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SYSTEMATIC REVIEW

Defining neonatal status epilepticus: A scoping review from the ILAE neonatal task force

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Abstract

Objective: To review the available literature concerning the definition of neonatal status epilepticus (SE) and/or seizure burden.

Methods: The International League Against Epilepsy Neonatal Task Force performed a scoping review of the definitions of neonatal SE. Following a systematic literature review, articles were screened and data were abstracted regarding: (1) article characteristics (author identification, publication year, journal name, digital object identifier, title, objective, and study design); (2) cohort characteristics (sample size, gestational age, seizure etiology); (3) definition of SE and/or seizure burden; and (4) the method used to identify and classify SE, including routine EEG (EEG), continuous EEG monitoring (cEEG), amplitude-integrated EEG (aEEG), or clinical features.

Results: The scoping review yielded 44 articles containing a definition of neonatal SE. Studies mainly included infants with hypoxic–ischemic encephalopathy or neonates considered at risk for seizures. SE identification and classification most often relied on cEEG. The majority of studies based the definition of SE on seizure duration, including summed duration of seizures comprising ≥50% of any 1-h epoch, recurrent seizures for >50% of the total recording time, or either electrographic seizures lasting >30 min and/or repeated electrographic seizures totaling >50% in any 1-h period. Seizure burden was reported in 20 studies, and the most commonly used approach assessed total seizure burden, defined as total duration of EEG seizures in minutes. Sixteen studies assessed the relationship between seizure burden and outcomes, and most identified a significant association between higher seizure burden and unfavorable outcomes.

For affiliations refer to page 10.

Significance: This scoping review demonstrates a substantial variation in neonatal SE definitions across the literature. The most common definitions were based around a 30-min seizure duration criterion, but evidence was insufficient to support that 30 min was a cutoff defining prolonged seizures or that seizures exceeding this burden were more likely to be pharmacoresistant or associated with worse outcomes. As a next step, the Neonatal Task Force intends to develop a standardized approach to assessing and describing neonatal seizure burden and defining neonatal SE.

Plain Language Summary: Prolonged seizures are a neurologic emergency, if untreated, can lead to permanent injury or death. In adults and children, seizures lasting longer than 30 min are believed to cause brain damage. However, it is not clear if this definition can be applied to neonates. The International League Against Epilepsy Neonatal Taskforce performed a scoping literature review which identified 44 articles containing a definition of neonatal status epilepticus. In this article, the authors reviewed the current used definitions for prolonged seizures in neonates to establish a relationship between seizure duration and neurological outcome. As a next step, the Neonatal Task Force intends to develop a standardized approach to assessing and describing neonatal seizure burden and defining neonatal SE.

KEYWORDS

neonatal, neurocritical care, outcome, seizure burden, seizures, status epilepticus

1 | INTRODUCTION

Seizures are the most common neurological emergency in the neonatal period. Most seizures in neonates occur in the context of an acute brain injury, while 10%–15% occur in the context of an epilepsy syndrome.[1–5] and may have distinct etiologies, clinical characteristics, and electroencephalographic (EEG) patterns.[4,6,7] Neonatal seizures are associated with mortality, neuroimaging abnormalities, and subsequent epilepsy and neurobehavioral disorders.[8,9]

Recent guidelines from the International League Against Epilepsy (ILAE) address the diagnosis and management of neonatal seizures, but details regarding neonatal status epilepticus (SE) were not addressed.[3–5] The definition of SE among neonates varies within the related literature and has evolved (Figure 1).[10–17] Many studies of neonates have extended the older 30-min time frame used to define SE in adults and older children has been extended to the neonatal period,[18,19] including definitions focused on seizure duration (e.g., continuous seizure lasting 30 min) or seizure percentage within an EEG epoch (e.g., ≥50% of 1-h epoch contains seizures) as proposed in the guidelines from the American Clinical Neurophysiology Society.[20] However, these definitions might be arbitrary given there is limited evidence as to the duration at which seizures become more refractory to treatment, cause secondary brain injury, or impact outcome in neonates.[18,19] Furthermore, the ILAE classification of SE in adults has become more nuanced and includes two operational dimensions. Time 1 (T1) is the duration at which a seizure is considered abnormally prolonged, and Time 2 (T2) is the duration of a seizure at which there is a risk of long-term consequences.[21] The proposed T1 and T2 durations vary by seizure type, including: (1) tonic–clonic SE (T1 5 min; T2 30 min),

Key Points

- There is a substantial variation on SE definition in neonates.
- Data are insufficient to support the 30 min seizure duration as a definition of SE in neonates.
- An evidence-based classification approach for neonatal seizure burden and a definition of neonatal SE is necessary.

