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Yield of conventional and automated seizure detection methods in the epilepsy monitoring unit

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ABSTRACT

Purpose: To investigate the performance of seizure detection methods and nursing staff response in our epilepsy monitoring unit (EMU).

Methods: We retrospectively reviewed 38 EMU patient admissions over a 1-year period capturing 133 epileptic and non-epileptic seizures with associated video-EEG data. We recorded detailed seizure event characteristics for further analysis.

Results: Rates of seizure detection, alarm usage, and time to nursing response varied by seizure type. Patients self-activated the push button (PB) alarm for 31.1% of all seizures, but only 8.9% of focal impaired awareness (FIAS) and focal to bilateral tonic-clonic seizures (FBTCS). In comparison, the Persyst automated seizure alarm reliably detected both electrographic seizures (76.2% of electrographic seizures) and FIAS/FBTCS (87.2% of FIAS/FBTCS), with a false positive alarm rate (FAR) of 0.14/hour, or every 7.3 h.

11.4% of all seizures went unrecognized by nursing staff, of which the majority (80.0%) were FIAS. The PB alarm was of higher yield for alerting nurses to focal aware seizures (FAS) and psychogenic non-epileptic seizures (PNES) versus FIAS and FBTCS ($p < 0.001$). In contrast, nurses relied more on the automated Persyst software alarm to detect FIAS ($p < 0.001$). Time to nursing response was no different following audible alarm onset for the PB compared to the Persyst alarms ($p = 0.14$).

Conclusion: Automated seizure detection software plays an important role in our EMU in seizure recognition, particularly for alerting nurses to FIAS. More rigorous studies are needed to determine the best utilization of various monitoring techniques and to promote high quality standards and patient safety in the EMU.

1. Introduction

Monitoring seizures with long-term video-electroencephalography (EEG) in the epilepsy monitoring unit (EMU) is one of the most useful diagnostic tools in the epileptologist's armamentarium. While clinically useful and largely safe, this procedure is not risk-free. Adverse events reported by epilepsy centers include falls, status epilepticus, postictal psychosis, fractures, infections, and the most feared complication, sudden unexpected death in epilepsy (SUDEP) [1]. A large retrospective study noted a SUDEP risk of 1.2 per 10,000 inpatient video-EEG monitoring admissions [2]. Increasing evidence suggests that unrecognized seizures lacking nursing staff response lead to increased morbidity and mortality in the EMU [2–4], and single-center studies report high rates of missed seizures ranging from 10% to 59.4% in patients undergoing surface or intracranial EEG monitoring [5–7]. Furthermore, methods of patient observation and supervision remain unstandardized among epilepsy centers, making it difficult to identify widely applicable solutions [1,8].

Automated alarms of various types can be employed in the EMU to improve seizure recognition and response times. Shin et al. noted that automated cardiac and oxygen saturation telemetry monitoring were important for detecting seizures with impaired awareness in their EMU [5]. Both single and multi-center trials have additionally demonstrated that wearable EMG devices can reliably detect seizures, predominantly

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those manifesting with bilateral tonic-clonic or other rhythmic motor phenomena [9–11]. Lastly, automated scalp EEG seizure detection algorithms report sensitivities for epileptic seizures between 75–90% and could be used to bolster conventional monitoring techniques in the EMU [12]. 15–19% of epilepsy centers in Europe utilize automated seizure detection software as standard practice [8,13]. In our study, we sought to determine rates of seizure recognition and nursing response by event type and detection method in our EMU.

2. Materials and methods

2.1. Inclusion criteria

Our study was approved by the Rutgers University Institutional Review Board. We retrospectively studied all admissions to the Robert Wood Johnson University Hospital (RWJUH) adult EMU during a 12-month period between 11/2013 and 10/2014. We reviewed the charts of 81 consecutive patients > 18 years of age electively admitted to the adult EMU by three epileptologists during that time period. Patients without epileptic or psychogenic non-epileptic seizure events captured during admission were subsequently excluded. We also excluded patients admitted for intracranial EEG monitoring. Consequently, 38 patients with events recorded were eligible for further analysis.

