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Seizures detection using multimodal signals: a scoping review

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Seizures detection using multimodal signals: a scoping review

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E-mail: fangyi.chen727@duke.edu**Keywords:** seizure, epilepsy, ML, wearable, sensors, detection, predictionSupplementary material for this article is available [online](#)**Abstract**

Introduction. Epileptic seizures are common neurological disorders in the world, impacting 65 million people globally. Around 30% of patients with seizures suffer from refractory epilepsy, where seizures are not controlled by medications. The unpredictability of seizures makes it essential to have a continuous seizure monitoring system outside clinical settings for the purpose of minimizing patients' injuries and providing additional pathways for evaluation and treatment follow-up. Autonomic changes related to seizure events have been extensively studied and attempts made to apply them for seizure detection and prediction tasks. This scoping review aims to depict current research activities associated with the implementation of portable, wearable devices for seizure detection or prediction and inform future direction in continuous seizure tracking in ambulatory settings. **Methods.** Overall methodology framework includes 5 essential stages: research questions identification, relevant studies identification, selection of studies, data charting and summarizing the findings. A systematic searching strategy guided by systematic reviews and meta-analysis (PRISMA) was implemented to identify relevant records on two databases (PubMed, IEEE). **Results.** A total of 30 articles were included in our final analysis. Most of the studies were conducted off-line and employed consumer-graded wearable device. ACM is the dominant modality to be used in seizure detection, and widely deployed algorithms entail Support Vector Machine, Random Forest and threshold-based approach. The sensitivity ranged from 33.2% to 100% for single modality with a false alarm rate (FAR) ranging from 0.096 to 14.8 d⁻¹. Multimodality has a sensitivity ranging from 51% to 100% with FAR ranging from 0.12 to 17.7 d⁻¹. **Conclusion.** The overall performance in seizure detection system based on non-cerebral physiological signals is promising, especially for the detection of motor seizures and seizures accompanied with intense ictal autonomic changes.

1. Introduction

An epileptic seizure is defined as transient symptoms due to the occurrence of abnormal electrical activity within the brain, and more than one unprovoked seizure occurring > 24 h apart or a single seizure with a high probability of recurrence is considered as epilepsy (Fisher *et al* 2014). Epilepsy is one of the most prevalent neurological disorders in the world, impacting around 65 million people of all ages globally (Mehndiratta and Wadhai 2015). Around 70% of epileptic cases can be controlled by the proper diagnosis and treatment; the remaining 30% of patients with epilepsy are medication refractory, a subset of whom may be controlled with surgery. Their unpredictability makes seizures extremely dangerous or even fatal, especially in an unsupervised environment. For example, the risk of sudden unexpected death in epilepsy (SUDEP), one of the common

causes of death among epileptic patients, is likely higher when there is a lack of attention and failure to provide urgent medical care, which may well explain a high risk of SUDEP during sleep periods at night (Nashef *et al* 1998, Lamberts *et al* 2012). Accidental injury/fatality related to seizures and SUDEP would potentially be reduced if caregivers and physicians could reliably know when a patient had a seizure. As a matter of fact, a continuous seizure detection and monitoring device is necessary in assisting caregivers and physicians to provide clinical support and diagnosis, thereby preventing severe seizure-related injuries and improving the quality of life for patients. Current options for seizure detection and monitoring are limited; for example, via video-EEG or ambulatory EEG, which are obtrusive and unsuitable for long-term continuous seizure monitoring outside clinical settings. A wearable device capable of acquiring non-cerebral physiological signals (ECG, EDA, EMG, acceleration, oxygen saturation etc) is an alternative method to overcome these barriers. Moreover, these non-cerebral manifestations may even precede the seizure onset as detected by scalp-EEG to forecast seizure events to allow for patients or caregivers to take early actions (Lacuey *et al* 2019).

Many studies have established the linkage between physiological signals obtainable in ambulatory settings and the occurrence of seizures (Ansakorpi *et al* 2000, Baumgartner *et al* 2001, Opherk *et al* 2002, Devinsky 2004). Seizures spreading to certain parts of central nervous system may alter normal autonomic function as they mimic the afferent action of the autonomic nervous system (ANS) (Devinsky 2004, Thijs 2019). The ANS is responsible for regulating involuntary physiological functions, such as heart rate, respiration, blood pressure, digestion, temperature, etc. Typically, the ictal or postictal state activates sympathetic nervous system, perceived as increased heart rate, blood pressure and breathing as well as facial flushing, pupillary dilatation (Devinsky 2004). It is also possible for parasympathetic system to be activated during ictal or preictal state, which leads to increased salivation, gastric acid secretion, decreased heart rates and blood pressure (Devinsky 2004). The systematic review conducted by Baumgartner's group presents a comprehensive overview of predominant ictal autonomic changes in cardiovascular, respiratory, gastrointestinal, cutaneous, pupillary and urinary aspects (Baumgartner *et al* 2001). Autonomic manifestations are often perceived in partial seizures but may sometimes remain unnoticed, resulting in a delayed or even missed diagnosis (Devinsky 2004). A potential high association has been reported between ictal central apneas (ICA) and focal epilepsy particularly mesial temporal lobe epilepsy (MTLE), and ICA can be the earliest clinical sign or even the sole manifestation of some seizures in MTLE (Lacuey *et al* 2019). Other biomarkers include but are not limited to changes of electrodermal activities (Vieluf *et al* 2020), inflammation-like responses (evaluated body temperature, white blood cell counts, or C-reactive protein levels) (Hong Seok *et al* 2016). These and other findings demonstrate the links between seizure and the ANS and have laid a solid foundation for developing algorithms to detect or predict seizure events based on physiological signals that can reflect status changes of the ANS. In addition, it can be anticipated that performance based on the single modality may not be optimal, but the integration of multimodalities would allow for more accurate seizure detection or prediction (van Westrhenen *et al* 2019).

A recently published International League Against Epilepsy (ILAE) guideline (Beniczky *et al* 2021) summarized wearable devices used for seizure detection as well as their performances, and seizure types recorded. The guideline targets on a specific group of audience, with a goal to inform and assist clinicians to utilize wearable devices for appropriate seizure type. In contrast, our paper has a wider audience targeting on clinicians, engineers, and researchers interested in algorithms behind, which caters to readers with various background and needs. Beyond that, we noticed that the guideline excluded some essential elements that are directly associated with the detection performance, such as extracted feature characteristics and deployed algorithms, which were captured and discussed by this scoping review. Another older and much shorter review paper (Leijten and Dutch TeleEpilepsy Consortium 2018) in the field selected 7 studies to summarize key algorithms and performance for seizure detection, limiting their scope to motor seizures that occur during nighttime and excluding the ones using single-modality signal, which also missed to document feature extraction processes and characteristics as well as the specific types of models being implemented. Instead, we included all relevant studies using wearable devices for routine seizure monitoring to better appreciate the variations across different types of seizures and how unimodal or multimodal devices affect performances. We believe that a more detailed description and analysis regarding the extracted features and algorithms would generate a comprehensive image of the current research activities in the field of ambulatory seizure detection/prediction and particularly help researchers in developing and advancing algorithms for seizure monitoring.

This scoping review is intended to provide a comprehensive mapping of current research activities associated with continuous seizure detection and monitoring solutions in ambulatory settings using wearable or implantable devices that are capable of recording physiological signals relevant to seizure detection. Several research questions were proposed and investigated: (i) what is known from current literature regarding the physiological signals used in ambulatory settings? (ii) what are the specifications of the devices used for recording these signals? (iii) what are the computational algorithms applied in processing signals? (iv) what is the performance of these algorithms? The anticipated outcome of the review is to inform the future direction in

Table 1. Database and keywords used in literature search.

| Electronic database | Searching keywords |
|---------------------|--|
| PubMed/IEEE | '(seizure* OR epileps*) AND (predict* OR monitor* OR alert* OR detect*) AND (device* OR wearable OR implant*)' |

continuous seizure detection or forecasting outside clinical settings and inspire further innovations in sustained seizure tracking based on the discussed signals.

2. Method

The scoping review was guided by the methodology framework proposed by Arksey and O'Malley (Levac *et al* 2010). During this work, five essential stages were identified in conducting scoping reviews, which involve identification of research question, identifying relevant studies, study selection, data charting and lastly summarizing and reporting the results.