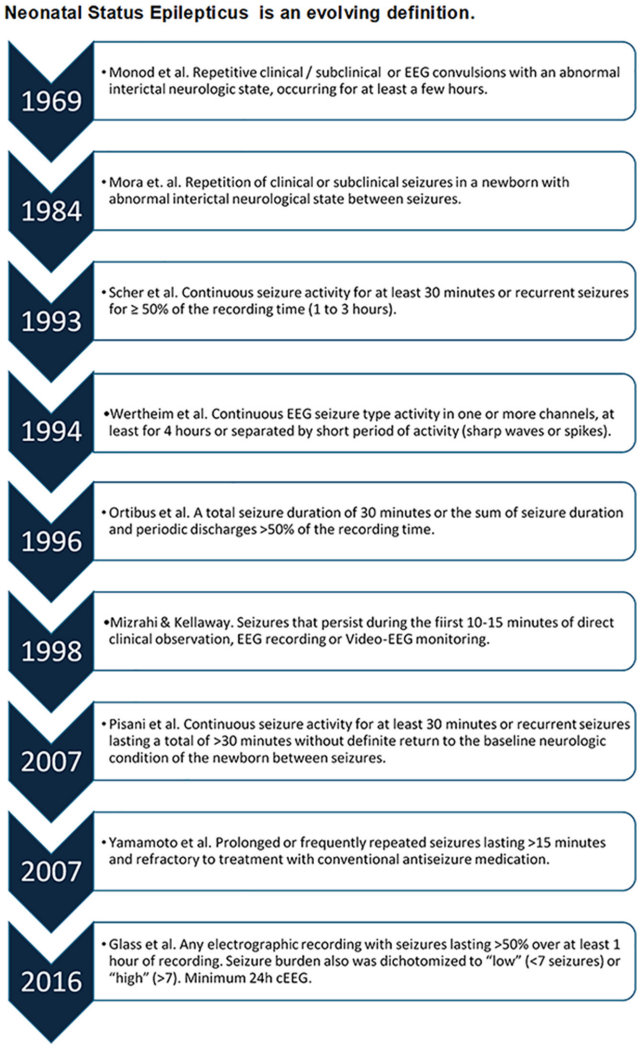

FIGURE 1 Neonatal Status Epilepticus is an evolving definition; this figure shows a timeline of previous definitions since 1969.

(2) focal SE with impaired awareness (T1 10 min; T2 >60 min), and (3) absence SE (T1 10–15 min; T2 unknown). The ILAE definitions of SE do not include neonates. Likewise, the American Clinical Neurophysiology Society has defined electrographic SE in critically ill children and adults as a continuous electrographic seizure lasting ≥10 min or electrographic seizures occurring for >20% of a 1-h epoch), but neonates were not included.[22]

Understanding when a seizure or seizures constitute SE in a neonate may be clinically important given increasing data that longer seizure duration and greater seizure burden are associated with lower responsiveness to antiseizure medications, higher mortality, longer length of hospital stay, and higher rates of abnormalities in the neurological examination at discharge.[1,7,9] Thus, seizure exposure may be a modifiable risk factor for unfavorable outcomes. A uniform definition of neonatal SE could help standardize future research protocols and guide acute management. Given the lack of consensus in the literature for the definition of neonatal SE, the ILAE Neonatal Task Force performed a scoping review of the definitions of neonatal SE and associations with neurodevelopmental outcome. This is a critical initial step in establishing an evidence-based definition of neonatal SE.

2 | METHODS

The ILAE Neonatal Task Force performed a scoping review focused on the definition of neonatal SE in a manner consistent with recent recommendations.[23–27] The Task Force opted for scoping review rather than systematic review due to the scarce evidence providing high certainty of evidence for the definition of status epilepticus.[28] Articles were selected using a systematic approach, and results were reported according to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) guidelines.[29]

The task force searched four online databases (PubMed, Cochrane, Lilacs, and Embase) over ten years for relevant peer-reviewed articles that met our eligibility criteria. There was an initial search (July 2012 to July 2022) and then an updated search (August 2022 to November 2023). Appendix A provides the search strategy. The key words that defined the search strategy were "infant, newborn," "infant, premature," "term birth," "neonate," "preterm," "SE," "convulsive SE," "non-convulsive SE," "refractory SE," "electrographic seizures," and "seizures." There were no language restrictions. The search results were merged, and duplicate articles were excluded.

Articles were screened for inclusion by two pediatric neurologists with neonatal neurology expertise (MLN, EGY) using independent review of titles and abstracts. Studies that did not assess SE or focused on non-neonatal cohorts were excluded. Abstracts, reviews, and editorials were excluded. Any disagreements about study characteristics or inclusion, including neonatal SE definitions, were resolved in consensus discussions with a third pediatric neurologist with neonatal neurology expertise (CJW). Figure 2 provides the PRISMA flow chart.