2.2. Overview of seizure detection methods

The RWJUH EMU is a six-bed unit on the neurology ward supported by neuroscience-trained nursing staff. Our standard monitoring protocol includes video-EEG screens with which nurses can observe EMU patients from a nearby centrally-located nursing station. There are also additional video-EEG monitors located in a different room allowing EEG technologists to observe each patient individually. While a staff member is expected to watch these screens continuously, this may not always be possible during patient emergencies or other extenuating circumstances. In special cases, a staff member may be assigned to observe a patient directly at bedside, but this is not usual practice at our center.

Patients alert nurses they are having a seizure by activating the event push button (PB) alarm. In addition to these monitoring techniques, we use Persyst Insight II software (Version 11; Persyst Development Corporation, Prescott, AZ) as another seizure detection measure. Once the software identifies a seizure, an audible alarm activates, and staff are informed that an event has occurred. The alarm sound for the Persyst automated seizure detection is distinct from the PB alarm, allowing nurses to easily distinguish these signals. EMU patients are also placed on remote cardiac telemetry monitoring as an additional safety precaution. The majority of patients share a large room with another neurology patient, separated by a cloth barrier. A minority of patients have a private room.

2.3. Data collection

A single reviewer (AY) examined EMU reports and video-EEG data for each patient event. Board-certified epileptologists (SW, BK, RM, KS) confirmed these findings and performed a final review.

The following characteristics were recorded for each event captured:

1) Event type, as determined by the treating epileptologist, using the International League Against Epilepsy (ILAE) operational terminology [14]: focal aware seizure (FAS), focal impaired awareness seizure (FIAS), focal to bilateral tonic-clonic seizure (FBTCS), psychogenic non-epileptic seizure (PNES), or generalized onset seizure
2) Clinical event start and end times by video observation
3) PB activation (yes/no), and if yes, time of audible alarm, and who activated the PB (patient, family/visitor, staff)
4) Persyst automated detection (yes/no), and if yes, time of audible alarm
5) Attendance of nursing staff to the event (yes/no), and if staff responded, time staff member present at bedside
6) Primary alarm type (AT) leading to event recognition, for attended events (defined as: already present at bedside, Persyst alarm, patient-initiated PB alarm, staff recognition of event, non-staff recognition of event [i.e. the patient's visitor or neighboring patient])

We also analyzed all Persyst seizure detection alarms and classified each detection as an electrographic seizure, epileptiform non-seizure abnormality, normal EEG background, or artifact (myogenic, ocular, chewing, hyperventilation, or electrode artifact).

2.4. Statistical analysis

We performed statistical analysis using SPSS version 24. Fisher's exact test was used to determine between-group differences for the proportion of attended seizures and the method of seizure recognition. Nursing response times by seizure event type were tested for normality using the Shapiro-Wilk's test and were not normally distributed ($p < 0.05$), and thus, we utilized the Kruskal-Wallis H test and follow-up Mann-Whitney U tests to compare response times. We later excluded generalized onset seizures from this analysis due to a low number of events captured. A probability value of < 0.05 was considered statistically significant, and we used the Bonferroni correction for multiple comparisons when appropriate. We did not perform a power analysis due to the retrospective and exploratory nature of this study.

3. Results

3.1. Patient and seizure characteristics

Patient and event type characteristics are summarized in Table 1. We analyzed video-EEG data for 38 patients (17 men and 21 women) with a combined total of 3957.23 h of monitoring. There were 144 clinical events captured with EEG data available for review (Table 1). Of note, we recorded only generalized onset myoclonic seizures and did not capture other types of generalized onset seizures. From here on, we will refer to these specifically as myoclonic seizures. Video recording was available for 132 of the 144 clinical events (14/15 FAS, 52/55 FIAS, 27/31 FBTCS, 36/40 PNES, and 3/3 myoclonic seizures).