2.1. Identify research question

To determine the applicable physiological signals and how they can be analyzed in seizure detection and monitoring in ambulatory settings and to provide a comprehensive summary of the relevant studies, the review was built upon four research questions:

- (1) What is known from current literature regarding the physiological/motor signals used in ambulatory settings?
- (2) What are the specifications of the devices being used for recording these signals?
- (3) What are the computational algorithms applied in the studies?
- (4) What is the performance of these algorithms?

2.2. Identify relevant studies

Literature search was performed in two databases: PubMed and IEEE (Institute of Electrical and Electronics Engineers). PubMed contains millions of published literatures in the field of biomedical and life science. To complement PubMed, IEEE is another source for identifying relevant studies with a focus on engineering and technology research. The keywords used for searching relevant articles are listed in table 1.

2.3. Selection of eligible studies

The selection process was guided by Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Page *et al* 2021). Identified articles went through several stages to be included in the scoping review. Two reviewers (FC and IC) performed double- blinded screening based on titles and abstracts to ensure that included articles were related to our topic. Senior authors (SRS and XH) were consulted to resolve any ambiguity or disagreement regarding whether to include specific articles. Articles were included if they met all of the following inclusion criteria:

- Related to seizure detection or prediction.
- Published between year 2011 and year 2021.
- Able to access full text.
- Used at least one physiological signal listed in table 2.
- Signals were collected using wearable or implantable devices.
- Algorithms were described in sufficient details.
- Clinical studies of either prospective or retrospective nature.

2.4. Data charting

The relevant information from the included articles was captured electronically in Microsoft Excel. A list of data elements that were extracted from each study is shown in table 3. We organized these elements into five

Table 2. Explanation of the commonly employed physiological signals in seizure detection/prediction.

| Physiological signals | Description |
|------------------------------|--|
| Electroencephalography (EEG) | Measurement in the change of electrical impulses in brain |
| Electrocardiogram (ECG) | Measurement of electrical activity of heartbeat |
| Accelerometry (ACM) | Quantification of movement changes in velocity and direction |
| Electrodermal activity (EDA) | Measurement of electrical conductance of skin in response to sweat |
| Electromyography (EMG) | Measurement of muscle activity |
| Photoplethysmography (PPG) | Utilize a light-based approach to sense the rate of blood flow |

Table 3. Lists of essential data elements captured from articles, organized in five categories.

| Categories of data elements | Data elements |
|-----------------------------|---|
| Study characteristics | <ul style="list-style-type: none"> • Study setting • Recorded status • Populations • Number of recruited and Number of analyzed • Length of recording • Reference/Ground Truth • Seizure types |
| Device characteristics | <ul style="list-style-type: none"> • Forms of implantation • Wearability/Ergonomic • Device brand • Data storage • Capacity on device |
| Signal characteristics | <ul style="list-style-type: none"> • Modality • Synchronization for multimodality • Sampling rate • Number of channels • Quality assessments and artifacts removal • Expert annotation with seizure onset/termination |
| Algorithm characteristics | <ul style="list-style-type: none"> • Intention • Real-time? • Feature domain • Algorithm • Patient-specific? |
| Performance | <ul style="list-style-type: none"> • Sensitivity • Accuracy • False alarm rate • Specificity • AUC • Positive predictive value |

categories: study characteristics, device characteristics, signal characteristics, algorithm characteristics, and algorithm performance. Most of the elements in the list are self-explanatory so we will focus on describing three more nuanced data elements: seizure type, feature domains, and performance metrics. Even though for ambulatory seizures detection/prediction tasks, the determination of seizure types is not the ultimate purpose, rather providing timely alerts when a seizure strikes regardless of the type. However, we included this element as to take the advantage of studies conducted at Epilepsy Monitoring Units (EMU)-based settings where seizure types are readily available. Such information would be helpful for researchers to develop seizure-specific algorithms as well as to provide insightful knowledge regarding the current choice of algorithms/modalities as related to seizure types. Besides, it helps to identify the groups of individuals suitable for using wearable devices for seizure monitoring, suggesting appropriate modalities and algorithms used for specific types of seizures.

Under the basic seizure classification guidelines proposed by ILAE, seizures can be categorized into three main groups based on onset: focal onset, generalized onset and unknown onset (Devinsky *et al* 2018). The

Table 4. Descriptions of data elements captured in performance category.

| Data elements | Description |
|---------------------------|--|
| Sensitivity | The number of seizures detected divided by the number of physician-annotated seizures |
| False alarm rate (FAR) | The number of false detections (normal activity classified as a seizure) over a certain period of time |
| Positive predictive value | The proportion of seizure cases that are correctly identified |
| Specificity | The proportion of actual non-seizure cases which are correctly identified |
| AUC | The area under the receiver operating characteristic (ROC) curve |

essential distinction between focal and generalized seizures is that, at onset, focal seizures affect only a region of the brain whereas generalized involve both hemispheres from the onset (Devinsky *et al* 2018). Focal onset seizures may spread from the region of onset to involve both hemispheres, in which case they are said to have become secondarily generalized. The category of unknown onset seizures is needed because it is not always possible to classify a seizure precisely based on the available clinical data. Focal (and unknown) onset can be further subdivided based on the presence or absence of impairment of awareness: focal with retained awareness (previously called simple partial seizures) and focal with impaired awareness (previously called complex partial seizures) (Devinsky *et al* 2018). All generalized onset seizures have impaired awareness. Depending on the type of seizures and the specific brain regions involved, the symptoms of seizures can be highly varied and can include motor (simple and complex), sensory, cognitive (confusion, loss of awareness), psychic and autonomic phenomenon (Stafstrom and Carmant *et al* 2015). For clinical classification purposes, the extent of motor symptoms is an important feature in assessing patients' conditions and examining potential treatment options with better outcomes. In the context of this paper, the recorded seizures were grouped in accordance with the classification guidelines proposed by ILAE (Fisher *et al* 2014), but with minor adjustments. We placed focal to bilateral tonic-clonic (FTBTC) into generalized-motor category, since the two types of seizure are highly similar clinically and can be hard to differentiate using non-EEG modality.

The feature domains were divided into 4 different categories (time, spatial, frequency, and nonlinear) to capture the feature characteristics being used for model construction. Time domain analysis depicts the changes in a physiological signal with respect to time, whereas for frequency domain features, the signals are quantified in given frequency bands. Spatial domain refers to the analysis in the variation for a signal across space. Lastly, nonlinear domain features include entropy, laminarity, recurrence rate, determinism and so on that aim to characterize dynamical evolution of the system that are presumably responsible for generating analyzed signals.

Different studies may choose to report different performance metrics. We therefore decided to capture all reported performance metrics including sensitivity, accuracy, false alarm rate, positive predictive value. Their corresponding definitions are given in table 4.

2.5. Collating, summarizing and reporting the results

Results collected from the data capture sheet were summarized in a narrative format along with data tabulation and visualization. To answer the proposed four research questions, results were grouped by the following categories (modality, device, applied algorithms, performance).

3. Results

The article selection procedure is depicted in figure 1. A total of 2927 records were initially identified. The initial search was concluded at the end of february 2021. During manuscript writing, additional citations drawn from related review articles and manual searching were screened to identify new articles to be included. We believe this update was necessary to ensure the timeliness of this review because the research in this field is accelerating. We thus identified five additional articles and a total of 30 articles were included.

As summarized from the included studies, current wearable devices for seizure detection or prediction heavily rely on ECG, ACM, EDA, EMG signals or various combinations of them. In 70% of studies, only a single modality was used to detect seizures with ACM being the most prevalent one and EDA never being used alone. Majority of recruited subjects were monitored on a continuous basis and around 83% of studies took place entirely in an inpatient EMU. Among all the modalities (table 6), many of the articles applied consumer-graded devices available in the market, analyzed data in an offline fashion, and focused on seizure detection. Many of them used video EEG (vEEG) as a gold standard to validate the developed algorithms. A comprehensive documentation for each article can be found in the supplementary materials (available online at stacks.iop.org/PMEA/43/07TR01/mmedia).