The full text of articles selected for inclusion was copied into an Excel (Microsoft 365) spreadsheet, and pairs of two members of the Task Force performed data extraction independently. Data were extracted using a standardized scoring form which included: (1) article characteristics (author identification, publication year, journal name, digital object identifier, title, objective, and study design);

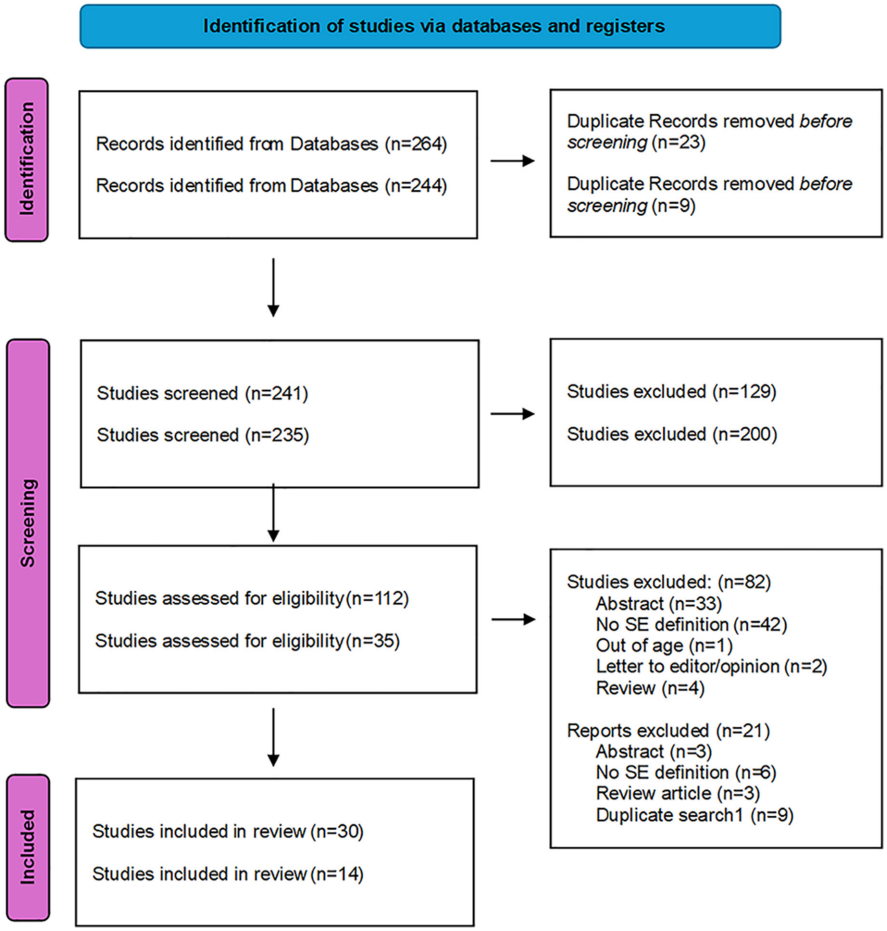

FIGURE 2 PRISMA Flowchart for the initial search (top) and update search (bottom).

(2) cohort characteristics (sample size, gestational age, seizure etiology); (3) definitions of SE and/or seizure burden; and (4) the method used to identify and classify SE, including routine EEG, continuous EEG monitoring (cEEG), amplitude-integrated EEG (aEEG), or clinical features.

3 | RESULTS

The scoping review yielded 44 articles containing a definition of neonatal SE.[1,16,30–71] Table 1 summarizes the article characteristics, cohort characteristics, SE and seizure burden definitions, and the methods used to identify and classify SE. Studies mainly included infants with hypoxic–ischemic encephalopathy (55%) or neonates considered at risk for seizures (e.g., extremely preterm or congenital heart defects). SE identification and classification most often relied on cEEG (with or without video) ($n = 21$, 48%), and less often used routine EEG (with or without video) ($n = 12$, 27%), aEEG alone ($n = 5$, 11%), or a combination of EEG/cEEG and aEEG ($n = 6$, 14%).

Most studies based the definition of SE on seizure duration (Table 1). Definitions included: (1) summed duration of seizures comprising ≥50% of any 1-h epoch,[32,33,38–40,42,45–47,66,69,70] (2) recurrent seizures for >50% of the total recording time,[1,33,44,47] or (3) either electrographic seizures lasting >30 min[50,56,65] and/or repeated electrographic seizures totaling >50% in any 1-h period.[16,52–54,59,62,63,67,68]

Among four studies that included clinical assessment of the neonate between recurrent seizures (specifically the return to baseline neurological condition),[16,37,43,62] the duration of the seizure required to constitute SE was shorter than in other studies. Schoaib and Jacobwitz defined SE as >5 min of continuous seizure or recurrence of seizure without recovery to baseline between seizures.[37,43] Pisani and Pavlidis defined SE as no return to the baseline neurologic condition between seizures after 30 minutes or recurrent seizures.[16,62] Studies also used several other approaches to define SE. Jacobwitz et al. defined SE as persistent seizures despite the use of two antiseizure medications.[31] Tarocco et al. defined super refractory SE as electroclinical seizures that continued for >24 h.[65] Two studies based the definition of SE on aEEG features.[50,68] Chen et al.[50] described that regular patterns of increased cortical activity with sawtooth pattern were suggestive of SE, and Mastrangelo et al.[68] defined SE as a continuous/prolonged increase of the lower and upper margin.

TABLE 1 Summary of the 44 articles included.

