Seizure Detection and SUDEP Prevention

Seizure detection and alerting devices hold promise for preventing sudden death in epilepsy.

By Cassandra Kazl, MD and Daniel Friedman, MD, MSc

For many of the 3 million adults and 470,000 children in the US (1.2% of the population) living with active epilepsy,[1] the unpredictable nature of seizures is unsettling for both patients and caregivers. Seizures can have many immediate negative consequences; the most significant is sudden unexpected death in epilepsy (SUDEP), the most common cause of premature death among people with epilepsy.[2] The pathophysiology of SUDEP often includes a terminal seizure.[3,4] Interventions that reduce seizure frequency (eg, epilepsy surgery or add-on drug therapy) also reduce SUDEP rates.[5,6]

The seizures that cause the majority of SUDEP cases are often unattended. Most SUDEPs occur during unsupervised times, and most commonly, the decedent is found by family or caregivers in the morning.[3,7] Persons with a history of seizures during unsupervised times may also be more vulnerable; a history of nocturnal seizures increases SUDEP risk.[8] Increased nighttime supervision appears to be protective; having a roommate or use of a nocturnal listening device is associated with reduced SUDEP risk.[9] This is likely because someone may be able to provide aid and resuscitation in the vulnerable postictal period when cardiopulmonary dysfunction may be reversible.[4] Even tactile stimulation and repositioning can decrease postictal respiratory dysfunction.[10]

There has been a growing interest in seizure detection and alerting devices for use in the home to notify caregivers of a seizure and turn unwitnessed seizures into attended seizures, as a method to reduce SUDEP risk. With the help of innovations in health technology, mobile sensors, and smartphones, many devices are in development and some have been commercialized. Recently 2 such devices were approved by the FDA for use as adjuncts to seizure monitoring.

Seizure Detection Methods

A range of biologic signals can be monitored for seizure detection (Figure), and these can be categorized as cerebral activity, seizure-related behavior (including movement and muscle contraction), and noncerebral, nonmotor physiologic changes (Tables 1 and 2).

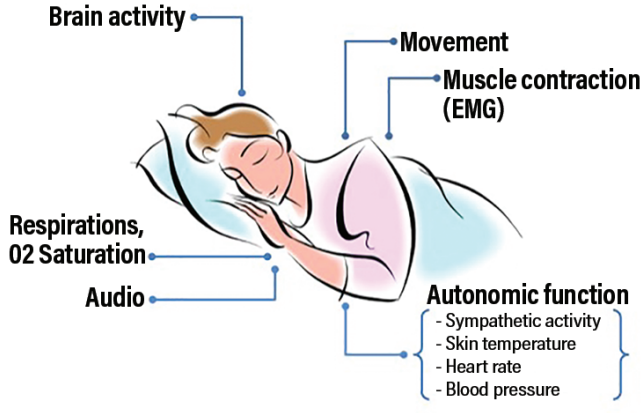

Figure. Measurable signals during seizures.

Cerebral Activity

Cerebral activity can be monitored using scalp electrodes or more invasive tools such as intracranial EEG (iEEG). The standard for seizure monitoring remains video EEG (vEEG). An advantage of monitoring cerebral activity is that seizure activity is detected early or may even be predicted before it is clinically evident.[11] All types of seizures can be detected by EEG even when brief or without major motor manifestations. Devices that measure EEG signals can be useful for quantifying overall seizure burden because many patients are unaware of some or all of their seizures.[12] Long-term monitoring of scalp EEG, however, requires application and maintenance of electrodes that may not be practical for long-term use. Implantable, intracranial seizure detection systems carry surgical risk that may not be acceptable and detection of subclinical or nonmotor seizures may not be necessary for SUDEP risk, as the majority of SUDEP follows generalized tonic-clonic seizure (GTCS). There has been an emphasis on developing practical noninvasive, noncerebral seizure detection methods.

