

eTable 1 Studies employing NIRS to investigate seizures in the critically ill

	Adelson et al. (1999)	Haginoya et al. (2002)	Alfonso et al. (2004)	Arca Diaz et al. (2006)	Giorni et al. (2009)
Study purpose	Pathophysiology	Pathophysiology	Pathophysiology	Treatment	Diagnostic
Study design	Case-series (n = 3)	Cohort / prospective (n = 15)	Case-report (n = 1)	Case-report (n = 1)	Case-report (n = 1)
# critically ill / SE (sex, age)	n = 1 (M, 4 months)	n = 1 (F, 13 year-old)	n = 1 (M, 3 week-old)	n = 1 (M, 2.5 months)	n = 1 (F, 2.5 months)
Clear seizures (#)	Yes (<i>NR</i>)	Yes (15)	Yes (7)	Yes (15)	Yes (<i>NR</i>)
Clear SE diagnosis (SE category)	Yes (CSE)	Yes (TSE)	Yes (MSE, NCSE/coma)	Yes (FMSE)	Yes (NCSE/coma)
Clinical manifestations	Yes	Yes	No	Yes	No
$\bar{x}$ seizures duration	<i>NR</i>	< 1min	32-45min	1-2min	“several minutes”
$\bar{x}$ inter-seizure- interval	180s to 60min	2-3min	<i>NR</i>	30s to 1.5min	<i>NR</i>
Treatment	Multiple ASMs	Multiple ASMs	Multiple ASMs	Multiple ASMs	Multiple ASMs
Underlying brain pathology	TBI	LGS	HME, TSC	CD	HIBI
NIRS device (technology / SR / #WL)	INVOS3100A (CW / <i>NA</i> / 2)	NIRO300 (CW-SRS / <i>NR</i> / 4)	INVOS5100 (CW / <i>NA</i> / 2)	INVOS300 (CW / <i>NA</i> / 2)	INVOS300 (CW / <i>NA</i> / 2)
NIRS biomarkers (absolute)	rSO ₂ (no)	[HbT/HbO/HbR] (no)	rSO ₂ (no)	rSO ₂ (no)	rSO ₂ (no)
# channels (cortical coverage)	4 (forehead U)	12 (forehead B)	4 (forehead U)	4 (forehead B)	4 (forehead B)
NIRSm duration (simultaneous EEG and/or systemic recording reported)	≈ 30h (Yes / No)	< 1h (Yes / No)	24h (Yes / No)	< 1h (Yes / No)	“several days” (Yes / Yes)
Results presentation	Continuous measurements	Continuous measurements	Continuous measurements	Continuous measurements	Continuous measurements

Pre-ictal changes	↑ rSO ₂	↓ [all]	NR	NR	NR
Ictal changes	↑ < ↓ rSO ₂	↑ [HbO] > [HbT] > [HbR]	↓ rSO ₂	↑↓ rSO ₂ (correlating with 69% of Sz)	↑↓ rSO ₂
		↓ amplitude [all] (over Sz course)			
		↑ [HbR], ↓↓ [HbO] and [HbT] (as Sz repeated)			
Post-ictal changes	NR	NR	↑↓ rSO ₂ , delayed baseline return	↓ rSO ₂	rSO ₂ normalization
Anatomical MRI collected (findings)	No	Yes (cerebral atrophy)	Yes (Right HME)	Yes (B frontoparietal CD)	No