FAS = focal aware seizures, FIAS = focal impaired awareness seizures, FBTCS = focal to bilateral tonic-clonic seizures, PNES = psychogenic non-epileptic seizures

3.2. Detection performance of the patient-activated push button alarm

The overall sensitivity of the patient-triggered PB alarm was 31.1%, as patients activated the PB themselves for 41/132 events. Patients initiated the PB alarm least often for FBTCS (7.4%, 2/27) and FIAS (9.6%, 5/52), followed by myoclonic seizures (33.3%, 1/3) and PNES

Table 1
Patient and Seizure Characteristics.

Number of patients	38	
Median age (range)	34.5 years (18-82)	
Gender	Men	17
	Women	21
Number and type of each event captured, in total	FAS	15
	FIAS	55
	FBTCS	31
	PNES	40
	Myoclonic seizure	3
	Total	**144**

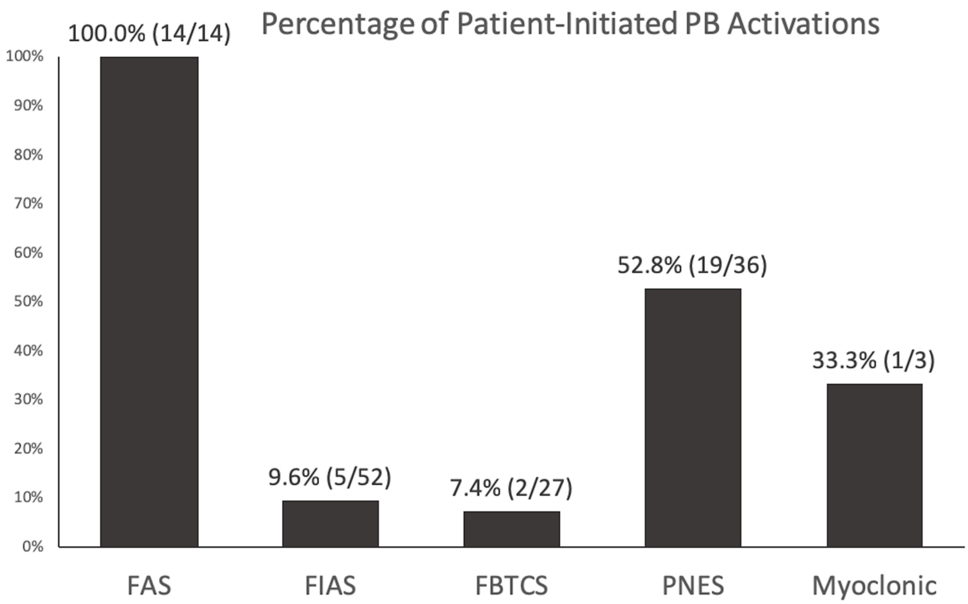

Fig. 1. Patient-initiated PB activation, by seizure type.
The x-axis represents each seizure event type recorded (FAS = focal aware seizures, FIAS = focal impaired awareness seizures, FBTCS = focal to bilateral tonic-clonic seizures, PNES = psychogenic non-epileptic seizures). The y-axis measures the proportion of each event type associated with a patient-initiated push button (PB) alarm activation, with absolute numbers in parentheses.