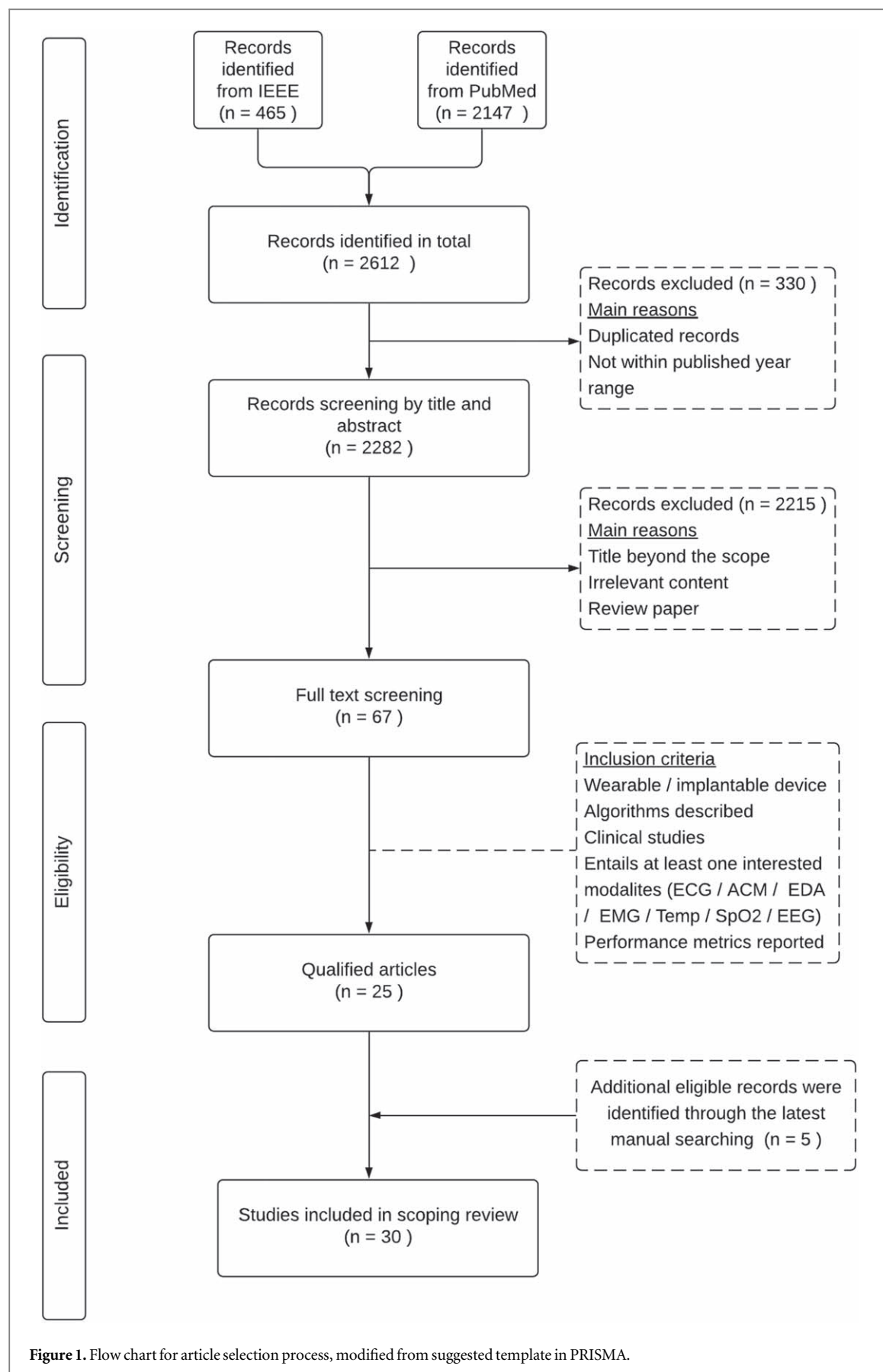


Figure 1. Flow chart for article selection process, modified from suggested template in PRISMA.

3.1. Study and device characteristics

table 7 shows findings according to the applied modalities and the target seizure types and device being used. Motor seizures (accompanied by some degree of involuntary muscle movements) were investigated and

Table 5. The mapping table for the 30 selected articles and the number ordering used in all tables in Results section, with respective references.

| Article number | Article title | Reference |
|----------------|--|-----------------------------------|
| 1 | Automated epileptic seizure detection based on wearable ECG and PPG in a hospital environment | Vandecasteele <i>et al</i> (2017) |
| 2 | Multimodal, automated detection of nocturnal motor seizures at home: Is a reliable seizure detector feasible? | van Andel <i>et al</i> (2017) |
| 3 | Multimodal nocturnal seizure detection in a residential care setting: a long-term prospective trial | Arends <i>et al</i> (2018) |
| 4 | Detection of seizure-like movements using a wrist accelerometer | Lockman <i>et al</i> (2011) |
| 5 | Measurement and quantification of generalized tonic-clonic seizures in epilepsy patients by means of accelerometry—An explorative study | Schulc <i>et al</i> (2011) |
| 6 | Automated real-time detection of tonic-clonic seizures using a wearable EMG device | Beniczky <i>et al</i> (2018) |
| 7 | Convulsive seizure detection using a wrist-worn electrodermal activity and accelerometry biosensor | Poh <i>et al</i> (2012) |
| 8 | Using wearable sensors for semiology-independent seizure detection—towards ambulatory monitoring of epilepsy | Heldberg <i>et al</i> (2015) |
| 9 | Multicenter clinical assessment of improved wearable multimodal convulsive seizure detectors | Onorati <i>et al</i> (2017) |
| 10 | Multi-biosignal analysis for epileptic seizure monitoring | Cogan <i>et al</i> (2016) |
| 11 | Seizure detection based on heart rate variability using a wearable electrocardiography device | Jeppesen <i>et al</i> (2019) |
| 12 | Wearable epileptic seizure prediction system with machine-learning-based anomaly detection of heart rate variability | Yamakawa <i>et al</i> (2020) |
| 13 | Evaluation of novel algorithm embedded in a wearable sEMG device for seizure detection | Conradsen <i>et al</i> (2012) |
| 14 | Ear-EEG detects ictal and interictal abnormalities in focal and generalized epilepsy—a comparison with scalp EEG monitoring | Zibrandtsen <i>et al</i> (2017) |
| 15 | Detection of generalized tonic-clonic seizures from ear-EEG based on EMG analysis | Zibrandtsen <i>et al</i> (2018) |
| 16 | Detection of generalized tonic-clonic seizures using surface electromyographic monitoring | Halford <i>et al</i> (2017) |
| 17 | A prospective, multicenter study of cardiac-based seizure detection to activate vagus nerve stimulation | Boon <i>et al</i> (2015) |
| 18 | Seizure detection using heart rate variability: a prospective validation study | Jeppesen <i>et al</i> (2020) |
| 19 | Detection of generalized tonic-clonic seizures by a wireless wrist accelerometer: a prospective, multicenter study | Beniczky <i>et al</i> (2013) |
| 20 | Accelerometry-based home monitoring for detection of nocturnal hypermotor seizures based on novelty detection | Cuppens <i>et al</i> (2014) |
| 21 | Tracking generalized tonic-clonic seizures with a wrist accelerometer linked to an online database | Velez <i>et al</i> (2016) |
| 22 | Spectral analysis of acceleration data for detection of generalized tonic-clonic seizures | Joo <i>et al</i> (2017) |
| 23 | User-based evaluation of applicability and usability of a wearable accelerometer device for detecting bilateral tonic-clonic seizures: a field study | Meritam <i>et al</i> (2018) |
| 24 | Tonic-clonic seizure detection using accelerometry-based wearable sensors: a prospective, video-EEG controlled study | Johansson <i>et al</i> (2019) |
| 25 | Automated detection of convulsive seizures using a wearable accelerometer device | Kusmakar <i>et al</i> (2019) |
| 26 | Machine learning from wristband sensor data for wearable, noninvasive seizure forecasting | Meisel <i>et al</i> (2020) |
| 27 | Computationally-efficient Algorithm for Real-Time Absence Seizure Detection in Wearable Electroencephalography | Dan <i>et al</i> (2020) |
| 28 | Detection of generalized tonic clonic seizures and falls in unconstraint environment using smartphone accelerometer | Zia <i>et al</i> (2021) |
| 29 | Non-invasive wearable seizure detection using long-short-term memory networks with transfer learning. Journal of neural engineering | Nasseri <i>et al</i> ((2021) |
| 30 | Seizure detection using wearable sensors and machine learning: setting a benchmark | Tang <i>et al</i> (2021) |

analyzed in every chosen article, except for some using ECG and PPG-based modality. Motor seizures can be further divided into focal-onset (originate in one hemisphere) and generalize-onset (originate on both sides). Focal-onset category contains temporal lobe seizure ($n = 2$) (please refer to table 5 [1], [15]), focal-impaired awareness ($n = 3$) (please refer to table 5 [10], [18], [25]), focal motor (hyper-motor, hyperkinetic) (please refer to table 5 [2], [3], [8]). Generalized tonic-clonic (GTC) seizure fell under the subcategory of generalize-onset, which was recognized as one prevalent seizure type investigated by 50% of the articles. For motor seizures, perceived as intense body motion, accelerometry is one frequently used modality to quantify acceleration and vibration of a subject's actions. Currently, there are many devices available in the market for acquiring such

