

Video Analyses of Sudden Unexplained Deaths in Toddlers

Laura Gould, MSc, Codi-Ann Reid, AB, Alcibiades J. Rodriguez, MD, and Orrin Devinsky, MD, for SUDC Video Working Group

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Correspondence

Ms. Gould
laura.gould@nyulangone.org

Abstract

Background and Objectives

More than 2,900 US children aged younger than 4 years die from unknown causes each year, accounting for more than 219,000 life years lost annually. They are mostly sleep-related and unwitnessed with unremarkable autopsies, limiting our understanding of death mechanisms. We sought to understand potential mechanisms of death by evaluating videos of sudden deaths in toddlers.

Methods

In our registry of 301 sudden unexplained child deaths, a series of 7 consecutively enrolled cases with home video recordings of the child's last sleep period were independently assessed by 8 physicians for video quality, movement, and sound.

Results

Four boys and 3 girls (13–27 months at death) with terminal videos shared similar demographic features to the 293 other registry cases without video recordings. Five video recordings were continuous and 2 were triggered by sound or motion. Two lacked audio. All continuous recordings included a terminal convulsive event lasting 8–50 seconds; 4 children survived for >2.5 minutes postconvulsion. Among discontinuous videos, time lapses limited review; 1 suggested a convulsive event. Six were prone with face down, and 1 had autopsy evidence of airway obstruction. Primary cardiac arrhythmias were not supported; all 7 children had normal cardiac pathology and whole-exome sequencing identified no known cardiac disease variants.

Discussion

Audio-visual recordings in 7 toddlers with unexplained sudden deaths strongly implicate that deaths were related to convulsive seizures, suggesting that many unexplained sleep-related deaths may result from seizures.

Introduction

Research on sudden deaths in infants and young children is limited because almost all are sleep-related and unwitnessed. For infant deaths, some risk factors were identified and public health campaigns undertaken. However, the incidence of unexpected infant and toddler deaths in the United States is unchanged for 2 decades.^{1–3}

In 2021, more than 2,900 children younger than 4 years died suddenly from unknown causes representing more than 219,000 life years lost; 92% were infants and 8% were 1–4 years.¹ These deaths were more common in the winter and among boys, non-Hispanic Blacks and American

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From the NYU Grossman School of Medicine (L.G., C.-A.R., A.J.R., O.D.), and NYU Comprehensive Epilepsy Center (L.G., C.-A.R., A.J.R., O.D.), New York.

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SUDC Video Review Group Members are listed in Appendix 2 at the end of the article.

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Glossary

SUDC = sudden unexplained death in childhood; **SUDCRRC** = SUDC Registry and Research Collaborative; **SUDEP** = sudden unexpected death in epilepsy.

Indians, and usually occurred in sleep in the prone position.³⁻⁵ Sudden infant death risk factors include prematurity, low birth weight, prenatal and postnatal smoke exposure, maternal alcohol and illicit drug use, and unsafe sleep environments. Breast feeding and pacifier use may reduce risk.^{3,6,7}

Research on sudden unexplained deaths in childhood (SUDCs), aged 1–18 years, is limited with less than 1% of research publications compared with sudden infant deaths. Most involve 1- to 4-year olds; the fifth leading category of death in this age group.¹ Two recent studies found that less than 20% of childhood cases had cardiac, neurologic, metabolic, genetic, and/or immunologic causes identified through a multidisciplinary review.^{8,9} A febrile seizure history was present in 30% of these children; a ~10-fold increase to the age-adjusted population.^{4,5,8,10} Hippocampal anomalies on neuropathology, supportive of potential epilepsy-related causes of deaths, have been identified in sudden explained child deaths.¹¹⁻¹⁵

Sudden unexpected death in epilepsy (SUDEP) risk factors and possible mechanisms of death align with sudden deaths in children.^{16,17} Among SUDEP cases recorded on video-EEG, almost all follow a generalized tonic-clonic seizure, with an early postictal, centrally mediated depression or cessation of respiration followed by cardiac arrest.¹⁸ Monogenic variants responsible for sudden unexplained death in childhood include calcium-mediated, sodium-mediated, and potassium-mediated channels in ~9% of cases; most were de novo variations in calcium channel genes expressed primarily in the heart.¹⁹ Pathogenic voltage-gated sodium channels can also contribute to cardiac (e.g., *SCN5A*) or neurologic (e.g., *SCN1A*) causes of death.²⁰ In SUDEP, diverse epilepsy-related genes have been identified, but it remains unresolved if they are markers of severe epilepsy or a tendency for convulsive seizures, or have a more specific role in SUDEP pathogenesis.²¹

Other genes implicated in epilepsy and SUDEP include *KCNA1*, which encodes the voltage-gated potassium channel Kv1.1; *HCN1* and *HCN2*, which encode hyperpolarization-activated cyclic nucleotide-gated cation channels; and *PRRT2*, which encodes a proline-rich transmembrane protein identified in an early-onset seizure disorder. Genes implicated in cardiac arrhythmias and SUDEP include long QT syndrome genes, such as *KCNQ1* and *KCNH2*, which encode potassium channels, and *RYR2*, which encodes a ryanodine receptor for intracellular calcium release.²⁰

Since SUDC is rarely witnessed and postmortem examinations are unrevealing, death mechanisms and causes of death

remain unknown. We analyzed terminal videos in a consecutive series of sleep-related child deaths from the SUDC Registry and Research Collaborative (SUDCRRC) to document observations and explore mechanism(s) of death.