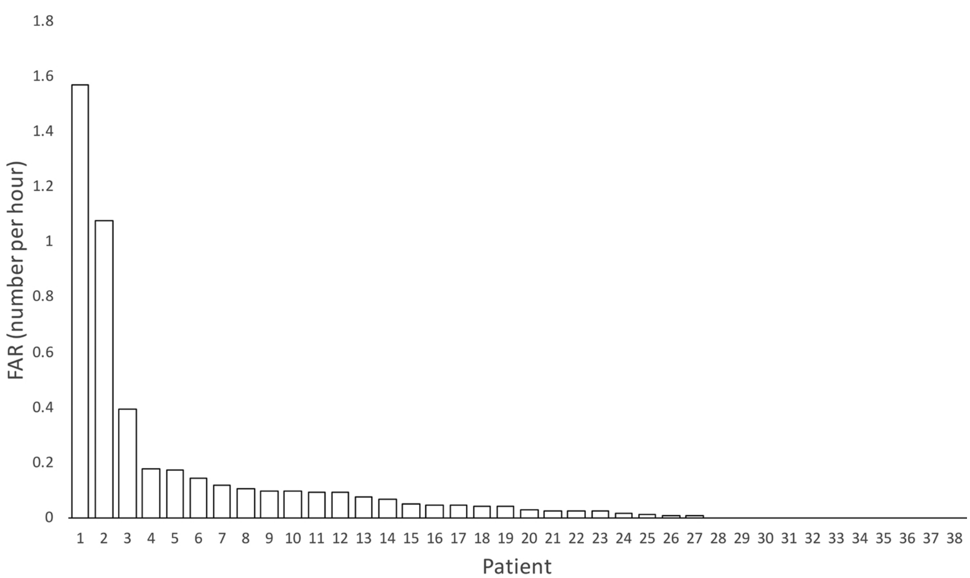

Fig. 2. Persyst seizure detection software FAR, per patient.
Each point on the x-axis corresponds to an individual patient (n = 38) in our study. The y-axis indicates the false positive alarm rate (FAR), quantified as the rate of false positive alarms per hour occurring over the course of the EMU admission for each individual patient.

(52.8%, 19/36). However, they activated the PB alarm for all FAS (100%, 14/14) (Fig. 1).

We further assessed the ability of patients to activate the PB alarm and alert nursing staff to seizure types that benefit from early recognition and clinical intervention, specifically, FIAS and FBTCS. We will refer to these going forward as "clinically relevant" seizure types. The sensitivity of the patient-activated PB alarm for detecting clinically relevant seizures was 8.9% (7/79 FIAS and/or FBTCS). For clinically relevant seizures, the positive predictive value (PPV) of the patient PB alarm was 17.1% (7/41), which we calculated as patient-PB activations for FIAS + FBTCS / all patient-PB activations. By contrast, the PPV for PNES by the patient-triggered PB alarm was 46.3% (19/41).

3.3. Detection performance of the Persyst automated seizure alarm

There was a total of 650 Persyst automated alarm detections for the 38 patients in our study; 108 of these were for accurately identified definite electrographic seizures, which we defined as any clinical or subclinical seizure with a clear EEG correlate per the treating epileptologist. The remainder of Persyst detections were for epileptiform non-seizure abnormalities (259), normal EEG (40), and various artifacts: myogenic (34), ocular (19), chewing (23), hyperventilation (1), and electrode (166).

The sensitivity of the Persyst automated seizure software for definite electrographic seizures was 76.2% (80/105 seizures). This differed by event type; the software detected 0/3 myoclonic, 2/10 (20.0%) FAS, 4/7 (57.1%) subclinical seizures, 27/31 (86.7%) FBTCS, and 48/55 (87.3%) FIAS. It therefore correctly identified 87.2% (75/86) of clinically relevant seizures.

The overall PPV of the Persyst software was 16.6% (108/650) for electrographic seizures. Of note, a single seizure could have multiple Persyst alarm detections, so we considered each alarm detection as a

Table 2
Nursing response by event type.