Seizure-Related Behavior

Seizure activity can be detected using extracerebral (or nonEEG) devices. Video motion detectors,[13-15] accelerometers,[16-19] or surface EMG (sEMG)[19-22] have been employed to detect the repetitive movements and muscle activity present during GTCS (Table 1). Audio recordings may be used to detect the unique sounds of GTCS such as ictal cry.[23] Movement detection devices are noninvasive and more widely applicable than intracerebral devices. Sensors to detect seizure-related movements include wrist-worn accelerometers, computer vision analysis of video signals, and piezo-electric mattress sensors.[24]

The movement signals recorded are not necessarily seizure specific; however, sophisticated algorithms are necessary to distinguish seizure-related motion from other forms of repetitive movements common in daily life (eg, running, chopping vegetables, or playing video games) to reduce false-detection rates. Some movement-detection sensors are location specific (ie, bed or mattress sensors), which can alleviate concerns for nighttime seizure detection but are not applicable to all forms of unattended seizures.

Accelerometer and Gyroscope. Accelerometers measure motion and velocity changes in more than 2 dimensions, whereas gyroscopic sensors measure angular and rotational acceleration. Both are low cost with low energy consumption. Small accelerometers can be worn easily on a limb and are much better tolerated by patients than EEG. Studies support that a wrist-worn motion detector should alert caregivers when GTCS occurs.[25] These units can be part of a commercially available smartwatch or an independent unit, either of which can connect to a smartphone to deliver alerts to caregivers. Accelerometers have high sensitivity for GTCS detection.[17,18] False positives varied in these studies from once every 5 days[17] to several times a day.[18,25]

Noncontact Movement Sensors. Pressure sensors can be placed under a mattress or sheet to detect patterns of abnormal movement, although sensitivity varies greatly; 1 study detected 89% of GTCS in adults,[26] whereas another study detected only 30% of GTCS in children.[27] There are several other problems with movement sensors such as high rates of false positives, faulty sensors, and an inability to differentiate seizures from other nighttime movements.[26] An advantage is that these sensors do not require physical contact with the patients, which can be helpful in young children.

Surface EMG. Changes in the electric activity of muscles are measured in surface EMG (sEMG) with electrodes placed on the skin rather than inserted into the muscle. Tonic and tonic-clonic seizures have characteristic sEMG patterns that can be used in detection devices.[28] In a prospective multicenter study, sEMG had sensitivity of 94% for GTCS detection.[20] A potential disadvantage of sEMG is that incorrect placement of a surface electrode can alter seizure detection accuracy and false-positive rate significantly (76% vs 100% and 2.52 vs 1.44 per 24 hours, respectively).[22]

TABLE 1. BIOSIGNALS PROPOSED FOR SEIZURE-DETECTION DEVICES

Brain activity	Extracranial EEG
	Intracranial EEG
Movement	Accelerometry/gyroscope
	Video detection systems
	Mattress sensors
Muscle contraction	Surface EMG (sEMG)
Respiratory	Respiratory monitor
	Oxygen saturation monitor
Cardiac	Electrocardiography (EKG)
	Blood pressure
Autonomic	Electrodermal activity (EDA)
	Skin temperature
Other	Audio
	Cerebral oxygen saturation sensors/ near infrared
	Near infrared spectroscopy (NIRS)
	Seizure-alert dogs

Video. Video observation is part of the standard for in-hospital monitoring of seizures; however, having a person review a live video stream is not feasible for home use. Advances in computer software have made automated detection of seizure-related behavior from a video stream a possibility.[13] Advantages of video-based methods include contactless monitoring, ease of use, and the ability to watch in real-time or play back an event for review. Disadvantages include the possibility of missing small seizure-related movements and restricted location of monitoring.