Table 6. Essential data elements shared by the included studies.

| Characteristics | ECG | | ACM | | EDA | | EMG | | EEG | | Multi-modality | |
|---|----------|-----|----------|-----|----------|---|----------|-----|----------|-----|----------------|-----|
| | <i>n</i> | % | <i>n</i> | % | <i>n</i> | % | <i>n</i> | % | <i>n</i> | % | <i>n</i> | % |
| In patients only | 5 | 100 | 8 | 80 | — | — | 3 | 100 | 2 | 67 | 6 | 67 |
| Mixed subjects: adults and pediatric recording > 24 h daily | 2 | 40 | 4 | 40 | — | — | 3 | 100 | — | — | 4 | 44 |
| | 4 | 80 | 6 | 60 | — | — | 3 | 100 | 3 | 100 | 7 | 78 |
| Multiple seizure types analyzed | 3 | 60 | 1 | 10 | — | — | — | — | 1 | 33 | 7 | 78 |
| Reference: Video-EEG | 5 | 100 | 9 | 90 | — | — | 3 | 100 | 3 | 100 | 7 | 78 |
| Consumer graded device | 4 | 80 | 10 | 100 | — | — | 3 | 100 | — | — | 9 | 100 |
| Artifact removal | 5 | 100 | 7 | 70 | — | — | — | — | 3 | 100 | 6 | 67 |
| Detection purpose | 5 | 100 | 10 | 100 | — | — | 3 | 100 | 3 | 100 | 8 | 89 |
| Threshold-based algorithm | 3 | 60 | 4 | 40 | — | — | 3 | 100 | 2 | 67 | 2 | 22 |
| Other algorithms | 2 | 40 | 6 | 60 | — | — | — | — | 1 | 33 | 7 | 78 |
| Off-line processed | 3 | 60 | 6 | 60 | — | — | 1 | 33 | 2 | 67 | 9 | 100 |
| Non-patient specific | 1 | 20 | 1 | 10 | — | — | — | — | 3 | 100 | 7 | 78 |

*Note: the percentage represents the ratio between number of articles in each modality with such characteristic and the total number of studies utilized that modality, round up to the nearest integer.

accelerometer signals, such as *SmartWatch* developed by Smart Monitor Inc., Nintendo, Epic-Care Free and Shimmer etc. Another common modality targeting generalized motor seizures is EMG. However, the acquisition of EMG signals typically requires several electrodes inserting into the skin, which could be painful for patients. We found 3 eligible studies (please refer to table 5 [6], [13], [16]) based on surface EMG (sEMG) modality that enables noninvasive monitoring. ECG or PPG-based modality is favorable in detecting seizure without accompanying intense motion, where the common acquisition device is *Epatch*, and wearable sensors developed by *Empatica*. We also compared the differences in choice of devices among the studies grouped by seizure types (non-motor, motor, mixtures), shown in table 9.

The average recording length for each brand of device is reported in table 8. The examination of user experience and data transmissions, if mentioned by the studies, were also recorded. Most of average recording length for the device were greater than 2 months, with the exception of three devices (*Nintendo*, *AspireSR* and *Cyberonics*). Within the scope of these studies, 7 brands of device acquired the interested physiological signals for more than 6 months. Majority of these wearable sensors are easy to implement without special training and assistance, and a few devices (e.g. Shimmer, custom-built: designed and built for research purpose, not available in commercial markets) reported connectivity issues during recording periods. Four studies (please refer to table 5 [11], [14], [16], [23]) reported adverse effects and they include the following: skin irritation, ear-discomfort (for wearable ear-EEG device), sweltering. Both *ePatch*, *Brain Sentinel* and *Epic-Care Free* were reported to cause some mild to moderate skin irritation after using the device (please refer to table 5 [11], [16], [23]). Zibbrandsten *et al* constructed a wearable ear-EEG sensor that required an expert assistant to place within the outer portion of the external meatus, where the majority of the patients complained of increasing tenderness and soreness in the external ear.

3.2. Algorithm

Algorithm 1(a) and 1(b) summarize the main algorithms from the articles organized by the seizure types, along with the corresponding modalities and feature domains. Time domain features derived from acquired signals were widely deployed in model construction, followed by frequency domain features. Fewer studies ($n = 4$) (please refer to table 5 [7], [8], [9], [20]) utilized nonlinear features (entropy, laminarity, deterministic and so on) in their algorithms. For ECG, the common features are HR, average HR, various metrics based on heart rate variability (HRV) analysis, cardiac sympathetic index (CSI), cardiac vagal index (CVI), laminarity, etc. Regarding EDA modality, the calculated features normally capture the variation in skin conductance response and skin conductance level between current and previous segments, which mostly reside in time domain category. Conversely, classifiers based on EMG and ACM signals often used frequency domain features, such as amplitude under high frequency (> 150 Hz). Half of these studies utilized threshold-based algorithms in which they determined the optimal passing value and duration for a case to be considered as an epileptic seizure event. In

Table 7. Summary of analyzed seizure types and employed devices in each study grouped by modality used, with article number and counts specified.

| Modality | | Targeted seizures | | Device brand | Studies |
|-----------------|---------------------------------|-------------------|--------------|--------------------------------|--|
| | | Seizure | # of Studies | | |
| Single-modality | ECG | Focal Onset | 2 | Faros | [1, 11, 12, 17, 18] |
| | | Generalized Onset | 3 | | |
| | PPG ACM | NCS | 1 | Epatch ($n = 2$) | [1] [4, 5, 19–22, 23 ^a , 24], [25, 28] ^a |
| | | iTC | 1 | AspireSR | |
| | | Focal Onset | 1 | Cyberonics | |
| | | | | Empatica | |
| | | | | Smart Monitor ($n = 3$) | |
| | | Generalized Motor | 9 | Nintendo | |
| | EDA EMG | | | Epi-Care Free ($n = 2$) | [6, 13, 16] |
| | | | | Apple iPod Touch | |
| | | | | RISE Acreo | |
| | | Focal Onset | 1 | Shimmer | |
| | | | | Custom- built | |
| | | — | — | — | — |
| | | Generalized Motor | 3 | IctalCare ($n = 2$) | [6, 13, 16] |
| | | | | Brain Sentinel ($n = 1$) | |
| | EEG | Generalized Motor | 2 | Custom-built ($n = 2$) | [14, 15, 27] ^a |
| | | Focal Onset | 1 | Medatec (BrainWalker 3) | |
| | | Generalized Onset | 1 | | |
| Multi-modality | ECG and ACM | Generalized Motor | 1 | Shimmer | [2] |
| | | Focal Motor | 1 | | |
| | | Clusters | 1 | | |
| | | | | | |
| | PPG and ACM | Generalized Motor | 1 | LivAssured BV | [3] ^a |
| | | Focal Motor | 1 | | |
| | | Clusters | 1 | | |
| | | | | | |
| | ACM and EDA | Generalized Motor | 2 | Custom- built ($n = 1$) | [7–9] |
| | | | | Empatica ($n = 2$) | |
| | | | | iCalm from MIT Lab ($n = 1$) | |
| | | | | | |
| | EDA and HR and SPO2 and EEG | Focal Motor | 1 | | [10] |
| | | Focal Non-motor | 1 | | |
| | | Generalized motor | 1 | Nonin (WristOX2) | |
| | | | | Affectiva (Q- Curve sensor) | |
| | EDA and ACM and BVP and TEMP | Focal Onset | 1 | | [26, 29 ^a , 30] |
| | | Generalized Onset | 1 | Empatica ($n = 3$) | |
| | | Generalized Motor | 1 | | |
| | | All types | 2 | | |

^a Study conducted under ambulatory settings: (please refer to table 5 [3, 23, 27, 28, 29]).

*Focal-onset seizure: Temporal lobe seizure (TLE), Focal impaired awareness (FIA), Focal-motor: Hyper-motor (HM), Focal hyperkinetic (HK).

*Generalized-onset seizure: Idiopathic generalized epilepsy (IGE), Generalized-motor: Tonic-clonic seizure (TC), Generalized tonic-clonic seizure (GTC), Focal to bilateral tonic-clonic (FTBTC), Generalized tonic (GT), Bilateral-tonic (BT).