Event Type	Proportion of attended events	Time RN at bedside after clinical seizure onset, median (range)
FAS	14/14 (100%)	32.5 (6-77) seconds
FIAS	40/52 (76.9%)	81.0 (0-313) seconds
FBTCS	25/27 (92.6%)	49.0 (0-216) seconds
PNES	35/36 (97.2%)	15.0 (0-435) seconds
Myoclonic seizure	3/3 (100%)	0.0 (0-772) seconds
Total	**117/132 (88.6%)**	

This table shows the proportion of each seizure event type with nursing attendance/response (column 1) and the time from clinical seizure onset until bedside nursing response (column 2). (FAS = focal aware seizures, FIAS = focal impaired awareness seizures, FBTCS = focal to bilateral tonic-clonic seizures, PNES = psychogenic non-epileptic seizures).

unique event. The calculated false positive alarm rate (FAR) was 0.14 times per hour, or every 7.3 h. After omitting non-ictal epileptiform Persyst detections, the PPV rose to 27.6% (108/391) and the FAR dropped to 0.07 times per hour, or once every 14.0 h. The FAR varied widely among patients, with a median rate of 0.04 per hour, but ranged from 0 to 1.57 times per hour (Fig. 2). Four patients accounted for 75.9% (462/609) of the false positive detections, and a single patient had 328 false positive Persyst alarms (53.9% of all false positives), mostly due to non-evolving runs of generalized epileptiform discharges (Fig. 2).

3.4. Seizure recognition by nursing staff

For seizures with accessible video data, 11.4% (15/132) seizure events went unattended by nursing staff (Table 2). There were no unrecognized FAS or myoclonic seizures, whereas 12/52 (23.1%) FIAS, 2/27 (7.4%) FBTCS, and 1/36 (2.8%) PNES lacked nursing response (Table 2). Unrecognized FIAS comprised the majority of missed seizures (80.0%, 12/15), and significantly more FIAS were missed when compared to all other seizure types ($p = 0.001$).

The alarm type (AT) by which nurses were alerted to a seizure based on detailed video analysis are diagrammed in Fig. 3 and varied by the event type. Staff were more likely to respond because of the patient-activated PB alarm for both FAS (100% of FAS, $p < 0.001$) and PNES (54.3% of PNES, $p < 0.001$) when compared to FIAS and FBTCS. In comparison, the Persyst automated seizure detector was the primary means of notification for FIAS (43.2% of FIAS), a significantly higher proportion than FAS and PNES ($p < 0.001$) (Fig. 3). There were no other major differences in the primary AT between the different seizure event types.

3.5. Time to nursing response by alarm and event type

Of the 119 attended seizures, we were unable to assess nursing responses for four of these due to video recording difficulties. We investigated nursing response times based on whether the chief AT was the PB alarm versus the Persyst seizure detection alarm. For this analysis, we considered all PB activations by any user, including the patient and family/visitor, if it was the primary AT signaling nursing staff. Nurses responded more quickly following clinical seizure onset if alerted by the PB alarm versus the Persyst seizure alarm by 107.0 s ($p < 0.001$) (Table 3). However, there was a median delay of 94.0 s (range 39.0–147.0) from clinical seizure onset until the Persyst automated detector sounded an audible alarm because the software requires time to determine the validity of a seizure in-progress. Consequently, the time of actual audible alarm onset to nursing response was not significantly different for the PB when compared to the Persyst alarm ($p = 0.14$) (Table 3).

We then determined nursing response times after clinical onset for each event type (Table 2). Nursing staff responded significantly earlier following clinical onset for PNES when compared to both FIAS (66.0 s earlier, $p < 0.001$) and FBTCS (34.0 s earlier, $p = 0.004$). After extensive review of the video recordings, this appeared to be related to the fact that the PB was the AT most frequently alerting our nurses to PNES (Fig. 3). In contrast, FIAS and FBTCS were frequently recognized by the Persyst alarm, which as noted above has a notable delay from EEG onset to audible alarm, while the PB alarm is instantaneous. There were no other significant differences in nursing response times by event type.