Audio. Many noises accompany seizures including ictal cry, vocalizations, certain automatisms (eg, lip smacking or sniffing), stridorous respirations, and secretions. Audio devices share some of the same advantages of video monitoring, (ie, comfort [contactless] and practicality) and are also more affordable. Baby monitors are one of the most widely used device types in the pediatric population. Disadvantages include relatively low-quality sound, background noise interference, and lack of visualization. Audio detection systems can be used with other modalities.[23]

Noncerebral Physiological Changes

Ictal and peri-ictal cardiorespiratory events seem to play an important role in the context of SUDEP.[4,29,30]

Autonomic changes have also been noted peri-ictally.[31,32] NonEEG seizure detection devices could employ one or a combination of these signals, including heart rate/EKG, blood pressure, O_2 saturation, respirations, and electrodermal activity (EDA), a measure related to sympathetic nervous system activation. Many of these signals can be recorded noninvasively.

Electrodermal Activity. Electrodermal activity is a measure of skin conductance and resistance caused by sweat gland activity, which is a direct reflection of sympathetic activity.[33] Seizures, and specifically GTCS, can lead to sympathetic activity that is reflected in peri-ictal EDA changes.[31] The mechanism of seizure-related sympathetic nervous system activation is not clear, although there are direct and indirect connections between cortical structures commonly involved in seizure networks (ie, frontal cortex, orcingulate gyrus) and medullary autonomic centers.[34] Electric stimulation of those structures can induce EDA changes.[35]

In addition to seizure detection, the EDA response amplitude has been proposed as a biomarker for SUDEP risk because it is correlated with longer EEG suppression, which is also considered a measure of SUDEP risk.[31] A disadvantage is that peri-ictal EDA changes have a relatively slow time course and may need to be combined with other methods to improve detection latency for seizure-monitoring devices.[36]

Electrocardiogram and Pulse Rate. Heart rhythm abnormalities, persistently elevated heart rate (HR), and decreased heart rate variability (HRV) are all predictors of sudden cardiac death in healthy populations and in people

TABLE 2. DEVICES CURRENTLY AVAILABLE AND IN DEVELOPMENT

Devices	Modality / sensor	Applications	Seizure types detected	Advantages
Brain Sentinel sensing, portable sEMG, analysis and characterization (SPEAC)[20-22]	Electrode patch - sEMG - audio recording	SPEAC2ME portal	GTCS, may detect some tonic	- Early detection in tonic phase - Wearable - Audio - Playback
Embrace by Empatica[31,49,50]	Smartwatch - EDA - Gyroscope - 3-axis accelerometer - Skin temperature sensor	- Alert app - Mate app (seizure diary)	GTCS	- Multiple detection modalities - Wearable - Relatively affordable - All ages - Multiple styles
Emfit Movement Monitor and Emfit QS[26,27]	Mattress sensor and bedside monitor -Quasi-piezoelectric sensor -Ballistocardiography (QS)	Emfit QS web application	GTCS, some focal motor, hypermotor	- Video - Contact-free - All ages
Epi-Care free and Epi-Care mobile by Danish Care Technology[17,51]	Wristband sensor with base unit (free) or smartphone app (mobile) -Accelerometer	Epi-Care mobile app for Android only	GTCS	- Wearable - All ages
Sleep activity monitor (SAMi)	Remote infrared video camera - Motion detector >15 seconds - Audio recording	SAMi app	GTCS, other seizures with prominent motor component	- Video - Audio - Immediate playback - Contact-free - All ages
SmartWatch Inspyre by SmartMonitor[16,52]	Smartwatch application -Accelerometer	App links to smartphone	GTCS	- Monthly subscription plan, multiple subscription options -Wearable - Relatively affordable - All ages - Audio (gold subscription) - Cancel false alarms

with medical conditions and are associated with ictal and post-ictal phases.[37] Seizure-related heart rate changes can include tachycardia, bradycardia, and asystole, and may be more associated with GTCS, temporal lobe seizures, and hypermotor frontal lobe seizures.[38]