Author/year	Population (n) % term/preterm	Definition of SE	Definition of SB	Based on	Etiology
Eberhard et al. 2024	(1) 100/0	Recurrent focal seizures of 1.5 to 2.5 min duration independently over the left and right posterior regions, without clear clinical change, occupying up to 55% of the recording	-	cEEG	Infection—meningitis (group B Streptococcus)
Jacobwitz et al. 2023	(28) Term and preterm	Persistent seizures despite two appropriately dosed antiseizure medications	-	EEG + clinical	Variety
Pin et al. 2023	(1) 0/100	Electrographic seizure activity totaling more than 30 min in any 1-h period (i.e., 50% seizure burden)		cEEG	HIE
Castro Conde et al. 2023	(39) 0/100	-	TSB	cEEG + video	HIE + others
Glass et al. 2023	(46) Term or late preterm	Summed duration of seizures comprising ≥50% of any 1-h epoch of recording		cEEG	HIE
Alharbi et al. 2023	(98) Term or late preterm (>36 weeks)		TSB and MHSB	cEEG for 48 h	HIE and others
Shoaib et al. 2023	(28 neonates—14 with SE) Term and preterm	Five minutes or more of continuous seizure activity or recurrence of seizure activity without recovery to baseline between seizures	-	EEG	Variety
Moeller et al. 2023	(107) Term and preterm	Total seizure burden adding up to ≥30 min of any given hour	LSB = ≤2 seizures per hour or total burden adding up to <20 min of any given hour. MSB= >2 seizures/hour or total burden adding up to ≥20 min and <30 min of any given hour	EEG	HIE and others
Danzer et al. 2023	(75) 0/100	Electrographic seizure activity totaling more than 30 min in any 1-h period (i.e., 50% seizure burden)	-	cEEG	ECMO Congenital diaphragmatic hernia
Bättig et al. 2023	(108) 18/82	The summed duration of seizures comprised ≥50% 1-h epoch.	-	EEG or aEEG	HIE and others
Simmons et al. 2022	(132) 4/96	Continuous seizure activity or recurrent seizures for more than 50% of 1–3 h of recording time	-	cEEG	Congenital brain malformation
Chen et al. 2022	(71) 39.5/60.5	Continuous electrographic seizures lasting at least 30 min or repeated electrographic seizures totaling more than 30 min in any 1-h period	-	cEEG + video	HIE and others
Nyman et al. 2022	(85) Term or late preterm (>36 weeks)	Seizures covering >50% of the given 1-h epoch.	TSB and MHSB	aEEG	HIE

(Continues)

TABLE 1 (Continued)

Author/year	Population (n) % term/ preterm	Definition of SE	Definition of SB	Based on	Etiology
Jacobwitz et al. 2022	(69 /13 neonates) 0/100	(1) as >5 min of continuous and/or electrographic seizure activity or recurrent seizure activity without recovery between seizures, (2) brief seizures totaling >5 min in an hour, seizure(s) >5 min, or both	-	EEG or aEEG	HIE and others
Massey et al. 2022	(354) 0/100	Summed duration of seizures comprising ≥50% of any 1-h epoch	-	EEG	Congenital heart/pulmonary disorders
Herzberg et al. 2022	(112) 71.4/28.6	Any electrographic recording with seizures lasting >50% over at least 1 h of recording	LSB (<7 EEG seizures/hour) or HSB (>7)	cEEG + video	Vascular hemorrhage
Pavel et al. 2022	(154) 0/100	Seizure burden in a minimum of 30 min within 1 h	TSB	EEG	Variety
Pittet et al. 2022	(31) Late preterm and term	>30 min of electrographic seizure activity occurring during a 1-h epoch	TSB and MHSB	cEEG	Congenital heart disease
Chalak et al. 2021	(364) 0/100	Multiple seizures with overall cumulative duration greater than 30 min and/or status epilepticus	-	aEEG	HIE
Basti et al.2020	(32) 0/100	≥30 min continuously seizure	HSB (seizure present >15 min in total per 1-h period) LSB (<15 min/hour)	aEEG	HIE
Chen et al. 2020	(23) Late preterm >35 weeks	Regular patterns of increased cortical activity with sawtooth pattern	-	aEEG	HIE
Rennie et al. 2019	(240) 0/100	-	TSB and MHSB	cEEG	HIE
Lloyd et al. 2017	(120) 100/0	Continuous or accumulative electrographic seizures present in>50% of a 1-h period	TSB	cEEG	Variety
Lin et al.2017	(99) Not available	Continuous 30 min electrographic seizures or electrographic seizures >30 min/hour	-	cEEG	ECMO
Buraniqi et al.2016	(52) 100/0	>30 min of continuous intermittent seizures in 1-h epoch	-	cEEG	Vascular hemorrhage
Elshorbagy et al. 2016	(39) 0/100	>30 min	-	cEEG + video	HIE
Kharoshankaya et al.2016	(47) 0/100	-	TSB and MHSB	cEEG	HIE
Glass et al. 2016	(426) 22/88	Any electrographic seizure lasting >50% over at least 1-h recording	LSB (<7 seizures) HSB (isolated EEG seizure, >7)	cEEG + video	HIE
Low et al. 2016	(19) 0/100	-	Hourly SB and MHSB	cEEG	HIE