Methods

Standard Protocol Approvals, Registrations, and Patient Consents

The New York University Sudden Unexplained Death in Childhood Registry and Research Collaborative (Registry), created in 2014, is approved by the New York University Langone Health Institutional Review Board and includes parental written consent (I14-01061) of those enrolled, as well as consent for publication of the data presented in this video series.⁴

The Registry's inclusion criteria include children aged 1 month through 18 years who died suddenly and unexpectedly where the final cause of death is unexplained or unclear after an autopsy report review.⁸ Cases were referred by medicolegal death investigation professionals, parents, or clinicians in the United States, United Kingdom, Canada, Germany, and Australia. Referrals are made through the study website (sudcrcc.org) or direct contact with Registry team members. The Registry enrolled 301 SUDC cases with complete data collection (i.e., birth and pediatrician records, medical examiner or forensic pathology biospecimens and reports [death scene and police investigations, autopsy, and toxicology], and parental/caregiver interviews by L.G.). The blinded multidisciplinary Registry review process occurred in parallel with child-parents trio whole-exome sequencing. The Registry's research has identified risk factors, genes and modes of inheritance, transcriptomic profiles and proteomic changes compared with explained pediatric deaths, and epidemiologic data that SUDC incidence is underestimated by the US death investigation system.^{4,8,12,14,15,19,20,22-26}

Cases

We reviewed the first 8 consecutively enrolled cases in the Registry with crib camera video recordings of the child's last sleep period. These 8 cases were similar to the other 293 Registry cases regarding demographics, clinical histories, and postmortem findings.

Materials

Videos from home security or commercial crib cameras recorded the child's death. Recordings were continuous or triggered by sound or motion with multiple timestamped videos.

Table 1 Characteristics of 301 Sudden Unexpected Pediatric Deaths Enrolled in SUDCRRC by Age

	≤60 mo (n = 248)	>60 mo (n = 53)
Age at death, mo, median (IQR)	20.4 (16.3–26.9)	151.6 (111–185.9)
% Male, n (%)	149 (60.1)	29 (54.7)
Born <37 wk gestation, n (%)	31/246 (12.6)	5/46 (10.9)
Attained milestones in normal range, n (%)	216 (87.1)	47 (88.7)
Febrile seizure, n (%)***	71 (29.4)	4 (7.5)
Afebrile seizure, n (%)	4 (1.6)	2 (3.8)
Cardiac arrhythmia, n (%)	3 (1.2)	2 (3.8)
Syncope, n (%)	1 (0.4)	1 (1.9)
First-degree family history febrile seizures, n (%)***	51 (20.6)	1 (1.9)
Circumstances of death, n (%)		
Cold symptoms and/or fever in past 48 h***	116 (46.8)	3 (5.7)
Death unwitnessed***	234 (94.4)	41 (77.4)
Sleep-related***	232 (93.5)	33 (62.3)
If sleep-related and unwitnessed (n = 264), n (%)		
Bedsharing*	11 (4.8)	6 (18.2)
Body found prone***	194 (83.1)	16 (48.5)
Face found prone**	125 (54.1)	9 (27.3)

Abbreviations: IQR = interquartile range; SUDCRRC = Sudden Unexplained Death in Childhood Registry and Research Collaborative. Significant by age: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; n is listed as fraction for any data with missing values.

Procedures

Parents transferred videos electronically, which were assessed for quality. Four with poor quality were enhanced by a forensic photographer to improve contrast for clarity and resized images to preserve details of child location. Where possible, videos were edited to include 5 minutes before abnormal motion or sound began and 5 minutes after the child's last sign of life.

Videos were reviewed independently by 6 forensic pathologists, a pediatric epileptologist, and a sleep medicine/epileptologist physician. Videos were assessed for image quality, audio content, motion, and child positioning for each 30-second segment for categorical choices and narrative descriptions of movement and sound. Assessments, using eTable 1 (links.lww.com/WNL/D313), were based on visual and audio data without other physiologic monitoring available.