*Non-convulsive seizures (NCS), ictal tachycardia (iTC) seizure.

particular, the compared metrics involved the rise of HR, numbers of high amplitude and frequency oscillations denoted as the number of zero crossing, duration for such increment and so on. Besides, 2/3 of the selected articles performed off-line processing, and a large portion of the real-time classifiers fell under the threshold-based algorithm that mostly targeted motor seizure events. In addition, a few articles ($n = 5$) (please refer to table 5 [10], [12], [14], [20], [27]) constructed patient-specific algorithms, where one of them was semi-patient specific (Arends *et al* 2018) model which was trained not only by the individual's data but others as well. Traditional machine learning algorithms (support vector machine, random forest, k-nearest-neighbor, etc)

Table 8. Comparison of durability and usability among all collected device brand^a.

| Device brand | Recording Length | | | | Usability | | |
|-------------------------------------|------------------|----------------------|--------------|------------|-----------------|-------------------------|-------------------------|
| | <= 10 days | 11 days ~ 1.5 Months | 2 ~ 6 Months | > 6 Months | User – friendly | Disconnections Reported | Adverse Effect Reported |
| <i>Empatica (E3,E4)</i> | | | | ✓ | ✓ | | |
| <i>Shimmer</i> | | ✓ | | | ✓ | ✓ | |
| <i>Smart Monitor (SmartWatch)</i> | | | ✓ | | ✓ | ✓ | |
| <i>Nintendo (Wii remote sensor)</i> | ✓ | | | | ✓ | | |
| <i>IctalCare (EDDI)</i> | | | ✓ | | ✓ | | |
| <i>iCalm from MIT Media Lab</i> | | | | ✓ | ✓ | | |
| <i>Nonin (WristOX2)</i> | | ✓ | | | ✓ | | |
| <i>Affectiva (Q-Curve sensor)</i> | | ✓ | | | ✓ | | |
| <i>ePatch</i> | | | ✓ | | ✓ | | ✓ |
| <i>LivAssured BV</i> | | | | ✓ | ✓ | | |
| <i>Brain Sentinel</i> | | | | ✓ | ✓ | | ✓ |
| <i>AspireSR</i> | ✓ | | | | | | |
| <i>Cyberonics</i> | ✓ | | | | | | |
| <i>Medatec (BrainWalker 3)</i> | | ✓ | | | | | |
| <i>Epi-Care Free</i> | | | | ✓ | ✓ | | ✓ |
| <i>RISE Acreo</i> | | | | ✓ | ✓ | | |
| <i>Apple iPod touch</i> | | | | ✓ | ✓ | | |
| <i>Custom-Built</i> | | | ✓ | | | ✓ | ✓ |

^a User- friendly: easy implementation of device without special trainings or assistance from experts.

appear to be dominant in the field of seizure detection. Nevertheless, deep learning recently started to emerge in performing seizure classification tasks or prediction using the data acquired from wearable devices, where 1D convolutional neural network and long short-term memory (LSTM) recurrent neural network were applied frequently. One recent study by Nasser *et al* implemented a LSTM model which was initially built from intracranial EEG (iEEG) data from 7 patients and adaptively trained by data acquired from wearable sensors developed by *Empatica* using a transfer learning approach. This study addressed the issue of deficiency of seizure data and minimized the amount of time in training LSTM model by taking the advantage of iEEG signal from both EMU patients and outpatients and reusing it for multimodal signals (ACM, EDA, BVP, Temp). Apart from that, visual inspection heavily relies on humans' empirical judgement and knowledge to determine seizure events, which were used in 2 articles using EEG and ear-EEG based modality (please refer to table 5 [14], [15]). To establish and validate the feasibility and reliability of using ear-EEG as a seizure detection tool, Zibbrandtsen's group manually inspected the acquired data and performed spectral analysis to compare the gold-standard vEEG and ear-EEG (Zibbrandtsen *et al* 2017, Zibbrandtsen *et al* 2018).

Algorithm 1a. Summary of input signal modality, extracted feature domain, real-time compatibility and patient specificity for each algorithm, specified by article number. Studies were motor seizure only^a.

| Algorithm | Modality | Feature Domain | | | Real-time Analysis | Patient-Specific | Studies |
|-------------------|------------------------------|----------------|-----------|-----------|--------------------|------------------|------------------------------------|
| | | Time | Frequency | Nonlinear | | | |
| SVM | ACM | ✓ | ✓ | - | - | - | [24], [28] ^a |
| | ACM ACM & EDA | ✓ | ✓ | ✓ | - | [7] | [7], [9], [20] |
| Random Forest | ACM | ✓ | ✓ | - | - | - | [24], [28] ^a |
| kNN | ACM | ✓ | ✓ | - | - | - | [24] |
| Threshold-Based | ACM | ✓ | - | - | [19] | - | [5], [19] |
| | ACM EMG / sEMG | - | ✓ | - | [6], [21] | - | [6], [16], [21], [23] ^a |
| | EMG | ✓ | ✓ | - | ✓ | - | [13] |
| Event Searching | ACM | ✓ | ✓ | - | ✓ | - | [4] |
| 1D CNN | EDA & ACC & BVP & TEMP | - | - | - | - | - | [26], [30] |
| RNN: LSTM | EDA & ACC & BVP & TEMP | - | - | - | - | - | [29] ^a |
| Visual Inspection | EEG Ear-EEG | ✓ | - | - | - | ✓ | [14] |
| Spectral Analysis | ACM | ✓ | ✓ | - | - | - | [22] |

^a Study conducted under ambulatory settings: [23, 28, 29].

Algorithm 1b. Summary of input signal modality, extracted feature domain, real-time compatibility and patient specificity for each algorithm, specified by article number. Study were focusing on mixed types seizures^a.

| Algorithm | Modality | Feature Domain | | | Real-time Analysis | Patient-Specific | Studies |
|--|--|----------------|-----------|-----------|--------------------------------------|-------------------|---|
| | | Time | Frequency | Nonlinear | | | |
| SVM | ECG PPG ACM | ✓ | - | - | - | - | [1], [25] |
| Random Forest | ACM & EDA | ✓ | ✓ | ✓ | - | - | [8] |
| kNN | ACM & EDA | ✓ | ✓ | ✓ | - | - | [8] |
| Threshold-Based | ECG ACM EEG / iEEG ECG & ACM PPG & ACM | ✓ | - | - | [3] ^a , [27] ^a | [27] ^a | [2], [3] ^a [11], [15], [18], [27] ^a |
| Event Searching | EDA & HR & SPO2 & EEG | ✓ | - | - | - | ✓ | [10] |
| Multivariate Statistical Process Control | ECG | ✓ | - | - | ✓ | ✓ | [12] |
| RNN: LSTM | EDA & ACC & BVP & TEMP | - | - | - | - | - | [26], [29] ^a |

^a Study conducted under ambulatory settings: [3, 27, 29].

Table 9. Summary of seizure types, modality, and wearable device.

| Seizure type | Modality | Device brand | Studies |
|------------------|---------------|-------------------------------------|---|
| Motor | ACM | <i>Smart Monitor</i> ($n = 3$) | [4, 5, 19, 20, 21] |
| | | <i>Nintendo</i> ($n = 1$) | [22, 23] ^a , [24, 28] ^a |
| | | <i>Epi-Care Free</i> ($n = 2$) | |
| | | <i>Shimmer</i> ($n = 1$) | |
| | | Other brands ($n = 1$) | |
| | ACM + EDA | <i>Custom-built</i> ($n = 1$) | [7, 9] |
| | | <i>Empatica</i> ($n = 1$) | |
| | | <i>iCalm</i> ($n = 1$) | |
| | Ear- EEG | <i>Custom-built</i> | [14] |
| | EMG / sEMG | <i>Ictal Care</i> ($n = 2$) | [6, 13, 16] |
| | | <i>Brain Sentinel</i> ($n = 1$) | |
| Non-Motor | ECG | <i>AspireSR</i> ($n = 1$) | [17] |
| | | <i>Cyberonics</i> ($n = 1$) | |
| | | | |
| Mixture | ACM | <i>Apple iPod touch</i> ($n = 1$) | [25] |
| | Ear-EEG | <i>Custom-built</i> ($n = 1$) | [15] |
| | ECG | <i>ePatch</i> ($n = 2$) | [1, 11, 12] |
| | | <i>Farps</i> ($n = 1$) | |
| | PPG | <i>Empatica</i> ($n = 1$) | [1] |
| | EEG | <i>Medatec (BrainWalker 3)</i> | [27] ^a |
| | Multimodality | <i>Empatica</i> ($n = 4$) | [2, 3 ^a , 8, 10, 18, 26, 29 ^a , 30] |
| | | <i>Shimmer</i> ($n = 1$) | |
| | | <i>LivAssured BV</i> ($n = 1$) | |
| | | <i>Nonin (WristOX2)</i> ($n = 1$) | |

^a Study conducted under ambulatory settings: [3, 23, 27]. [28, 29].

