	6
11	2	M	CHD	ECPR	151	A – IJ / NECK	10	30	130	Present, L<R asymmetry	Benign, Seizures, L<R asymmetry	68/65%, No asymmetry	US, Left IVH	1	6
12	24	F	MA -> LCOS	VA	89	CA – IJ / NECK	Mis	76	144*	Present, No asymmetry	Malignant, no seizures, No asymmetry	85/77%, No asymmetry	N/A	1	6
13	36	F	CM	VA	119	CA – IJ/ NECK	Mis	71	Mis	Present, No asymmetry	Benign, no seizures, No asymmetry	83/81%, No asymmetry	N/A	1	5
14¥	180	M	CHD	ECPR	69	A – IVC+ LA / NECK	19	37	56	Present -> unilateral (L) absence, L<R asymmetry¥	Benign, no seizures, No asymmetry	86/79%, No asymmetry	CT, Left SDH	2	4

Table 1: Descriptive statistics, outcome, and the results of study interventions. CHD: Congenital heart defect; MC: Myocarditis; CM: Cardiomyopathy; MA: Metabolic acidosis; LCOS: Low cardiac output state; ECPR: extracorporeal cardiopulmonary resuscitation; ->: leading to; A – RA: Aorta – Right Atrium; A – LA & RA: Aorta – Left Atrium & Right Atrium; A – IVC & LA: Aorta – Inferior Vena Cava & Left Atrium; CA – IJ: Carotid Artery & Internal Jugular Vein; Mis: Missed study intervention; ¥: An illustration of SSEP evolution provided in figure 2; SSEP: Somatosensory evoked potential; EEG: Electroencephalography; NIRS: Near-infrared spectroscopy; L: Left; R: Right; US: Ultrasound; CT: Computed tomography; MRI: Magnetic resonance Imaging; N/A: Not assessed; IVH: Intraventricular haemorrhage; SDH: Subdural haemorrhage; PCPC: Pediatric Cerebral Performance Category. *Indicates an intervention performed during ECMO decannulation or ECHO stress test.

Neurological complications

The majority of SSEP (8/14, 57%), EEG (8/14, 57%) and NIRS (11/14, 79%) recordings were symmetrical and considered normal as they did not meet the thresholds described for possible neurological injury.

Asymmetries in SSEP amplitude were noted in 4/14 (29%) patients which correlated with subdural (*n*=1) or intraventricular haemorrhage (*n*=2) and scattered foci of haemosiderin within cerebral hemispheres (*n*=1) on US/CT/MRI imaging. SSEPs evolved from normal to absent (*n*=1), and a progressive asymmetry resulted in unilateral absence (*n*=1) (Figure 2).

EEG asymmetries were noted in 4/14 (29%) patients and these correlated with ipsilateral US abnormalities in 2/14 (14%). Benign EEG consisted of age-appropriate polyrhythmic theta and delta activity in most (8/11, 73%) and this was interspersed by intermittent rhythmic delta activity (a non-specific EEG abnormality) in 3/11 (27%). Malignant EEG recordings (3/14, 21%) were suppressed, either with high amplitude irregular bursts of EEG activity interspersing the background (i.e., a burst-suppression pattern) (*n*=2) or without (*n*=1). Subclinical seizures were successfully treated in 1/14 (7%).

NIRS asymmetries (>20% hemispheric difference in $SctO_2$) in 3/14 (21%) were associated with a unilateral lesion in 1/3 (33%) but no specific US/CT/MRI abnormalities in 2/3 (66%). Imaging (US/CT/MRI) that was performed in 10/14 (71%) was normal in 6/10 (60%), detected intraventricular or subdural haemorrhage in 3/10 (30%) and scattered foci of cerebral haemosiderin in 1/10 (10%).

[insert Figure 2]

Seven patients (50%) had poor outcome, which was more common in neonates, CHD patients, and following ECPR. Two died soon after decannulation, one remained cannulated (2nd ECMO run) in a comatose state, and three had died within 30 days. One patient developed right sided weakness following a left sided haemorrhage.

All patients with absent SSEPs, malignant EEG, or seizures had poor outcome. NIRS indices of neurological complications (>20% asymmetry or <56% mean $SctO_2$) were identified in two patients with poor outcome and one patient with good outcome.

DISCUSSION

In the challenging PIC environment, we established that non-invasive neuro-monitoring during ECMO is feasible. We achieved a 70% recruitment rate and demonstrated that multimodal neuro-monitoring consisting of SSEP, EEG and NIRS could be acquired and interpreted in all patients with no adverse events or reactions to study interventions.

We performed and interpreted SSEP/EEG/NIRS data and collected all planned clinical information. Most failed recruitment occurred within the first months of study set up, and each failed recruit was discussed at monthly meetings to prevent a similar failure moving forward. Non-invasive neuro-monitoring of SSEP/EEG/NIRS detected all neurological injuries identified via US/CT/MRI, and predicted poor outcome. The success of this feasibility study justifies a larger trial which could provide more definitive evidence of SSEP/EEG/NIRS neuro-monitoring utility.