All video cases completed a comprehensive multidisciplinary review per SUDCRRC's methodology⁸ and cause of death certification followed national guidelines.²⁷ Deaths considered unexplained detailed potential intrinsic and extrinsic (environmental) factors that may increase risk of death but do not explain the death.²⁷

Statistical Analysis

Our primary analysis included video analyses for movement and sound classified as normal, abnormal, or unsure/none with narrative descriptions. Majority consensus across 6 forensic pathology reviewers was combined into 1 rater opinion and agreement measured using Kappa statistic. We then assessed percentage agreement across 3 raters: 1 combined forensic pathology opinion, 1 pediatric epileptologist (O.D.), and 1 epileptologist/sleep medicine physician (A.R.).

We compared demographic and clinical histories for all Registry cases (n = 301) divided by age (\leq or >60 months) with 2-tailed *t* tests for continuous variables with 95% CIs and the χ^2 test with Yates correction for categorical variables in a 2 × 2 contingency table ($\alpha < 0.05$ significant). All statistical analyses performed with IBM SPSS version 28.0 by L.G.

Data Availability

Consent forms will be released by contacting corresponding author. Qualified researchers may request access to individual deidentified imaging data with parental consent through request to author, approval of SUDCRRC Principal Investigator, and data sharing agreement with NYU Langone Health.

Table 2 Child Characteristics and Video Analyses (N = 7)

Child characteristics and significant death investigation findings								Video analysis						
No.	Age (mo)/ Sex	Medical history	Personal history seizures	Family history seizures	Terminal history past 72 h	Face position found	Whole-exome sequence results ^a	SUDCRRC final cause of death	Video type	Video quality ^b	Movement	Sound	Overall video assessment	
1	23/male	Chronic otitis media, s/p bilateral myringotomy tubes	No	No	Cold symptoms × 5 wk	Side	None	Unexplained sudden death with possible infection, terminal seizure with tongue contusion; found prone with airway obstruction by the foreign material (food)	Continuous	Low	Abnormal	Abnormal	Convulsive seizure with agonal type breathing preconvulsive and postconvulsive event	
2	17/female	Egg allergy	No	No	Cough and fever × 48 h	Prone	None	Asphyxia due to obstruction of airway by enlarged pharyngeal tonsil in the setting of viral and bacterial infections including COVID-19, influenza A, and <i>Haemophilus influenzae</i>	Continuous	Medium	Abnormal	Abnormal	Convulsive seizure with unusual side-to-side trunk movements and abnormal vocalizations followed by the absence of motion or sound	
3	17/male	Fraternal twin, 4 fraternal seizures (onset 12 mo)	Yes, febrile seizures	Yes, febrile seizure and epilepsy	Family member with flu	Prone	None	Unexplained sudden death with flu A positive, witnessed seizure before death, personal history of febrile seizures, family history of febrile seizures and epilepsy, hamartia of left amygdala; found prone faced down	Continuous	Medium	Abnormal	Abnormal	Convulsive seizure with face prone into adjacent pillow with subsequent labored breathing that decreases in frequency and effort over time	
4	27/female	None	No	No	None	Prone	None	Unexplained sudden death with terminal convulsive event; found prone faced down	Continuous	Low	Abnormal	n/a	Convulsive seizure primarily of trunk and legs	
5	13/female	None	No	No	Diaper rash, teething	Prone	None	Unexplained sudden death with <i>Haemophilus influenzae</i> type f sepsis, unilateral acute otitis media; and found prone faced down	Motion-triggered	High	Indeterminant		Unremarkable movement and sound overall	
6	25/male	None	No	No	Cough × 24 h	Prone	None	Unexplained sudden death with fever, cough (URI symptoms), tracheobronchitis and bronchiolitis, possible recent COVID-19; and found prone, face down	Motion-triggered	High	Abnormal	Abnormal	Appears congested with face movement into pillow. Unclear if voluntary or arousal due to parasomnia. Then, abnormal vocalization before lack of movement; suggests convulsive event	
7	15/male	Born 35 wk gestation 5 lbs–6 oz, fraternal twin, otitis media 2 wk prior	No	No	None	Prone	None	Unexplained sudden death with probable febrile seizure, respiratory syncytial viral infection, parainfluenza viral infection, Coxsackie B1 viral infection, preterm birth, low birth weight; and found face down following possible seizure	Continuous	Medium	Abnormal	n/a	Likely seizure with rhythmic truncal movements appearing to be a hypermotor seizure	

Abbreviations: COVID-19 = coronavirus disease 2019; s/p = status post; SUDCRRC = Sudden Unexplained Death in Childhood Registry and Research Collaborative; URI = upper respiratory infection.

^a Whole-exome sequencing results: none = no likely pathogenic or pathogenic variants identified.

^b Video quality: low, medium, high.