TABLE 1 (Continued)

Author/year	Population (n) % term/ preterm	Definition of SE	Definition of SB	Based on	Etiology
Pressler et al. 2015	(14) 0/100	-	TSB	cEEG	HIE
Naim et al. 2015	(161) Term and preterm	Any single seizure >30 min or if recurrent seizures together lasted for more than 30 min in any 1-h epoch (50% SB)	-	cEEG + video	Congenital cardiopathy
Srinivasakumar et al. 2015	(72) 0/100	-	Cumulative SB	Video EEG	HIE
Lynch et al. 2015	(23) 0/100	-	TSB and MHSB	cEEG + aEEG	HIE
Pavlidis et al. 2015	(n = 47) 40.5/59.5	Continuous seizure activity ≥30 min or recurrent seizures lasting a total of>30 min without definite return to the baseline neurologic condition of the newborn between seizures or (hourly seizure burden range: ≥50%–100%)	-	Video EEG	Variety
Low et al. 2014	(9) 0/100	Continuous or accumulative electrographic seizure activity lasting ≥50% of a 1-h period	-	EEG aEEG+ clinical observation	Vascular- stroke
Glass et al. 2014	(90) 0/100	Continuous electrographic seizure lasting at least 30 min, or recurrent electrographic seizures for at least 50% of 1–3 h of recording time	-	cEEG	HIE
Vesoulis et al. 2014	(95) 100/0	A single ictal episode with a duration greater than 30 min	Cumulative daily SB	aEEG	Vascular hemorrhage
Tarocco et al. 2014	(1) 100/0	Super refractory SE defined as electroclinical seizures continue more than 24 h	-	Video EEG	Genetic + Structural (migration disorder)
Shah et al. 2014	(85) 0/100	Seizure >30 min in any 1-h period	HSB (seizures >15 min in total/1-h period) LSB (<15)	EEG + aEEG	HIE
Mastrangelo et al. 2013	(28) 0/100	(a) continuous seizure activity for at least 30 min, or (b) recurrent seizures for >50% of the recording time ranging from 1 to 3 h or (c) a continuous electrographic seizure longer than 15 minand/or more than 1 electrographic seizure over a 10-min period on the EEG. aEEG = status epilepticus was depicted as continuous increase of the lower and upper margin	-	EEG+ aEEG	HIE and others

(Continues)

TABLE 1 (Continued)

Author/year	Population (n) % term/preterm	Definition of SE	Definition of SB	Based on	Etiology
Srinivasakumar et al. 2013	(69) 0/100	Continuous or cumulative electrographically documented seizure activity lasting for at least one-half of each 1-h period	SB = total duration of EEG seizures in seconds	Video EEG	HIE
Low et al. 2012	(107) 0/100	Continuous or cumulative electrographic seizure activity lasting ≥50% of each 1-h period	TSB	EEG	HIE
Pisani et al. 2007	(160/ 26 with SE) Preterm and term	Continuous seizure activity for ≥30 min or recurrent seizures lasting a total of >30 min without definite return to the baseline neurologic condition of the newborn between seizures	-	Video EEG	Variety
Scher et al. 2002	(1) 0/100	Eight electrographic/clinical events over a 40-min recording	-	Video EEG	Vascular – stroke

Abbreviations: aEEG, amplitude integrated EEG; cEEG, continuous EEG; ECMO, extracorporeal membrane oxygenation; HIE, hypoxic ischemic encephalopathy; HSB, high seizure burden; HSB, hourly seizure burden; LSB, low seizure burden; MHSB, maximum hourly seizure burden; MSB, moderate seizure burden; SE, status epilepticus; TSB, total seizure burden.

Seizure burden was reported in 20 studies. The most commonly used approach assessed total seizure burden, defined as total duration of EEG seizures in minutes (11 studies, 55%). Other approaches included maximum hourly seizure burden (8 studies),[36,38,42,47,51,56,57,61] cumulative seizure burden defined as the total duration of electrographic seizures in seconds (2 studies),[60,69] hourly seizure burden (1 study),[58] and daily seizure burden (1 study).[65] High/moderate and low seizure burden were categorized in five studies[1,38,44,49,66] which used varied definitions for the number of seizures classified as high/moderate or low (Table 1).