3.3. Performance

Table 10(a) reports the distribution of motor seizure studies categorized by different algorithms used, and based on three key performance metrics, sensitivity, FAR and PPV, whereas table 10b reports performances for mixture seizure studies. Within the scope of these studies, all 30 of them reported sensitivity as one of the performance metrics. In addition, 27 studies reported FAR and 15 studies reported PPV, with each study reporting at least one of the two metrics. To compile results, if the study involved multiple models of the same algorithm, the best performance is reported. If a model was tested on multiple patient groups, the average performance is given.

Across all studies, the range of sensitivity spans from 47% to 100%, FAR varies from 0 to 43.2 d⁻¹, and PPV ranges from 2.15% to 100%. Twenty-two out of the 30 studies achieved sensitivity above 80%, and 21 out of 27 studies reported FAR below 5 d⁻¹. Regarding threshold-based algorithms, 12 out of 14 studies achieved sensitivity higher than 85%, among which 1/3 reached 100% sensitivity. However, the lowest sensitivity of threshold-based algorithm was 57.14% from a surface-EMG study which had a small sample size of 7 seizures from five patients, resulting in a standard deviation of 0.125. Meanwhile, 8 of the 13 threshold-based studies reported false alarm rate less than 1 d⁻¹, with a range of 0 to 17.7 d⁻¹ and a standard deviation of 5.41. The only threshold-based study (Zibrandtsen *et al* 2018) that did not use FAR as a metric reported a PPV value of 95% instead. As for studies using SVM algorithm (please refer to table 5 [1], [7], [9], [20], [24], [25], [28]), five out of the seven had sensitivities above 90%, and the other two had sensitivities between 70% and 80%, resulting in a smaller standard deviation of 0.109. Among the seven studies using SVM as the classifier, more than half reported FAR less than 1 d⁻¹, whereas highest FAR is 43.2 d⁻¹ from Vemdecastele *et al*'s study based on PPG signal, so the standard deviation of FAR in SVM classifiers is 19.01. For Random Forests, all three studies (please refer to table 5 [8], [24], [28]) achieved sensitivities above 80% and one of them scored 100% in both sensitivity and PPV (Zia *et al* 2021). Heldberg *et al*'s study evaluated both Random Forest and kNN models on EDA and ACM signals: kNN had 89.1% sensitivity and 93.1% specificity while Random Forest had 87.3% sensitivity and 95.2% specificity. Studies using event-searching algorithms and visual inspections mostly had low FAR below 1 d⁻¹ and low sensitivities below 80% (please refer to table 5 [10], [14]).

Figures 2(a) and (b) show the correlation between the two most commonly reported performance metrics among all studies. The 25 studies that reported both sensitivity and FAR are plotted separately by seizure types (motor and mixture seizure) as two scatterplots of respective article numbers positioned by both metrics. Figure 2(a) has a much smaller range of FAR than figure 2(b), indicating that motor seizure studies tend to have

Table 10a. Summary of three most reported performance metrics for motor seizure studies, categorized by algorithms used^a.

| Algorithm | Sensitivity | | | FAR | | | PPV | | |
|--------------------------|-------------------|-------------------|--------------------------|--------------------------------|----------------------------|-------------------------------|------------------|--------------------------|-------------------|
| | <i>Below 80%</i> | <i>80%–95%</i> | <i>Above 95%</i> | <i>Above 10 d⁻¹</i> | <i>1–10 d⁻¹</i> | <i>Below 1 d⁻¹</i> | <i>Below 10%</i> | <i>10%–90%</i> | <i>Above 90%</i> |
| <i>Threshold-based</i> | [13] | [6, 19, 21] | [5, 16, 23] ^a | — | [16, 21] | [6, 13, 19, 23] ^a | [16] | — | [5] |
| <i>SVM</i> | [28] ^a | [7, 9, 24] | [20] | — | [7] | [9, 24] | — | [9, 20, 28] ^a | — |
| <i>Random forest</i> | — | [24] | [28] ^a | — | — | [24] | — | — | [28] ^a |
| <i>kNN</i> | — | [8] | [24] | — | [24] | — | — | — | — |
| <i>Event searching</i> | — | [4] | — | — | [4] | — | — | — | — |
| <i>Visual inspection</i> | [14] | — | — | — | — | [14] | — | — | [14] |
| <i>MSPC</i> | — | — | — | — | — | — | — | — | — |
| <i>Spectral analysis</i> | — | — | [22] | — | [22] | — | — | [22] | — |
| <i>LSTM</i> | — | [29] ^a | — | — | [29] ^a | — | — | — | — |

^a Study conducted under ambulatory settings: [23, 28, 29].

Table 10b. Summary of three most reported performance metrics for mixtures seizure studies, categorized by algorithms used^a.

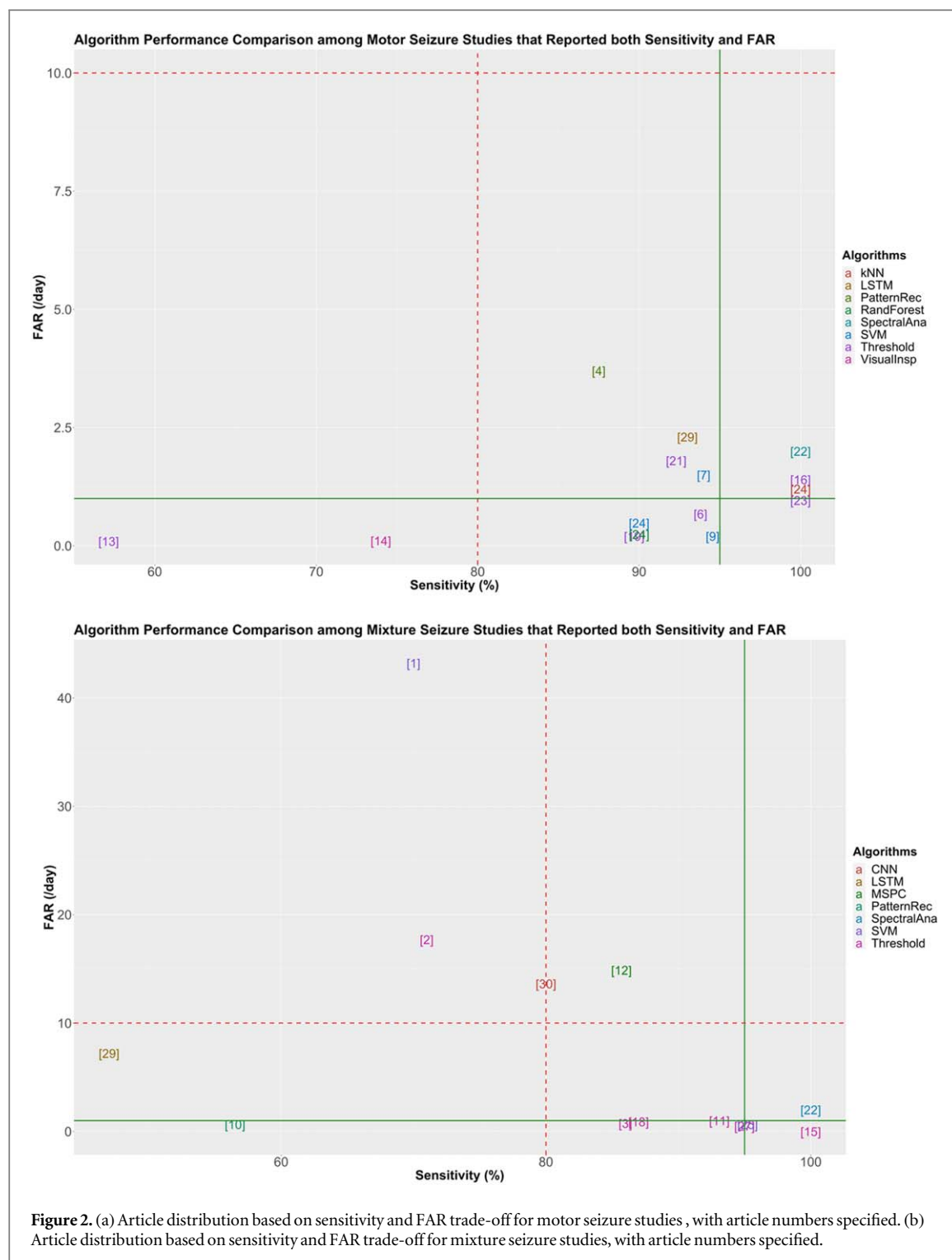
| Algorithm | Sensitivity | | | FAR | | | PPV | | |
|--------------------------|-------------------|--------------------------|-----------------------|--------------------------------|----------------------------|--|------------------|-------------------------|------------------|
| | <i>Below 80%</i> | <i>80%–95%</i> | <i>Above 95%</i> | <i>Above 10 d⁻¹</i> | <i>1–10 d⁻¹</i> | <i>Below 1 d⁻¹</i> | <i>Below 10%</i> | <i>10%–90%</i> | <i>Above 90%</i> |
| <i>Threshold-based</i> | [2] | [3, 11, 18] ^a | [15, 27] ^a | [2] | [11] | [3 ^a , 15, 18, 27] ^a | — | [2, 3, 18] ^a | — |
| <i>SVM</i> | [1] | — | [25] | [1] | — | [25] | [1] | [25] | — |
| <i>Random forest</i> | — | [8] | — | — | — | — | [8] | — | — |
| <i>kNN</i> | — | — | — | — | — | — | [8] | — | — |
| <i>Event searching</i> | [10] | — | — | — | — | [10] | — | — | — |
| <i>Visual inspection</i> | — | — | — | — | — | — | — | — | — |
| <i>MSPC</i> | — | [12] | — | [12] | — | — | — | — | — |
| <i>Spectral analysis</i> | — | — | — | — | — | — | — | — | — |
| <i>CNN</i> | [26] | [30] | — | [30] | — | — | — | — | — |
| <i>LSTM</i> | [29] ^a | — | — | — | [29] ^a | — | — | — | — |