Results

Analysis of 301 Sudden Unexplained Pediatric Deaths by Age

Table 1 summarizes 301 consecutive Registry cases with a complete medical record review and family interview, stratifying children younger than or older than 60 months at death. These age groups did not differ by sex, race, ethnicity, prematurity, low birth weight, meeting developmental milestones, personal or first-degree family history of afebrile seizures, arrhythmias, syncope, or sudden death.

Compared with older children, those who died younger than 60 months ($n = 248$) were more likely to have a history of febrile seizures ($p \leq 0.001$), first-degree family history of febrile seizures ($p < 0.001$), upper respiratory infection or fever in past 48 hours of life ($p < 0.001$), unwitnessed ($p < 0.001$), sleep-related ($p < 0.001$), body prone ($p < 0.001$), face down ($p < 0.003$), and less likely to bedshare ($p < 0.011$).

Case Reviews of 7 Sudden Pediatric Deaths With Terminal Videos

Of the 301 Registry cases, 8 (2.7%) had terminal videos. One video was recorded at a daycare center during a group nap period; visibility of the child was poor and was excluded. The 7 remaining videos included 4 boys and 3 girls aged 13–27 months (Table 2). Cases 1 through 5 were in a crib, case 6 was in a converted crib (side rail removed), and case 7 was in a portable crib.

Three cases had no significant medical history. Four had common pediatric conditions: preterm birth with recent otitis media, chronic otitis media and bilateral myringotomies, egg allergy, and febrile seizures. The child with febrile seizures had first-degree relatives with febrile and afebrile seizures. All children had normal developmental milestones including independent ambulation.

Cases with videos were similar to cases younger than 60 months in the full Registry cohort. All deaths were sleep-related; most during nocturnal sleep (6/7) and 1 during daytime nap. Four had disorders during the past 72 hours of life: cold symptoms, cough and fever, cough, diaper rash, and teething; 3 did not. All children were discovered prone with face down into bedding, except for one's face to the side significant for airway obstruction at autopsy. Whole-exome sequencing failed to identify likely or definite pathogenic, inherited or de novo, variations in any case. Six cases had postmortem evidence of infection with mild pathology not considered significant for primary cause of death.

Formal neuropathologic examination of the brain was performed on 6 of 7 cases, 3 of which had hippocampal dentate

gyrus changes previously reported in SUDC (cases 1, 2, and 4). None of these cases had a reported history of febrile seizures, whereas 1 case with a reported history of febrile seizure had hippocampi that were microscopically within normal limits.

The Registry's multidisciplinary case review process concluded 6 of 7 cases as "Unexplained Sudden Deaths" with associated factors as recommended by the National Association of Medical Examiners Panel on Unexpected Deaths Pediatrics and detailed in Table 2.²⁷ Case 2 was considered asphyxia due to airway obstruction by enlarged pharyngeal tonsils due to viral and bacterial infections.

Video Analyses of 7 Sudden Pediatric Deaths

The video devices continuously recorded in 5 cases and were motion triggered in 2. Video quality was high in 2, moderate in 3, and low in 2. Two lacked audio.

The 6 forensic pathologists displayed moderate agreement in evaluating convulsive activity across the 7 videos ($K = 0.641$, 95% CI 0.473–0.808, $p < 0.001$). The final 3 raters (combined forensic pathologists, pediatric epileptologist, and epileptologist/sleep medicine physician) had 100% agreement across 4 cases (1–4), 67% agreement for 1 (case 7), and 33% agreement for 2 (cases 5 and 6) for the presence of convulsive event.

Abnormal movements were identified in 6 videos. In all 5 continuously recorded videos, a convulsive event was identified shortly before death. All convulsive events were 8–50 seconds. The 2 motion-triggered videos had time gaps: one had indeterminant movement and the other had abnormal movements suggesting a convulsive event.

Abnormal sounds were identified in 4 of 5 audio-recorded events; all were respiratory sounds or vocalizations. Agonal, labored, or deep breathing was identified in 5 cases by audio or visual analysis. Of the 5 continuous videos, all had convulsions and 4 were alive postconvulsion for at least 2.5 minutes. Two of these 4 had abnormal postictal respirations. One case deemed because of asphyxia was indeterminant for signs of life post convulsion due to limited video duration (case 2). Case 1 had a convulsive event with emesis and suspected postictal aspiration.

Semiology of Convulsive Events

Case 1 was a 13-minute continuous video recorded at the onset of daytime nap period. The child was prone with face to right and brief agonal breathing after an ~8-second convulsive seizure. Subsequent agonal type breathing lasted ~5 minutes.

Case 2 was a 90-second continuous video. The child was prone with face down and had a ~30-second convulsive seizure with side-to-side truncal movements and abnormal "whimpering" vocalization followed by cessation of motion or sound.

Case 3 was a 30-minute continuous video. The child was prone with face to side initially. A ~40-second convulsive seizure caused the face to turn more prone into the pillow near the child's face. Labored breathing followed, decreasing in frequency and depth over 25 minutes until there was no movement or sound.