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	Wallois et al. (2009)	Cooper et al. (2011)	Silas et al. (2012)	Singh et al. (2014)	Monrad et al. (2015)
Study purpose	Pathophysiology	Pathophysiology	Pathophysiology	Pathophysiology	Pathophysiology
Study design	Case-report (n = 1)	Cohort / prospective (n = 4)	Case-report (n = 1)	Case-report (n = 1)	Case-series (n =)
# critically ill / SE (sex, age)	n = 1 (M, 10 day-old)	n = 4 (NR, 8 day-old)	n = 1 (M, < 4 day-old)	n = 1 (F, 10 day-old)	n = 1 (M, 10 year-old)
Clear seizures (#)	No (12)	No (NR)	Yes (13)	Yes (7)	Yes ()
Clear SE diagnosis (SE category)	No	No	Yes (NCSE/coma)	No	Yes (ESES)
Clinical manifestations	No	No	No	No	NR
$\bar{x}$ seizures duration	$\approx$ 28s	NR	$\approx$ 8min	54.3s	NR
$\bar{x}$ inter-seizure- interval	407s	393.6s	15min-20h	441.3s	NR
Treatment	Phenobarbital	Multiple ASMs	Therapeutic hypothermia and phenobarbital or phenytoin or midazolam	Multiple ASMs	NR
Underlying brain pathology	Acute fetal distress	Stroke, sepsis, hypoglycemia	HIE	HIE	NR
NIRS device (technology / SR / #WL)	Imagent (CW-FM / NR / 2)	UCL Optical Topography System™ (CW-FM / 10Hz / 2)	NIRO200 (CW-SRS / NR / 4)	UCL Optical Topography System™ (CW-FM / 10Hz / 2)	INVOS (CW / NA / 2)
NIRS biomarkers (absolute)	[HbT/HbO/HbR] TOI, FTOE (no)	[HbT/HbO/HbR] (no)	TOI (yes)	[HbT/HbO/HbR] (no)	rSO ₂ (no)
# channels (cortical coverage)	8 (parietal B)	60 (whole-head)	NR (frontoparietal U)	58 (whole-head)	2 (forehead U)
NIRSm duration	1.5h	1.5h	20-24h	1h	< 1h

(simultaneous EEG and/or systemic recording reported)	(Yes / Yes)	(Yes / No)	(Yes / Yes)	(Yes / No)	(Yes / No)
Results presentation	Continuous measurements and mean changes	Continuous measurements	Continuous measurements	Continuous measurements	Continuous measurements
Pre-ictal changes	NR	NR	NR	↑ [HbO] + ↑ [HbR] + ↑ [HbT]	NR
Ictal changes	↑ [HbR] → ↓ [HbR] + ↑ [HbO] + ↑ [HbT] ↓ TOI (slightly) ↑ FTOE Some variability between events	↑ [HbO] + ↑ [HbR] + ↑ [HbT] → ↓ [HbO] + ↓ [HbR] + ↓ [HbT] [HbR] not significant [HbO] and [HbR] out of phase	8 Sz (62%): ↑ TOI in 5 Sz, decrease in 3 Sz – ↑ MABP in 7 Sz, ↓ MABP in 1 Sz 5 Sz (38%): no change in TOI – ↑ MABP in 1 Sz	↑ [HbO] + ↑ [HbR] + ↑ [HbT] until max, then ↓ [HbO] + ↓ [HbR] + ↓ [HbT] Significant spatial variability	↑ rSO ₂
Post-ictal changes	NR	NR	NR	↓ [HbO] + ↓ [HbR] + ↓ [HbT] (prolonged)	NR
Anatomical MRI collected (findings)	No	No	Yes (acute hypoxic-ischemic changes)	No	Yes (normal)

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	Sokoloff et al. (2015)	Mitra et al. (2016)	Mitra et al. (2016)	Martini et al. (2019)	Parcella et al. (2020)
Study purpose	Treatment	Pathophysiology	Pathophysiology	Pathophysiology	Prognostic
Study design	Cohort / prospective (n = 20)	Case-report (n = 1)	Case-report (n = 1)	Case-report (n = 1)	Cohort / retrospective (n = 62)
# critically ill / SE (sex, age)	n = 11 (10M, “fully term neonates”)	n = 1 (NR, 9.5 day-old)	n = 1 (NR, 10 day-old)	n = 1 (NR, 9 day-old)	38 (18M, < 3 day- old)
Clear seizures (#)	Yes (40)	Yes (4)	Yes (16)	Yes (10)	23/38 patients (NR)
Clear SE diagnosis (SE category)	No	Yes (NCSE/coma)	No	Yes (TSE)	No
Clinical manifestations	NR	No	No	Yes	NR
$\bar{x}$ seizures duration	$\approx$ 120s	$\approx$ 5min	$\approx$ 90s	$\approx$ 10min	NR
$\bar{x}$ inter-seizure- interval	NR	3-8min	NR	15-30min	NR
Treatment	Phenobarbital	Therapeutic hypothermia	Multiple ASMs	Therapeutic hypothermia and multiple ASMs	Therapeutic hypothermia
Underlying brain pathology	HIE, neonatal epilepsy, stroke, sepsis, ICH, SVT	HIE	Stroke	HIE	HIE
NIRS device (technology / SR / #WL)	INVOS5100 (CW / 0.2Hz / 2)	Homemade system (CW / NR / NR)	Homemade system (CW / NR / NR)	NR (NR)	INVOS (CW / NA / 2)
NIRS biomarkers (absolute)	rSO ₂ , FTO ₂ (no)	[HbO/HbR /HbT/HbD/CCO]	[HbO/HbR /HbT/HbD/CCO]	rSO ₂ (no)	rSO ₂ (no)
# channels (cortical coverage)	4 (parietal B)	6 (forehead B)	6 (forehead B)	NR (NR)	2 (forehead U)
NIRSm duration (simultaneous EEG and/or systemic)	1h (Yes / Yes)	1.5h (Yes-quantitative / Yes)	3h (Yes-quantitative / Yes)	6h (Yes-quantitative / Yes)	72h (Yes / Yes)