This study utilised clinical scientists in neurophysiology to capture non-invasive neuro-monitoring data, which may be possible to replicate in other centres. Further approaches

would require training and investment from ECMO or PIC teams, so that SSEP/EEG/NIRS results can be obtained before, during, and immediately after cannulation. This would allow for the identification of whether a neurological injury was acquired before or during ECMO.

Similar non-invasive neuro-monitoring programmes have been successful elsewhere[28–30] and within our institution[31]. This demonstrates that SSEP/EEG acquisition can be performed by specifically trained PIC healthcare professionals under neurophysiology supervision. On-line SSEP averaging is recommended, meaning that analysis is done at the point of data capture (i.e., real time analysis). This would allow rapid SSEP results and injury detection, in conjunction with NIRS and EEG data.

ECMO patients at our institution have qEEG monitored continuously for 24 hours to detect, treat and manage seizures. This consists of amplitude integrated EEG (aEEG) and a colour density spectral array (CDSA) of EEG activity. On-line detection of possible neurological injury using the SSEP/EEG/NIRS indices described would be feasible, although continuous and quantitative SSEP monitoring may be more problematic.

However, quantitative SSEP data was arguably more important in this cohort because current management (daily US in high-risk patients and CT following abnormal cranial nerve examination, qEEG and NIRS) was insufficient to detect and monitor two patients with poor outcome whose deterioration was only detected via SSEPs.

The first had normal SSEPs with a slight but not clinically significant asymmetry before and during decannulation, which when repeated (following recannulation) was absent. This injury may have been the result of low cardiac output post decannulation, a cardiac arrest which required recannulation, or iatrogenic injury during recannulation.

The second patient had SSEP asymmetry 19 hours post ECMO initiation which over time deteriorated and was absent during decannulation (Figure 2). This injury may have been present prior to ECMO, during CHD repair, when weaning from bypass; as a result of cardiac arrest soon after surgery or during ECPR initiation. ECMO factors such as circuit heparinisation and laminar cerebral blood flow cannot be excluded. Unfortunately, it was impossible to determine at which time point the injury occurred.

Previous studies investigating the utility of non-invasive neuro-monitoring during ECMO have shown promising results in detecting neurological injury and predicting poor outcome[32,33] but do not utilise SSEP monitoring. Although we detected several SSEP/EEG/NIRS abnormalities which correlated with neuroimaging findings, our preliminary results should be interpreted with caution due to the small sample of patients recruited. More evidence is required and future prospective research is recommended.

Absolute $SctO_2$ did not correlate with neuroimaging indices of neurological injury. NIRS asymmetries were identified in two poor outcome patients and one good outcome patient. A mean $SctO_2$ <56% in the first 48 hours following Norwood procedure in neonates has predicted poor outcome with 79% specificity[26]. In our neonatal subgroup (4/14, 29%), $SctO_2$ decreased below 56% in one patient with poor outcome. Our findings are similar to those who report absent and asymmetric SSEPs[34,35], malignant EEG[36,37] and seizures[38] as indices of neurological injury and poor prognosis.

Although there was no obvious distinction in mean $SctO_2$ between good and poor outcome groups, a mean NIRS $SctO_2$ <56% may not have been an accurate index of possible neurological injury as this was taken from data in neonates. Although the quality of

evidence supporting NIRS cerebral ischaemia monitoring is low[39–41], future studies could focus on significant asymmetries between left and right hemisphere measurements.

This study has several limitations. We chose a selective high-risk population to neuro-monitor during VA ECMO support. Our results may not be generalisable to other ECMO populations (e.g., VV ECMO for respiratory failure). The PCPC scale may not have been suitable to assess subtle long-term neurological disability, which may not be present 30 days post cannulation[42]. Neuroimaging was at the discretion of the clinician and there was no formalised neuropsychological and neuro-developmental assessment. As such, mild or delayed neurological injury may have been unrecognised. Future studies would need to incorporate clinical and MRI follow-up several months after decannulation.

In conclusion, our study protocol for non-invasive neuro-monitoring in high-risk paediatric patients during ECMO appears feasible and safe. Important diagnostic and prognostic information was obtained and there appeared to be a trend to towards correlation with neurological injury. A future large-scale, prospective study is justified to examine the utility of neuro-monitoring in the management of these patients.

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Conflicts of interest

The Authors declare that there is no conflict of interest.

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Contribution

William M McDevitt: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Visualization, Project administration

Margaret Farley: Investigation, Resources, Writing - Review & Editing

Darren Martin-Lamb: Investigation, Resources, Writing - Review & Editing

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Stefano Seri: Conceptualization, Methodology, Validation, Resources, Writing - Review & Editing, Supervision.

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