Case 4 was a 20-minute continuously recorded video without audio. The child was prone with initial face position indeterminate. A ~50-second convulsive seizure primarily involved trunk and lower extremities followed by rhythmic lower extremity clonic activity alone before ~5-minute postconvulsion. The child's face was prone when found.

Case 5 included ~11-second video segments triggered by a sound or movement, presumably the child's. Across 6 segments over 105 minutes of the final sleep period, the child was in prone with face prone or to the side. No abnormal movement or sound were identified.

Case 6 included ~10-second video segments triggered by sound or movement, presumably the child's. Across 4 segments over a 100-minute sleep period, the child appeared congested with face movement into his pillow. It was unclear if the movement was voluntary. The second segment recorded 1 deep inspiration. The third segment recorded an abnormal vocalization (sneeze-like sound), while the child extended his trunk rapidly from the child's prone position to sitting, then returned quickly to prone face down into pillow position. Clinicians considered this suggestive of a seizure, possibly hypermotor or convulsive, but determination was limited by discontinuous recording.

Case 7 was a 15-minute continuously recorded video. The child was prone with face prone initially followed by a ~25-second paroxysmal motor event primarily involving the trunk, appearing to be a hypermotor seizure. This followed with rhythmic hip motions and simultaneous irregular deep and shallow breathing motions until no further movement or sound ~5-minute postictal.

The supplement includes eFigure 1 (links.lww.com/WNL/D313), which visualizes the temporal relationship of abnormal movement and sound.

Discussion

Audio-visual recordings in 7 toddlers with unexplained sudden deaths strongly implicated convulsive seizures. Primary cardiac arrhythmias were not supported; all 7 children had normal cardiac pathology and whole-exome sequencing failed to identify any pathogenic cardiac variations. All 5 cases with continuous recordings revealed convulsions before death. Two cases with noncontinuous motion-triggered recordings were less definitive: one suggested a

convulsion and the other had indeterminate movement. Convulsive seizures may be related to most sudden unexplained deaths in young children. Of 6 cases with suggestive or definite convulsive movements before death, only 1 had a febrile seizure history. Beyond unexplained toddler deaths, seizures may be related to unwitnessed, sleep-related, autopsy-negative deaths in individuals with and without a history of seizures across all ages. Febrile seizures are approximately 10-fold more frequent in sudden unexplained toddler death cohorts than controls.^{4,5,10,24} Among our 248 Registry cases who died before 60 months, 29.4% had febrile seizures, consistent with previous studies implicating febrile seizures in some of these deaths.^{20,24} Seizures may also contribute to toddler deaths explained by other factors. Febrile seizures occurred in 22% of toddlers whose deaths were certified explained because of infections and accidents, more than 5-fold higher than in the age-matched controls.⁴ This supports that febrile seizures were the mechanism of deaths attributed to other causes by current death certification practices.

Seizures may be responsible for some sudden infant deaths, which are usually unwitnessed during sleep. Infant seizures are often subtle and may cause isolated apneas, leading to underdiagnosis. Among 6 infants with recurrent life-threatening events with normal interictal electroencephalograms, 23 seizures were recorded in which initial electroencephalographic changes were followed by tachycardia and oxygen desaturations (27 seconds after electrographic onset) and apneic pauses, despite resuscitation.²⁸ Post-mortem neuropathologic and molecular phenotyping studies identify epilepsy syndromes in some autopsy-negative cases otherwise attributable to sudden infant death syndrome.^{11,22,29}

Seizures involved in sudden unexplained nocturnal deaths in young adults are sometimes misclassified as sudden cardiac death³⁰ but typically lack evidence such as cardiac hypertrophy, coronary artery disease, congenital abnormalities, or other findings. One consecutive series of adult sudden cardiac deaths in San Francisco County found that 17% of nonarrhythmogenic cases had a seizure history that was later determined as the definite or likely causes of death in most.³¹ Asian cultures named this syndrome after the "loud groan" heard during sleep before death, suggesting a possible "ictal vocalization."³²

Seizure-related deaths can occur in people without a history of seizure. Only one of our cases had a (febrile) seizure history. Yet their postconvulsive course paralleled typical sudden unexpected deaths in epilepsy recorded in epilepsy-monitoring units: postconvulsive tachycardia and breathing instability were followed by death, often during sleep and prone.¹⁸ The specificity of hippocampal dentate gyrus changes in SUDC has been questioned.^{12,15} Hippocampal findings in our cases did not correlate with a febrile seizure history; in case 2, they were unrelated to

death due to tonsillar obstruction. Four cases with definite terminal convulsions were alive following their convulsion; 2 had postictal respiratory dysfunction. All 7 cases had asphyxia risk: discovered prone faced down positioning or airway obstruction at autopsy. Postictal depression of arousal and reflexes likely contributed as well.