^a Study conducted under ambulatory settings: [3], [27], [29].

lower FARs in comparison to mixture seizure studies. In addition, motor seizure studies also had higher sensitivities (13 out of 15 studies reported sensitivity above 85% and FAR below 5 d⁻¹), achieving an overall better performance.

table 11 summarizes the model performance metrics grouped by modality used by each study. Among studies using single modality, ECG had the tightest sensitivity range of 85.7%–93.1% as well as largest FAR range from 0.58 to 14.88 d⁻¹. Vandecasteele *et al*'s study is the only study that used PPG signal alone, and it scored a sensitivity of 33.2% and a FAR of 43.2 d⁻¹. There is no study using EDA signal alone for seizure detection yet. Studies using EMG and EEG reported sensitivities with a broad distribution from 50% to 100%, and FAR below 2 d⁻¹ on average. Among the 9 multi-modality studies (please refer to table 5 [2], [3], [7], [8], [9], [10], [26], [29], [30]), 7 of them have reported sensitivity whereas 4 also reported FAR. Three studies (please refer to table 5 [7], [8], [9]) used ACM and EDA combined signals and all achieved sensitivity between 85% and 95%, with FARs below 1 d⁻¹. The study [3] using ACM-PPG combined modality had similar performances, with 85% sensitivity and 0.12 d⁻¹ FAR. Cogan *et al*'s study using EDA, HR, SPO2 and EEG was able to achieve 100% sensitivity and reported specificity between 73% and 100%.

Table 12 summarizes the model performance metrics for different seizure types and modalities. Among all articles, 16 studies involved only motor seizures, including 13 GTCS (generalized tonic-clonic seizure) studies (please refer to table 5 [4], [5], [6], [7], [9], [13], [14], [16], [19], [20], [21], [22], [28]) and 9 studies based on ACM modality (please refer to table 5 [4], [5], [19], [20], [21], [22], [23], [24], [28]). These motor seizure studies overall achieved sensitivities above 73% and false alarm rates below 3.7 d⁻¹. Specifically, for studies detecting GTCS, the range of sensitivity is 83.64%–100% and the range of FAR is 0–1.8 d⁻¹. The study (please refer to table 5 [17]) on cardiac-based seizure detection (Boon *et al* 2015) analyzed only non-motor types of seizure and achieved a sensitivity of 80% and false positive rates from 0.5 to 7.2 h⁻¹ for all model settings, among which it reported best



performance of 100% sensitivity and 0.49 h^{-1} FAR for the ictal tachycardia (iTC) seizure type. The rest of studies ($n = 14$, listed in 'Mixture' section of table 4) tested models on a mixture of motor and non-motor seizures, including TLE (temporal lobe epilepsy), focal seizures, dialeptic seizures, etc. The mixture studies reported detection accuracies evaluated on all types of seizure, where the sensitivities ranged from 32% to 100% and the FAR ranged from 0 to 50 d^{-1} .

Drawing from table 13, no significant difference in performance between ambulatory and EMU settings was found. In addition, there seems to be no preference on the selection of feature characteristics and algorithms under different study settings. However, it would require more evidence to corroborate the above finding, given that a limited number of ambulatory studies (please refer to table 5 [3], [23], [27], [28], [29]) were included in this analysis. Thus, we were ineligible to draw any conclusions in terms of the differences between studies under ambulatory and EMU settings.

Table 11. Summary of algorithm performance ranges, compared across different modalities.

| Modality | | Sensitivity | False alarm rate | Specificity | PPV |
|------------------------|--------------------|-----------------|-------------------------------|---------------|-------------|
| Single Modality | ECG | [85.7%–93.1%] | [0.58–14.88 d ⁻¹] | — | [2.15%] |
| | PPG | [33.2%] | [43.2 d ⁻¹] | — | [1.12%] |
| | ACM | [87.5%–100%] | [0.2–2 d ⁻¹] | [99%] | [40%–100%] |
| | EDA | — | — | — | — |
| | EMG | [50%–100%] | [0.096–2.25 d ⁻¹] | [11%–20%] | — |
| | EEG | [56%–100%] | [0.5–2.25 d ⁻¹] | [87%–100%] | — |
| Multi-Modality | ACM, PPG | [85%] | [0.12 d ⁻¹] | — | [56%] |
| | ACM, EDA | [83.64%–94.55%] | [0.29 d ⁻¹] | [93.1%–95.2%] | [7.5%–8.2%] |
| | ACM, ECG | [71%] | [17.7 d ⁻¹] | — | — |
| | EDA, ACC, BVP, EMP | [51.2%] | — | — | — |
| | EDA, HR, SPO2 | [100%] | — | [73%–100%] | — |

Table 12. Summary of algorithm performance group by seizure type.

| Seizure Type | Modality | Performance | | | |
|--------------------------|---------------------|-----------------|--------------------------------|---------------|---|
| | | Sensitivity | False alarm rate | PPV | Article |
| Motor | ACM | [87.5%–100%] | [0.2–3.7 d ⁻¹] | [60.04%–100%] | [4, 5, 19, 20, 21, 22, 23 ^a , 24, 28] ^a |
| | EMG | [76%–100%] | [0–2.24 d ⁻¹] | [11%–20%] | [6, 13, 16] |
| | EEG | [73.6%–92%] | [0.1 d ⁻¹] | [92.59%] | [14] |
| | ACM, EDA | [83.64%–94.55%] | [0.2–1.5 d ⁻¹] | [39%–51%] | [7, 9] |
| | ACM, EDA, BVP, TEMP | [93%] | [2.3 d ⁻¹] | — | [29] ^a |
| Non-motor Mixture | ECG | [81.8%–100%] | [11.76–172.8 d ⁻¹] | — | [17] |
| | ACM | [95.23%] | [0.64 d ⁻¹] | [40%] | [25] |
| | ECG | [38.9%–87%] | [0.58–50 d ⁻¹] | [2.15%–86.2%] | [1, 11, 12, 18] |
| | EEG | [95%–100%] | [0–0.5 d ⁻¹] | — | [15, 27] ^a |
| | PPG | [32%] | [43.2 d ⁻¹] | [1.12%] | [1] |
| | ACM, ECG | [71%] | [17.7 d ⁻¹] | [50%] | [2] |
| | ACM, PPG | [86%] | [0.75 d ⁻¹] | [49%] | [3] ^a |
| | ACM, EDA | [89.1%] | — | [7.5%] | [8] |
| | EDA, HR, SPO2, EEG | [57%] | [0.64 d ⁻¹] | — | [10] |
| | ACM, EDA, BVP, TEMP | [47%–80%] | [7.3–13.63 d ⁻¹] | — | [26, 29 ^a , 30] |
| | | | | | |

^a Study conducted under ambulatory settings: [3, 23, 27]. [28, 29].