Although there are advantages to this form of monitoring, such as portability and being able to monitor variables with as little as 2 leads, several important disadvantages remain. For instance, solely cardiac-based detection has failed to discriminate some types of seizures from other activities such as exercise, arousal from sleep,[32] and even psychogenic nonepileptic seizures.[39]

Pulse Oximetry. Oxygen saturation (SpO_2) uses infrared waves to detect blood-oxygen concentration (a saturometer) and a plethysmograph. It can be easily monitored by a sticker or strap on a distal extremity or even an earlobe. When combined with an HR and an EDA detector, it was found that SpO_2 decrease caused an alert after HR change and before EDA change.[36] When SpO_2 thresholds are set to 80% to 86%, SpO_2 detectors alone are able to detect 63% to 73% of generalized convulsions and 20% to 28% of focal seizures.[40] Because SpO_2 detection has a relatively high false alarm rate, they are usually combined with other sensors in a multimodal system.

Near-Infrared Spectroscopy. Using the near-infrared region of the electromagnetic spectrum, near-infrared spectroscopy (NIRS) measures hemodynamic changes (eg, cerebral O_2 saturation) during epileptic seizures. In children with epilepsy, an association was seen between convulsive seizures and cerebral blood volume; however,

	Disadvantages	Performance (tested vs vEEG) /regulatory approval	Overall sensitivity (GTC)	False positive rates
	- Not yet widely commercially available - Requires precise placement - Adhesive must be reapplied - Not practical for long-term use or young children	Yes; FDA approved trial: NCT02371200	Med-high - sEMG 53%-100%[28] - 93.8%/95% mean per patient (EMU)[20] - 76-100% (EMU)[30] - 95% (EMU)[21]	- 0.67/24 h[20] - 1.44-2.52/24 h[22]
	- Daily recharging - Long charging time	Yes; FDA approved trial: NCT03207685	High - EDA 86-100%, accelerometry 80-100%[28] - 94% (EMU)[49] - 94.55%[50]	- 0.74/24 h[49] - 0.2/24 h[50]
	- Limited to sleep - Not wearable - Expensive - Weight limit	Yes; not FDA approved trial: NCT02661919	Low-med - Mattress sensor 0-75%[28] - 89% (EMU)[26]	- 0.18/24 h[26]
	- Sensor must be within 65 ft from base unit or 30-50 ft from smartphone - Expensive - Android-compatible only	Yes; CE mark, available in Europe only	High - Accelerometry 80-100%[28] - 91% (EMU)17 - 90% (outpatient setting)[51]	- 0.2/24 h (EMU)[17] - 0.1/24 h (outpatient)[51]
	- Limited to sleep - Not wearable - Expensive - High false-alarm rate (eg, pets)	No	Med-high - Video detection system 75-100%[28]	NA
	- Daily recharging - Must purchase smartwatch separately	Yes; not FDA approved	High - Accelerometry 80-100% - 92.3% (EMU)[51]	- 81 false detections, 48% of total, no time denominator available[52]

the same study also showed no change to mild change in absence seizures, an initial decrease in some convulsive seizures, and an initial increase followed by decrease for tonic status epilepticus.[41] Another study suggests that NIRS can distinguish patterns of cerebral oxygenation that differ in focal unaware seizures and focal to bilateral tonic-clonic seizures.[42] There are still limitations including the size of the wearable device and conflicting evidence regarding low positive predictive value for seizures.[43,44] More data are required to assess the sensitivity of NIRS as a reliable seizure detector.

Available Devices

Several commercially available seizure monitoring devices are available or in development (Table 2). Many have been tested against the standard vEEG in patients admitted to epilepsy-monitoring units. Most target GTCS with reported sensitivities of 53% to 100% and false-positive rates between 0.1 and 2.52 per 24 hours in the epilepsy-monitoring unit.

Alerting Methods

Devices differ in how caregivers are alerted. Some pair with an application on the patient's smartphone to issue text alerts or voice calls to prespecified responders, and others use a paired receiver that issues an audio alarm. At this time, no device links directly to first responders or centralized call centers, which is a concern for patients who live alone or are socially isolated without nearby friends or family to provide peri-ictal assistance.