Death certifications commonly default to cardiac causes when autopsies are unrevealing.^{30,33} Unwitnessed deaths in adults with epilepsy are often attributed to cardiac causes based on age-related cardiac pathologies that do not differ from age-matched controls.³⁴ Neither cardiac arrhythmias nor terminal seizures have pathognomonic autopsy findings. Tongue contusions complicate some epileptic convulsions, including one of our cases, but cannot be reliably distinguished from a convulsion resulting from cardiac-induced cerebral hypoxia.^{17,35} Cardiac causes are unlikely in our cases because whole-exome sequencing was negative for pathogenic or de novo cardiac disease sequence variations (although sequence variations may exist in genes or regulatory elements not currently known to influence cardiac arrhythmia risk), cardiac pathology was unrevealing, all were sleep-related and most were found face down.³⁶ Thus, the preterminal convulsive movements in our cohort were most likely due to an epileptic seizure.

Our study is limited by sample size, absence of contemporaneous physiologic monitoring to objectively distinguish abnormal movement, convulsions and seizures, variable quality and duration of audio-video recordings, and SUDCRCC case ascertainment that may be biased and possibly not representative of the overall SUDC population. However, these recordings of sudden childhood deaths are a unique data set providing compelling evidence that terminal seizures may be much more common than medical histories suggest. The demographic profiles of these cases overlap with our full SUDCRCC cohort, suggesting that many other unwitnessed sleep-related deaths in young children could result from seizures. The causes of the convulsive events in our cases are unknown; mild infections may have lowered the seizure or febrile seizure threshold.

In a consecutive series of audiovisual recordings of deaths in 7 children, a convulsion preceded death in 6 cases, including all 5 with continuous recordings. Without video evidence, death investigations would not have implicated seizures. Seizure-related deaths are underrecognized in patients with epilepsy and unrecognized in people without epilepsy. Accurate diagnosis is limited by lack of pathognomonic evidence of terminal seizure because autopsies are normal or show incidental findings, and identification of perimortem seizures may be challenging or absent. Terminal seizures may play a role in many unwitnessed sleep-related deaths in toddlers and potentially in infants, older children, and adults.

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Disclosure

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Appendix 1 Authors

Name	Location	Contribution
Laura Gould, MSc	NYU Grossman School of Medicine, and NYU Comprehensive Epilepsy Center, New York	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data
Codi-Ann Reid, AB	NYU Grossman School of Medicine, and NYU Comprehensive Epilepsy Center, New York	Major role in the acquisition of data; analysis or interpretation of data
Alcibiades J. Rodriguez, MD	NYU Grossman School of Medicine, and NYU Comprehensive Epilepsy Center, New York	Major role in the acquisition of data; analysis or interpretation of data
Orrin Devinsky, MD	NYU Grossman School of Medicine, and NYU Comprehensive Epilepsy Center, New York	Drafting/revision of the manuscript for content, including medical writing for content; major role in the acquisition of data; study concept or design; analysis or interpretation of data

Appendix 2 Coinvestigators

Name	Location	Role	Contribution
Alison Krywaczyk, MD	Cuyahoga County Medical Examiner's Office, Cleveland, OH	Forensic and Cardiac Pathologist Co-Investigator	Data acquisition and reviewer of videos, review of manuscript
Kristen Landi, MD	NYC Office of the Chief Medical Examiner, New York	Forensic and Pediatric Pathologist Co-Investigator	Data acquisition and reviewer of videos, review of manuscript
Melissa Guzzetta, DO	Office of the County Medical Examiner, Middlesex, NJ	Forensic Pathologist Co-Investigator	Data acquisition and reviewer of videos, review of manuscript
Heather Jarrell, MD	Office of the Medical Investigator, University of New Mexico Health Sciences Center, Albuquerque	Forensic and Neuropathologist Co-Investigator	Data acquisition and reviewer of videos, review of manuscript
Kelly Lear, MD	Arapahoe County Coroner's Office, Centennial, CO	Forensic Pathologist Co-Investigator	Data acquisition and review of manuscript
Tara Mahar, MD	Erie County Medical Examiner's Office, Buffalo, NY	Forensic Pathologist Co-Investigator	Data acquisition and reviewer of videos, review of manuscript
Katherine Maloney, MD	Erie County Medical Examiner's Office, Buffalo, NY	Forensic Pathologist Co-Investigator	Data acquisition and review of manuscript
Declan McGuone, MBBCh	Yale Medical School, New Haven, CT	Forensic and Neuropathologist Co-Investigator	Data acquisition and reviewer of videos, review of manuscript
Alex Williamson, MD	Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY	Forensic and Pediatric Pathologist Co-Investigator	Data acquisition and reviewer of videos, review of manuscript
Kathryn Pinneri, MD	Montgomery County Forensic Services, Conroe, TX	Forensic Pathologist Co-Investigator	Data acquisition and reviewer of videos, review of manuscript
Victoria Delavale, MPH	NYU Grossman School of Medicine, New York	Research Coordinator Co-Investigator	Collection of materials and communication of team members in review process
Daniel Friedman, MD	NYU Grossman School of Medicine, New York	Neurologist Co-Investigator	Strategic support to SUDCRRC