4. Discussion

Our single-center retrospective observational cohort study over one-year demonstrated differences in nursing responses when categorized by seizure event and alarm type in the EMU. Our findings suggest that automated seizure detection software can bolster conventional methods of monitoring and alert staff to both FIAS and FBTCS. In comparison, PNES were primarily recognized by PB activation and associated with more consistent and timely nursing interventions.

FIAS can be clinically subtle depending on the localization and semiology, and indeed, were the event type most often lacking nursing response in our study, with 23.1% of all FIAS going unrecognized. Patients with FIAS or FBTCS may be unable to alert staff in a reliable or timely fashion, particularly in the EMU when medication tapering can lead to faster onsets or atypical seizure presentations. Moreover, post-ictal amnesia is common; some patients are completely unaware they have suffered a seizure at all. Studies conducted at other epilepsy centers have similarly found that FIAS frequently go unrecognized, at rates ranging from 15 to 33% [5,7]. Another study found that 38.1% of patients with electrographic seizures recorded with ambulatory EEG were incognizant of some or all of their focal seizures [15]. While perhaps not as concerning as unrecognized generalized tonic-clonic seizures, missed FIAS can certainly lead to complications in the EMU such as falls, patient injury, or status epilepticus. In addition, seizures lacking an ictal examination and interview are also less clinically informative and could further prolong the EMU length of stay. We found that the Persyst software was responsible for alerting nurses to a high proportion (43.2%) of recognized FIAS in our study. Without a control group, we cannot definitively conclude that more seizures would have gone unrecognized, but we suspect the rate of missed seizures would be much higher in our EMU without the use of this technology.

Multiple studies since the 1980s have shown that automated seizure detection software can reliably identify epileptic seizures. As continuous video-EEG became in vogue, challenges surrounding storing and reviewing large quantities of EEG data surfaced accordingly [16]. It was then apparent that relying solely on patient or bystander observation resulted in missed seizures. An early study by Gotman found that an automated seizure algorithm detected at least 41% of electrographic seizures that were otherwise clinically unrecognized [17]. The Persyst software detector correctly identified 76.2% of all electrographic seizures in our study, nearly identical to the sensitivity of 76% previously seen with this algorithm [18]. Other researchers report seizure detection rates ranging between 75–90% [12] and have robustly demonstrated the broad applicability of automated seizure software technology in as many as 205 patient admissions across multiple different epilepsy centers [19].

One potential concern regarding the use of automated EEG seizure software is a high rate of false positive alarms. Indeed, the false positive rate in our study was significant, comprising 83.4% of all Persyst detections with a FAR of 0.14 times per hour, or every 7.3 h. However, we noted that one patient accounted for a majority (53.9%) of the false positive detections; if this patient were excluded from the analysis, the overall Persyst FAR drops markedly to 0.09 times per hour, or once every 11.7 h. Other studies report seizure detection software FARs ranging from 0.1 to as many as 5 times per hour [12,18]. High numbers