Table 2 summarizes 16 studies which assessed the relationship between seizure burden and a variety of outcomes, including brain injury and response to antiseizure medication.[1,34,36,38,42,46,49,51,52,56,57,60,64,66,69,70] The relationship between seizure burden and neurodevelopment outcomes at ages from 18 to 48 months was assessed in eight studies.[1,34,36,42,49,56,60,63] Except for one report,[64] these studies identified a significant association between higher seizure burden and unfavorable outcomes. Three studies assessed etiology, and a high seizure burden occurred with stroke, severe hypoxic–ischemic encephalopathy, intraventricular hemorrhage type III-IV, and structural lesions on neuroimage.[51,53,66] Five studies used seizure burden to assess the effectiveness of treatment (pharmacological and therapeutic hypothermia).[38,46,57,68,70]

4 | DISCUSSION

A previous ILAE report on SE definitions and classification noted that in the neonatal period (0 to 30 days for term babies), SE may be difficult to recognize, but it did not explore further aspects among neonates.[21] Thus, to expand work addressing common terminology and classification approaches for SE, this scoping review aimed to assess and categorize the definitions of neonatal SE available in the literature as an initial step in establishing an evidence-based definition of neonatal SE. The review indicated that: (1) studies have used variable definitions of SE; (2) most SE definitions rely on assessment using EEG (most often cEEG but sometimes aEEG); and (3) most studies define SE in relation to 30 min, including continuous seizure activity lasting 30 min or brief seizures totaling 30 min within a 1-h epoch (50% seizure burden).[32,33,38–40,42,44–48,67,70,71] The validity of criteria focused on return to a normal neurological state is questionable in critically ill neonates who may be sedated and/or paralyzed and who are often encephalopathic or comatose given the underlying acute brain injury etiology causing the SE.

TABLE 2 Relationship of seizure burden and different outcomes ($n = 16$ studies).

Study	Outcome measured
Castro-Conde et al. 2023	Abnormal neurodevelopment was significantly associated with total SB >25 min (odds ratio 95% 1.72–142.86, $p = 0.026$)
Alharbi et al. 2023	Higher SB during neonatal encephalopathy was independently associated with worse cognitive and language scores at 18 months
Moeller et al. 2023	The standardized, SB-based protocol for the treatment of neonatal seizures improved short-term patient outcomes. The use of a continuous midazolam infusion was reduced by 53.7%, duration of EEG monitoring decreased, the proportion of infants discharged without antiseizure medications increased by 68%
Nyman et al. 2022	Although neonatal SB was associated with post neonatal epilepsy at group level, at individual level aEEG background is more accurate for prediction of epilepsy
Pavel et al. 2022	Significantly lower SB burden and fewer seizures were noted in the infants treated with antiseizure medication within 1 h of seizure onset ($p = 0.029$ and 0.035, respectively)
Basti et al. 2020	A high SB correlates with a persistent abnormal aEEG trace, tissue injury on MRI and abnormal developmental outcome at age 18–24 months
Rennie et al. 2019	Neonates with stroke and severe HIE tended to have the largest SB
Lloyd et al. 2017	An association among higher SB and severe IVH (grade III-IV) in preterm infants was suggested
Low et al. 2016	Phenobarbitone immediately reduced SB but the effect was not significant within 4 h of treatment. Doses of phenobarbitone at 20 mg/kg, rather than 10 mg/kg, were significantly more effective in reducing SB
Kharoshankaya et al. 2016	In HIE, a high electrographic SB is significantly associated with abnormal outcome (at 24–48 months), independent of HIE severity or treatment with hypothermia. The odds of an abnormal outcome increased over ninefold if a neonate had a total seizure burden of more than 40 min ($p = 0.001$), and eightfold if a neonate had a MHSB >13 min per hour ($p = 0.003$)
Glass et al. 2016	High SB was associated to need of ≥2 antiseizure medications, death or abnormal examination at discharge. Greater seizure burden was associated with increased morbidity and mortality
Srinivasakumar et al. 2015	EEG monitoring and treatment of electrographic seizures results in significant reduction in SB. SB is associated with more severe brain injury and significantly lower performance scores across all neurodevelopment domains on Bayley III
Vesoulis et al. 2014	No association was found between high SB on either day 1, 2 or 3 and children's subsequent motor, cognitive and language scores at age 2 years
Shah et al. 2014	In multivariate logistic regression, high SB was independently associated with greater injury on MRI (OR 5.00, 95% CI 1.47 to 17.05 $p = 0.01$)
Srinivasakumar et al. 2013	Therapeutic hypothermia was associated with reduced electrographic SB in mild neonatal HIE and in the ones with mild and moderate MRI injuries.
Low et al. 2012	A decreased SB burden was seen in neonates with moderate HIE who received cooling.

Abbreviations: aEEG, amplitude integrated EEG; CI, confidence interval; HIE, hypoxic ischemic encephalopathy; IVH, intraventricular hemorrhage; MHSB, maximum hourly seizure burden; MRI, magnetic resonance image; SB, seizure burden.