recording reported)					
Results presentation	Continuous measurements and mean changes	Continuous measurements	Continuous measurements and mean changes	Continuous measurements	Continuous measurements and mean changes
Pre-ictal changes	$\bar{x}$ rSO ₂ $\approx$ 79.4 %	NR	NR	NR	NR
Ictal changes	↓ rSO₂, ↑ FTOE (within physiological range) (↑ with ↑ phenobarbital dose) Independent from systemic changes	↑ [CCO] → ↓ [CCO] → ↑ [CCO] (after aEEG peak) ↓ [HbT] + ↓ [HbD] → ↑ [HbT] + ↑ [HbD] (after aEEG peak)** No systemic changes	Asymmetric ↓ [HbO], [HbR], and [CCO] (↓ stroke hemisphere > non-stroke hemisphere) No systemic changes	↑↓ rSO₂ → delayed ↓ rSO₂ → ↑ rSO₂ close to the end (correlating with ↑ Sz amplitude) rSO₂ baseline increased with each subsequent Sz	rSO₂ was higher in severe group (i.e., patients with seizures)
Post-ictal changes	rSO ₂ normalization	NR	↓ [HbO] + ↓ [HbR] + ↓ [CCO] → slow ↑ [HbO] + ↑ [HbR] + ↑ [CCO]	rSO ₂ normalization	NR
Anatomical MRI collected (findings)	No	Yes (abnormal + ↓ signal intensity)	Yes (↓ signal intensity + restriction diffusion)	No	Yes (all abnormal)

Abbreviations= # = number, $\bar{x}$ = average, $\approx$ = approximately, **M** = male, **F** = female, **SE** = status-epilepticus, **CSE** = convulsive SE, **TSE** = tonic SE, **MSE** = myoclonic SE, **FMSE** = focal motor SE, **NCSE** = nonconvulsive SE, **ESES** = electrical status epilepticus of slow-wave sleep, **ASMs** = antiseizure medications, **DRE** = drug-resistant epilepsy, **SR** = sampling rate, **WL** = wavelength, **LGS** = Lennox-Gastaut syndrome, **HME** = Hemimegalencephaly, **TSC** = tuberous sclerosis complex, **CD**= cortical dysplasia, **HIBI** = hypoxic-ischemic brain injury, **HIE** = hypoxic-ischemic encephalopathy, **ICH** = intracranial hemorrhage, **SVT** = sinus venous thrombosis, **Sz** = seizure, **CW** = continuous-wave, **SRS** = spatially-resolved spectroscopy, **FM**= frequency multiplexed, **NIRSm**= NIRS monitoring, **rSO₂**= regional cerebral oxygen saturation, **[HbO]** = oxy-hemoglobin concentration, **[HbR]** = deoxy-hemoglobin concentration, **[HbT]** = total hemoglobin concentration, **[HbD]** = difference between oxy- and deoxy-hemoglobin concentration, **[CCO]** = cytochrome c-oxidase concentration, **TOI** = tissue oxygen index, **FTOE** = fractional tissue oxygen extraction, **aEEG** = amplitude EEG, **B** = bilateral, **U** = unilateral, ↑↓ = fluctuation, **NR** = not reported.