References

- Centers for Disease Control and Prevention; National Center for Health Statistics. *Mortality 2018-2021 on CDC WONDER Online Database, released in 2021. Data are from the Multiple Cause of Death Files, 2018-2021, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program.* Accessed February 2, 2023. wonder.cdc.gov/ucd-icd10-expanded.html.
- Shapiro-Mendoza CK, Woodworth KR, Cottengim CR, et al. Sudden unexpected infant deaths: 2015-2020. *Pediatrics.* 2023;151(4):e2022058820. doi:10.1542/peds.2022-058820
- Moon RY, Carlin RF, Hand I; NEWBORN TFOSIDSATCOFA. Sleep-related infant deaths: updated 2022 recommendations for reducing infant deaths in the sleep environment. *Pediatrics.* 2022;150(1):e2022057990. doi:10.1542/peds.2022-057990

- Crandall LG, Lee JH, Stainman R, Friedman D, Devinsky O. Potential role of febrile seizures and other risk factors associated with sudden deaths in children. *JAMA Netw Open.* 2019;2(4):e192739. doi:10.1001/jamanetworkopen.2019.2739
- Hefti MM, Kinney HC, Cryan JB, et al. Sudden unexpected death in early childhood: general observations in a series of 151 cases: Part 1 of the investigations of the San Diego SUDC Research Project. *Forensic Sci Med Pathol.* 2016;12(1):4-13. doi:10.1007/s12024-015-9724-2
- Parks SE, DeSisto CL, Kortsmit K, Bombard JM, Shapiro-Mendoza CK. Risk factors for suffocation and unexplained causes of infant deaths. *Pediatrics.* 2023;151(1):e2022057771. doi:10.1542/peds.2022-057771
- Polavarapu M, Klonoff-Cohen H, Joshi D, Kumar P, An R, Rosenblatt K. Development of a risk score to predict sudden infant death syndrome. *Int J Environ Res Public Health.* 2022;19(16):10270. doi:10.3390/ijerph191610270
- Crandall LG, Lee JH, Friedman D, et al. Evaluation of concordance between original death certifications and an expert panel process in the determination of sudden unexplained death in childhood. *JAMA Netw Open.* 2020;3(10):e2023262. doi:10.1001/jamanetworkopen.2020.23262
- Haas EA. Sudden unexplained death in childhood: an overview. In: Duncan JR, Byard RW, eds. *SIDS Sudden Infant and Early Childhood Death: The Past, the Present and the Future.* University of Adelaide Press; 2018.
- Smith DK, Sadler KP, Benedum M. Febrile seizures: risks, evaluation, and prognosis. *Am Fam Physician.* 2019;99(7):445-450.
- Kinney HC, Haynes RL, Armstrong DD, Goldstein RD. Abnormalities of the hippocampus in sudden and unexpected death in early life. In: Duncan JR, Byard RW, eds. *SIDS Sudden Infant and Early Childhood Death: The Past, the Present and the Future.* University of Adelaide Press; 2018.
- McGuone D, Leitner D, William C, et al. Neuropathologic changes in sudden unexplained death in childhood. *J Neuropathol Exp Neurol.* 2020;79(3):336-346. doi:10.1093/jnen/nlz136
- Hefti MM, Cryan JB, Haas EA, et al. Hippocampal malformation associated with sudden death in early childhood: a neuropathologic study: Part 2 of the investigations of The San Diego SUDC Research Project. *Forensic Sci Med Pathol.* 2016;12(1):14-25. doi:10.1007/s12024-015-9731-3
- McGuone D, Crandall LG, Devinsky O. Sudden unexplained death in childhood: a neuropathology review. *Front Neurol.* 2020;11:582051. doi:10.3389/fneur.2020.582051
- Leitner DF, McGuone D, William C, et al. Blinded review of hippocampal neuropathology in sudden unexplained death in childhood reveals inconsistent observations and similarities to explained paediatric deaths. *Neuropathol Appl Neurobiol.* 2022;48(1):e12746. doi:10.1111/nan.12746
- Devinsky O, Ryvlin P, Friedman D. Preventing sudden unexpected death in epilepsy. *JAMA Neurol.* 2018;75(5):531-532. doi:10.1001/jama.2018.0400