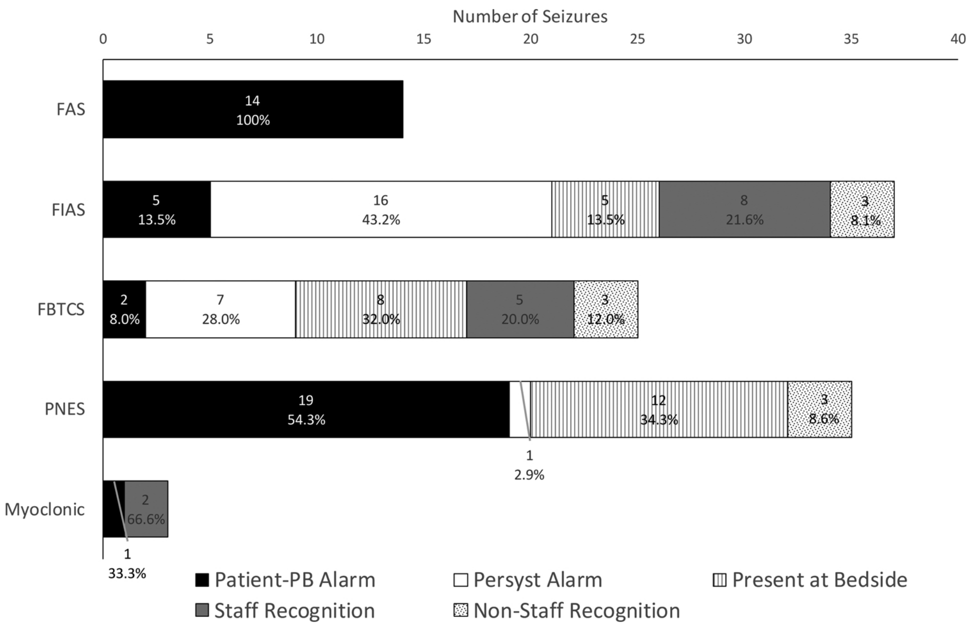

Fig. 3. Primary means of seizure detection by nursing staff, by event type.
Each point on the y-axis corresponds to a seizure event type, with the x-axis showing the proportion and total number of seizures detected by each specific alarm type. (FAS = focal aware seizures, FIAS = focal impaired awareness seizures, FBTCS = focal to bilateral tonic-clonic seizures, PNES = psychogenic non-epileptic seizures, PB = push button, Persyst = automated Persyst seizure detection software).

Table 3
Nursing response times after push button versus Persyst alarms. We calculated the time to bedside nursing response following clinical seizure onset (row 1) or audible alarm onset (row 2) for the patient-initiated push button (column 1) and the automated Persyst (column 2) primary alarm types. Nursing response was significantly faster following clinical seizure onset for the push button alarm compared to the Persyst alarm. However, there was no difference in nursing response time following audible alarm onset, attributable to a delay in seizure recognition by the Persyst automated software.

	Push button alarm	Persyst automated alarm	P-value
Time RN at bedside after clinical onset, median (range)	30.0 (0-772) seconds	137.0 (0-248) seconds	$p < 0.001$
Time RN at bedside after audible alarm onset, median (range)	18.0 (0-770) seconds	28.0 (0-196) seconds	$p = 0.14$

of false positive detections can have relevant clinical consequences, and our major concern was that staff will not react promptly to automated alarms if they perceive them as low-yield for true seizure events. Building on previous work by Fürbass and colleagues, we have now demonstrated that not only does an automated seizure detector perform well in theory, but just as importantly, nursing staff can and will use it to recognize seizures in a real-world EMU setting [19]. Indeed, nursing response times in our EMU were no different following the audible Persyst alarm when compared to the PB alarm. However, addressing ways to combat alarm fatigue among nursing staff is critical, since the rate of false positive detections will probably rise as increasingly multimodal automated alarm systems are deployed in the EMU.

Although automated seizure detection software seems promising, many EMUs do not utilize this and primarily rely on patient, visitor, or staff recognition of seizures [8]. The PB alarm was most reliable in detecting FAS, as expected, due to the subjective nature of FAS/auras with preserved consciousness allowing for consistent patient-initiated PB activation. The PB alarm also alerted nurses to a high proportion of PNES, which has been likewise noted by other investigators [5]. We found that nurses additionally responded about 30–70 seconds earlier to bedside following clinical onset for PNES when compared to FIAS and FBTCS. We suspect this is related to a limitation of the Persyst software, which requires some time to accurately determine if an epileptic seizure is occurring. In support of this, we noted a delay from clinical onset to nursing bedside response for seizures detected by the Persyst software when compared to the PB alarm, but no difference in time to response following the onset of the actual audible alarm when comparing these ATs (Table 3). Another potential explanation for more timely detection of PNES could include a difference in clinical presentation, as PNES often manifests with prominent motor movements and early vocalization [20]. PNES with these features are probably more easily recognized by nursing staff in comparison to FIAS characterized by bland staring.