The generalizability and validity of any of the neonatal SE definitions are unknown. Further, there is little evidence that the definitions used in the studies, including the 30-min cutoff to define SE, provide an evidence-based approach to defining an abnormally prolonged seizure (T1 in the ILAE definition for adults), identifying a seizure duration which might reduce responsiveness to antiseizure medications, or identifying a seizure duration associated with secondary brain injury and worse outcomes (T2 in the ILAE definition for adults).[21] Although higher seizure burden has been associated with unfavorable outcomes,[1,33,36,42,49,56,60,63] the definition of "high" seizure burden has not been uniform. Several studies have been published after the inclusion search for this article. In a study of 39 neonates with moderate–severe hypoxic–ischemic encephalopathy enrolled in a clinical trial undergoing cEEG undergoing cEEG, maximal pretreatment seizure burden predicted successful response to seizure treatment better than other seizure burden measures.[72] In a study if 70 neonates with hypoxic–ischemic encephalopathy, seizures were not associated with death or neurodevelopmental impairment after adjustment for clinical and imaging variables, including for severe seizures.[73]

Experimental studies provide insight on the importance of defining the seizure duration which could impact neurodevelopmental outcomes.[74–76] Data suggest that the immature brain is more resistant to structural damage as a result of seizures.[75] Furthermore, etiology may impact the relationship between seizure burden and brain injury;

a rat model of ischemic stroke indicated that the harmful effect of kainic acid on brain injury was not related to duration of SE.[76] These findings suggest that the context related to prior insults and underlying etiology may influence the seizure burden which in turn contributes to secondary brain injury.

In conclusion, this scoping review demonstrated substantial variation in neonatal SE definitions across the literature, in the methods used for recognition of SE (EEG, cEEG with and without video, aEEG), and in the population studied. The most common definitions were based around 30-min duration criteria. However, evidence was insufficient that seizures exceeding 30 min were more likely to be pharmacoresistant or associated with worse outcomes. Given the variability in neonatal SE definitions identified in this scoping review, there is an urgent need to develop a standardized and evidence-based classification approach for neonatal seizure burden and a definition of neonatal SE that could be applied rigorously in research studies and extended to clinical practice. Similar to adults and non-neonatal children,[22] a uniform approach and definitions will enable comparison of data across studies and translation of data from studies into clinical practice. This approach may help establish T1 and T2 timepoints aligned with the ILAE approach for non-neonates. As a next step, the ILAE Neonatal Task Force intends to develop a standardized approach to assessing and describing neonatal seizure burden and defining neonatal SE using an inter-disciplinary team of selected experts providing consensus-recommendations through a structured and rigorous Delphi process.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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ANNEX A

SEARCH STRATEGY

Aim: review definitions of status epilepticus in neonates.

Time frame: 10 years.

Key words and search terms

Infant, Newborn", "Infant, Premature", Term Birth"
Neonate # Preterm
status epilepticus
convulsive status epilepticus
non convulsive status epilepticus
refractory status epilepticus
electrographic seizures

EMBASE

("Absence Status" OR "Complex Partial Status Epilepticus" OR "Electrographic Status Epilepticus" OR "Generalized Convulsive Status Epilepticus" OR "Generalized Status Epilepticus" OR "Grand Mal Status Epilepticus" OR "Non Convulsive Status Epilepticus" OR "Non-Convulsive Status Epilepticus" OR "Petit Mal Status" OR "Simple Partial Status Epilepticus" OR "Status Epilepticus, Complex Partial" OR "Status Epilepticus, Electrographic" OR "Status Epilepticus, Generalized" OR "Status Epilepticus, Generalized Convulsive" OR "Status Epilepticus, Grand Mal" OR "Status Epilepticus, Non Convulsive" OR "Status Epilepticus, Non-Convulsive" OR "Status Epilepticus, Simple Partial" OR "Status Epilepticus, Subclinical" OR "Status, Absence" OR "Status, Petit Mal" OR "Subclinical Status Epilepticus" OR "electrographic seizures" OR "refractory status epilepticus") AND **("Infant, Newborn"** OR "Infants, Newborn" OR "Neonate" OR "Neonates" OR "Newborn" OR "Newborn Infant" OR "Newborn Infants" OR "Newborns" OR "Infant, Preamture" OR "Infant, Preterm" OR "Infants, Premature" OR "Infants, Preterm" OR "Neonatal Prematurity" OR "Premature Infant" OR "Premature Infants" OR "Prematurity, Neonatal" OR "Preterm Infant" OR "Preterm Infants" OR "**Term Birth**" OR "Birth of Full Term Infant" OR "Birth of Full Term Newborn" OR "Birth of Full-Term Infant" OR "Birth of Full-Term Newborn" OR "Birth, Fullterm" OR "Birth, Term" OR "Births, Fullterm" OR "Full-Term Infant Births" OR "Fullterm Birth" OR "Fullterm Births" OR "Term Births" OR Preterm)

PUBMED

("Absence Status" OR "Complex Partial Status Epilepticus" OR "Electrographic Status Epilepticus" OR "Generalized Convulsive Status Epilepticus" OR "Generalized Status Epilepticus" OR "Grand Mal Status Epilepticus" OR "Non Convulsive Status Epilepticus" OR "Non-Convulsive Status Epilepticus" OR "Petit Mal Status" OR "Simple Partial Status Epilepticus" OR "Status Epilepticus, Complex Partial" OR "Status Epilepticus, Electrographic" OR "Status Epilepticus, Generalized" OR "Status Epilepticus, Generalized Convulsive" OR "Status Epilepticus, Grand Mal" OR "Status Epilepticus, Non Convulsive" OR "Status Epilepticus, Non-Convulsive" OR "Status Epilepticus, Simple Partial" OR "Status Epilepticus, Subclinical" OR