- Middleton OL, Atherton DS, Bundock EA, et al. National Association of Medical Examiners position paper: recommendations for the investigation and certification of deaths in people with epilepsy. *Acad Forensic Pathol.* 2018;8(1):119-135. doi:10.23907/2018.009
- Ryvlin P, Nashif L, Lhatoo SD, et al. Incidence and mechanisms of cardiorespiratory arrests in epilepsy monitoring units (MORTEMUS): a retrospective study. *Lancet Neurol.* 2013;12(10):966-977. doi:10.1016/S1474-4422(13)70214-X
- Halvorsen M, Gould L, Wang X, et al. De novo mutations in childhood cases of sudden unexplained death that disrupt intracellular Ca(2+) regulation. *Proc Natl Acad Sci USA.* 2021;118(52):e2115140118. doi:10.1073/pnas.2115140118
- Harowitz J, Crandall L, McGuone D, Devinsky O. Seizure-related deaths in children: the expanding spectrum. *Epilepsia.* 2021;62(3):570-582. doi:10.1111/epi.16833
- Devinsky O, Hesdorffer DC, Thurman DJ, Lhatoo S, Richerson G. Sudden unexpected death in epilepsy: epidemiology, mechanisms, and prevention. *Lancet Neurol.* 2016;15(10):1075-1088. doi:10.1016/S1474-4422(16)30158-2
- Halvorsen M, Petrovski S, Shellhaas R, et al. Mosaic mutations in early-onset genetic diseases. *Genet Med.* 2016;18(7):746-749. doi:10.1038/gim.2015.155
- Crandall L, Devinsky O. Sudden unexplained death in children. *Lancet Child Adolesc Health.* 2017;1(1):8-9. doi:10.1016/S2352-4642(17)30003-2
- Hesdorffer DC, Crandall LA, Friedman D, Devinsky O. Sudden unexplained death in childhood: a comparison of cases with and without a febrile seizure history. *Epilepsia.* 2015;56(8):1294-1300. doi:10.1111/epi.13066
- Leitner DF, William C, Faustina A, et al. Proteomic differences in hippocampus and cortex of sudden unexplained death in childhood. *Acta Neuropathol.* 2022;143(5):585-599. doi:10.1007/s00401-022-02414-7
- Halvorsen M, Petrovski S, Shellhaas R, et al. Mosaic mutations in early-onset genetic diseases. *Genet Med.* 2016;18(7):746-749. doi:10.1038/gim.2015.155
- Bundock EA, Corey TS, Andrew TA, et al., eds. *Unexplained Pediatric Deaths: Investigation, Certification, and Family Needs.* Academic Forensic Pathology International; 2019. <https://www.ncbi.nlm.nih.gov/books/NBK577018/>
- Hewertson J, Poets CF, Samuels MP, Boyd SG, Neville BG, Southall DP. Epileptic seizure-induced hypoxemia in infants with apparent life-threatening events. *Pediatrics.* 1994;94(2 pt 1):148-156. doi:10.1542/peds.94.2.148
- Brownstein CA, Goldstein RD, Thompson CH, et al. SCN1A variants associated with sudden infant death syndrome. *Epilepsia.* 2018;59(4):e56-e62. doi:10.1111/epi.14055
- Zheng J, Zheng D, Su T, Cheng J. Sudden unexplained nocturnal death syndrome: the hundred years' enigma. *J Am Heart Assoc.* 2018;7(5):e007837. doi:10.1161/JAHA.117.007837
- Devinsky O, Friedman D, Cheng JY, Moffatt E, Kim A, Tseng ZH. Underestimation of sudden deaths among patients with seizures and epilepsy. *Neurology.* 2017;89(9):886-892. doi:10.1212/WNL.0000000000004292
- Tanchaiswad W. Is sudden unexplained nocturnal death a breathing disorder? *Psychiatry Clin Neurosci.* 1995;49(2):111-114. doi:10.1111/j.1440-1819.1995.tb01872.x

33. Krahn AD, Behr ER, Hamilton R, Probst V, Laksman Z, Han HC. Brugada syndrome. *JACC Clin Electrophysiol.* 2022;8(3):386-405. doi:10.1016/j.jacep.2021.12.001
34. Nascimento FA, Tseng ZH, Palmiere C, et al. Pulmonary and cardiac pathology in sudden unexpected death in epilepsy (SUDEP). *Epilepsy Behav.* 2017;73:119-125. doi:10.1016/j.yebeh.2017.05.013
35. Brigo F, Storti M, Lochner P, et al. Tongue biting in epileptic seizures and psychogenic events: an evidence-based perspective. *Epilepsy Behav.* 2012;25(2):251-255. doi:10.1016/j.yebeh.2012.06.020
36. Thosar SS, Butler MP, Shea SA. Role of the circadian system in cardiovascular disease. *J Clin Invest.* 2018;128(6):2157-2167. doi:10.1172/JCI180590