Accessibility

A survey showed that the majority of people with epilepsy are familiar with multiple digital technologies, making them a good population for wearable technology.[45] There are limited data about the usefulness of wearable devices, in part because both patients and their health care providers lack knowledge of the devices.

A majority of persons with epilepsy prefer devices that are wearable, portable, and discrete.[45,46] Cost is also a major factor, with a majority of patients surveyed wanting to use a device only if it was covered by insurance, and a few expressing interest if it were not covered but affordable.[45] Multimodal devices for long-term use are also preferred.[46]

Seizure-Detection Device Caveats

Real-World Data

Most data regarding the accuracy of seizure detection devices come from studies in the epilepsy-monitoring unit, but that is not an accurate representation of real-world use because of patients' limited range of activity in the unit and the presence of study staff to apply and position devices.[22] Little data exist for ambulatory patients and there are currently no standards for assessing accuracy. A set of outcome measures and standards for reporting have been proposed,[47] but not all prior studies meet those standards. There is also the issue of patient adherence. Even if the device is readily available and applied correctly, there is no way of ensuring it is always used.

Options Limited for Those Who Live Alone

People with epilepsy are more likely to live alone after they become independent from their parents.[48] For these people, seizure detection does not equate to timely intervention. A recent case report highlighted this for a patient who, despite using a device that detected a convulsive seizure and issued an alert, died before his parents (the prespecified responders) arrived 15 minutes later.[53]

Unknown Life-Saving Efficacy

There are no studies yet that demonstrate seizure detection and alerting devices reduce SUDEP risk and, because of the relatively infrequent occurrence of SUDEP even in the highest risk populations, these studies may be difficult to perform.[9] Seizure detection may fail to prevent all SUDEP because although the majority of witnessed SUDEP occurred following GTCS, approximately 10% occurred following focal unaware seizures.[3] Concurrent vEEG monitoring[54] and ambulatory intracranial monitoring[55] has shown that SUDEP can occur without antecedent seizures. In these cases, devices that detect only GTCS would not prevent SUDEP. It is also possible for SUDEP to occur despite immediate peri-ictal intervention by trained personnel, suggesting that simple resuscitative efforts may not always be enough to reverse the cascade of events leading to death.[56]

Conclusions and Future Directions

Noninvasive devices to detect GTCS and alert caregivers are becoming readily available. Although performance of some of these devices is uncertain, especially in the outpatient setting, there is sufficient information available to help choose between available options and determine which device may work best for a particular patient. Despite the lack of direct evidence that seizure detection devices prevent SUDEP, they may be a good tool to augment nocturnal supervision as a SUDEP-prevention strategy. The use of these seizure detection devices should be put in the context of SUDEP risk, seizure types, independence, and patient and family preferences.

The intersection of technology and health is constantly evolving, and there are a few things that we can expect to see going forward. The most common methods for detection discussed in this review may eventually play more of a role in a closed-loop warning system able to provide rapid

treatment or prevention of seizures.[57] As this technology is improved upon, seizure forecasting/prediction devices will emerge for the purpose of treatment and not just alerting. This will give the patient and family even more confidence and peace of mind, improving the quality of life of all parties involved. Although many patients can achieve seizure freedom, the population of people refractory to treatment remains and they are entitled to the same quality of life as their healthy counterparts. ■

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Cassandra Kazl, MD
Clinical Neurophysiology Fellow
Department of Neurology
NYU Comprehensive Epilepsy Center
New York, NY

Daniel Friedman, MD, MSc
Associate Professor, Department of Neurology
Co-Director, Video-EEG Laboratory
Director of Medical, Cardiac and Neurosurgical ICU
Epilepsy Monitoring Services
Co-Director, Special Procedures for the Epilepsy Service
NYU Comprehensive Epilepsy Center
New York, NY

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