"Status, Absence" OR "Status, Petit Mal" OR "Subclinical Status Epilepticus" OR "electrographic seizures" OR "refractory status epilepticus") AND **("Infant, Newborn"** OR "Infants, Newborn" OR "Neonate" OR "Neonates" OR "Newborn" OR "Newborn Infant" OR "Newborn Infants" OR "Newborns" OR **"Infant, Premature"** OR "Infant, Preterm" OR "Infants, Premature" OR "Infants, Preterm" OR "Neonatal Prematurity" OR "Premature Infant" OR "Premature Infants" OR "Prematurity, Neonatal" OR "Preterm Infant" OR "Preterm Infants" OR "**Term Birth**" OR "Birth of Full Term Infant" OR "Birth of Full Term Newborn" OR "Birth of Full-Term Infant" OR "Birth of Full-Term Newborn" OR "Birth, Fullterm" OR "Birth, Term" OR "Births, Fullterm" OR "Full-Term Infant Births" OR "Fullterm Birth" OR "Fullterm Births" OR "Term Births" OR Preterm)

LILACS

("Absence Status" OR "Complex Partial Status Epilepticus" OR "Electrographic Status Epilepticus" OR "Generalized Convulsive Status Epilepticus" OR "Generalized Status Epilepticus" OR "Grand Mal Status Epilepticus" OR "Non Convulsive Status Epilepticus" OR "Non-Convulsive Status Epilepticus" OR "Petit Mal Status" OR "Simple Partial Status Epilepticus" OR "Status Epilepticus, Complex Partial" OR "Status Epilepticus, Electrographic" OR "Status Epilepticus, Generalized" OR "Status Epilepticus, Generalized Convulsive" OR "Status Epilepticus, Grand Mal" OR "Status Epilepticus, Non Convulsive" OR "Status Epilepticus, Non-Convulsive" OR "Status Epilepticus, Simple Partial" OR "Status Epilepticus, Subclinical" OR "Status, Absence" OR "Status, Petit Mal" OR "Subclinical Status Epilepticus" OR "electrographic seizures" OR "refractory status epilepticus") AND ("Infant, Newborn" OR "Infants, Newborn" OR "Neonate" OR "Neonates" OR "Newborn" OR "Newborn Infant" OR "Newborn Infants" OR "Newborns" OR "Infant, Premature" OR "Infant, Preterm" OR "Infants, Premature" OR "Infants, Preterm" OR "Neonatal Prematurity" OR "Premature Infant" OR "Premature Infants" OR "Prematurity, Neonatal" OR "Preterm Infant" OR "Preterm Infants" OR "Term Birth" OR "Birth of Full Term Infant" OR "Birth of Full Term Newborn" OR "Birth of Full-Term Infant" OR "Birth of Full-Term Newborn" OR "Birth, Fullterm" OR "Birth, Term" OR "Births, Fullterm" OR "Full-Term Infant Births" OR "Fullterm Birth" OR "Fullterm Births" OR "Term Births" OR Preterm)

COCHRANE

("Absence Status" OR "Complex Partial Status Epilepticus" OR "Electrographic Status Epilepticus" OR "Generalized Convulsive Status Epilepticus" OR "Generalized Status Epilepticus" OR "Grand Mal Status Epilepticus" OR "Non Convulsive Status Epilepticus" OR "Non-Convulsive Status Epilepticus" OR "Petit Mal Status" OR "Simple Partial Status Epilepticus" OR "Status Epilepticus, Complex Partial" OR "Status Epilepticus, Electrographic" OR "Status Epilepticus, Generalized" OR "Status Epilepticus, Generalized Convulsive" OR "Status Epilepticus, Grand Mal" OR "Status Epilepticus, Non Convulsive" OR "Status Epilepticus, Non-Convulsive" OR "Status Epilepticus, Simple Partial" OR "Status Epilepticus, Subclinical" OR "Status, Absence" OR "Status, Petit Mal" OR "Subclinical Status Epilepticus" OR "electrographic seizures" OR "refractory status epilepticus") AND ("Infant, Newborn" OR "Infants, Newborn" OR "Neonate" OR "Neonates" OR "Newborn" OR "Newborn Infant" OR "Newborn Infants" OR "Newborns" OR "Infant, Premature" OR "Infant, Preterm" OR "Infants, Premature" OR "Infants, Preterm" OR "Neonatal Prematurity" OR "Premature Infant" OR "Premature Infants" OR "Prematurity, Neonatal" OR "Preterm Infant" OR "Preterm Infants" OR "Term Birth" OR "Birth of Full Term Infant" OR "Birth of Full Term Newborn" OR "Birth of Full-Term Infant" OR "Birth of Full-Term Newborn" OR "Birth, Fullterm" OR "Birth, Term" OR "Births, Fullterm" OR "Full-Term Infant Births" OR "Fullterm Birth" OR "Fullterm Births" OR "Term Births" OR Preterm)