However, we found that patients did not reliably self-activate the PB alarm for FIAS and FBTCS, which we termed “clinically relevant” seizure types with an associated risk of harm if unrecognized. The patient-initiated PB alarm sensitivity for these was only 8.9% (7/79 of FIAS and/or FBTCS). It may be unrealistic to expect patients to alert nursing staff to these types of seizures, but this severely restricts a nurse’s ability to provide prompt ictal testing and various rescue interventions. This limitation has further implications outside of the EMU for neurostimulation devices such as the vagal nerve stimulator (VNS). The VNS features an additional patient-activated magnet stimulation option, with evidence of seizure termination or diminution with its use [21,22]. The majority of patients who are unable to recognize their focal seizures may benefit more from other neurostimulation strategies that do not rely on patient-activation. For example, the newest VNS model (AspireSR®) delivers automatic stimulation in response to ictal tachycardia, which has been shown to provide an additional reduction in seizure frequency for patients previously implanted with the traditional VNS system [23]. Thus, alternative methods of detection could represent not only potential solutions for boosting nursing response in the EMU, but also provide seizure detection and therapeutic intervention on an outpatient basis.

Limitations of our study include the small overall sample size and heterogenous population, which included both epilepsy and PNES patients. We did not further sub-categorize focal seizures to comment on any differences in seizure response comparing motor and non-motor phenomenology, or other further cerebral localization. The single-center bias also limits overall generalizability, as monitoring methods, staff expertise, and training vary widely among epilepsy centers. What may be a good solution for our center may not be useful or feasible for others.

Nevertheless, this is compelling preliminary evidence that automated seizure detection software can play an important adjunctive role in safety and seizure detection in the EMU. SUDEP, well-known to be most strongly associated with FIAS and FBTCS, has an established risk of 1.2 per 10,000 video-EEG monitoring admissions [2]. With a median of 330 annual admissions at level four epilepsy centers in the US [24], a single center can expect one case of SUDEP approximately every 25 years. While the relative risk reduction of SUDEP for convulsive seizures associated with nursing care interventions is unknown, all of the cases of monitored SUDEP in the MORTEMUS study notably occurred with a delay to resuscitation from seizure termination of 18 min or more [2]. Seyal and colleagues further demonstrated that early periictal nursing interventions reduced the duration of respiratory dysfunction and post-ictal generalized EEG suppression, both thought to contribute to the pathophysiology of SUDEP [25]. An outpatient case-control study of SUDEP determined that precautions such as nighttime checks or a listening monitoring device were protective against SUDEP, with an odds ratio of 0.1 [26]. If improved monitoring and nursing response in the EMU were equally protective, then the SUDEP rate would theoretically fall to one case every 252 years in a single EMU. These are obviously imprecise estimates but should provide all EMUs, especially high-volume centers, with a strong motivation to improve safety and prevent this dreaded outcome.

5. Conclusion

What combination of automated detectors (seizure detection software, cardiac/oxygen telemetry, or wearable devices) that can best aid nurses in seizure recognition without providing overly burdensome false positive alarm rates remains unknown. Prospective rigorous studies utilizing various methods of monitoring, and ideally conducted in multiple EMUs, are needed to create more definitive safety recommendations and guidelines. While there can be a reluctance to publish one's own EMU data, further research in this area is necessary to ensure best patient safety practices.

Declarations of interest

None

Conflict of Interest and Authorship Conformation Form

- All authors have participated in (a) conception and design, or analysis and interpretation of the data; (b) drafting the article or revising it critically for important intellectual content; and (c) approval of the final version.
- This manuscript has not been submitted to, nor is under review at, another journal or other publishing venue.
- The authors have no affiliation with any organization with a direct or indirect financial interest in the subject matter discussed in the manuscript

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