4. Discussion

Typically, definitive diagnoses and detection of epileptic seizures, along with some clinical interventions and treatments, require continuous long-term EEG monitoring of patients, which could be quite expensive, cumbersome, and significantly restrain the mobility of patients, making it infeasible for use outside clinical settings. Given the fact that the association between physiological signals related to the ANS and certain seizure manifestations has been well established (Ansakorpi *et al* 2000, Baumgartner *et al* 2001, Opherke *et al* 2002, Devinsky, 2004), more approachable signals were suggested to address the issues. This scoping review intended to investigate four research questions we proposed to guide a scoping review of this nascent but active field. Our research questions are answered by collecting, analyzing, and synthesizing data elements that are organized into five categories (study, device, signal, algorithm and performance characteristics) and we designed an easy-to-use data capture form to allow multiple reviewers collect data. Overall findings from this scoping review show that it is promising to use non-EEG signals acquired from wearable sensors to detect or even anticipate seizure events in ambulatory settings. However, we also identified large variations among reviewed studies in terms of describing types of seizures and choices of performance metrics to evaluate algorithms. These variations have made it difficult to compare and synthesize results from different studies. Therefore, our scoping review is best considered as a snapshot of a field of studies that is rapidly advancing and can be used to inform directions of future research. In the following, we discuss our findings for each research question, present some recommendations of essential data elements for future studies to include in their reports, and summarize the limitation of this scoping review.

Table 13. Performance grouped by study settings (ambulatory, non-ambulatory).

| Settings | Sensitivity | | | FAR | | | PPV | | |
|-----------------------|------------------------|---|-------------------------------------|--------------------------------|----------------------------|--|------------------|--------------------------|------------------|
| | <i>Below 80%</i> | <i>80%–95%</i> | <i>Above 95%</i> | <i>Above 10 d⁻¹</i> | <i>1–10 d⁻¹</i> | <i>Below 1 d⁻¹</i> | <i>Below 10%</i> | <i>10%–90%</i> | <i>Above 90%</i> |
| <i>Ambulatory</i> | [28, 29] | [3, 29] | [23, 27, 28] | — | [29] | [3, 23, 27] | — | [3, 28] | [28] |
| <i>Non-Ambulatory</i> | [1, 2, 10, 13, 14, 26] | [4, 6], [7–9], [11, 12], [18, 19], [21, 24], [30] | [5, 15], [16, 17, 20, 22], [24, 25] | [1][2], [12], [17], [30] | [4, 7, 11, 16, 21, 22, 24] | [6, 9, 10, 13, 14], [15, 18], [19, 24], [25] | [1][8] [16] | [2, 9], [18, 20, 22, 25] | [5, 14] |

4.1. Physiological and mobility signals

Most of the articles focused on GTCS, where the most frequently used signal modalities are ACM and EMG. Convulsive seizures are accompanied by dramatic motor activity, which have been identified as the high-risk factor for physical injury and sudden unexpected death in epilepsy (SUDEP) (Kanner 2011). SUDEP is a common cause of death in epilepsy, which may be attributed by cardiac and respiratory alternations related with GTCS (Kanner 2011). One study investigating witnessed cases of SUDEP found out that 12 out of 15 SUDEP cases followed after a GTCS (Langan *et al* 2000). This association with SUDEP along with risk of accidental injury makes a compelling case that convulsive seizures are more critical to detect than non-convulsive seizures (NCS). NCS may cause less immediate harm to patients but their detection and prompt intervention may prevent any ensuing injury. Furthermore, NCSs often go undetected, which greatly delays the identification and treatment process. Correspondingly, a wider coverage of the seizure types is critical for seizure management in ambulatory settings. Based on results from this scoping review, detection of a wide category of seizure types would be best approached by integrating multiple signal modalities.

4.2. Device characteristics

With respect to the device used among the studies, all wearable devices, except for some custom-made devices (wearable ear-EEG device), are consumer-graded and easy to access the data via Bluetooth transmission towards mobile devices or local stations. A stable data transmission is essential for data collection, processing, and model construction, enabling for implementing real-time detection or prediction systems. Among all the examined papers, 3 types of devices (Shimmer, *SmartWatch*, custom-built) were reported to experience disconnections during the recording stages due to sensor failures or poor connection to base station. Consequently, a more robust sensor design along with the transmission system warrants further exploration. Regarding the side effect found in the device, mild to moderate skin irritations are the most frequently reported adverse effects but appear to be transient. Both research studies (Zibrandtsen *et al* 2017, Zibrandtsen *et al* 2018) implementing custom built wearable ear-EEG device found that one of the major drawbacks was the increasing discomfort on the external ears when continuously wearing the device. Besides, even though its performance appears identical to EEG, the burden for specialists in correcting the electrode gels and wearing the device remains unsolved. A softer earpiece material was suggested to enhance the user experience, but its actual effect remains unknown until conducting further studies.

None of studies we collected reported any assessment of the wearable devices in terms of their signal quality. Instead, they documented the encountered data transmission issues and user-experiences of using such wearable devices. However, quantification of signal quality is essential in constructing accurate and realizable seizure detection models that would reject low quality signal segments. Nasseri *et al* (Nasseri *et al* 2020) evaluated several commercial wearable devices (*Empatica E4*, *Biovotion Everion*, *Byteflies Sensor Dots*, *Activinsights GENEActiv watch*) regarding their signal quality by calculating respective signal quality indexes. According to their findings, the aforementioned commercial devices could generate high-quality signals and the recruited patients showed strong preferences in wearing wrist-worn devices as opposed to the ones worn on upper arm during the study period. As mentioned by the study, although the reliability of these devices was established, the potential for continuous long-term clinical usage remains unknown. In future studies, the integration of automated signal quality measurements may be helpful in enhancing the performance of real-time detection models.

4.3. Algorithm characteristics

Algorithms used to classify signals in the collected studies can be divided into traditional machine learning (SVM, kNN, random forest, decision tree etc), deep learning (1D CNN, LSTM), and others (threshold-based, event searching, visual inspection etc). Despite the fact that most of them were implemented off-line with a goal of differentiating seizure events, some potential was shown for seizure prediction if the signals capture ANS changes that precede the EEG discharges (Leutmezer *et al* 2003, Thijs 2019). Mesile *al* etc constructed 1D CNN and LSTM based on multimodal signals (EDA, ACM, BVP and temperature) acquired from E4 wristbands to predict seizure events, demonstrating significantly better than chance in 43% of the patients where among them, mean sensitivity was around 75%. At the same time, the results looked less promising across all the recruited subjects, with a mean sensitivity around 51%. There certainly exist opportunities for further enhancement in prediction tasks. Conversely, algorithms designed purely for detection purpose generated much better performance (sensitivity above 90% with less than 1 FAR/day). Regardless of the success in seizure detection using non-EEG signals, a large portion of them conducted off-line signal processing and the outcome may differ when applied in real-time scenarios. Toshitaka's team developed multivariate statistical process control for anomaly detection to recognize tonic-clonic and non-convulsive seizures in real-time. HRV features are extracted from the raw data, and control limits (detection threshold) are determined individually and adjusted off-line prior to real time implementation. Overall, they reported a high sensitivity (95%) but with high false alarm rates (14 d^{-1}). Many studies found in this scoping review captured the signals in settings where patients' mobility was often restricted. To minimize the FAR and better differentiate seizure events from seizure mimic events in free-living settings, Jeppesen *et al* instructed patients to perform exercise tests (biking, cognitive stress tests), if possible, to mimic the activities which would cause dramatic autonomic changes. In the end, they reported a sensitivity of 93.1% and FAR of 1 per day. During recording stages, special instructions like requesting patients to perform physical exercises or allowing patients to engage in their typical activities under careful supervision could be beneficial in building a more robust classifier with low FAR.

4.4. Performance characteristics

In selection of comparable performance metrics, accuracy is not a valid measure of model performance when the dataset is imbalanced. Sensitivity, which is the ratio of correct seizure predictions to total seizure occurrences, provides information about a model's performance on false negatives (incorrect prediction of seizure as non-seizure). On the other hand, PPV or precision gives a model's performance on false positives (incorrect prediction of non-seizure as seizure) and directly characterizes seizure alert burdens. In the circumstances of seizure detection, the false negatives are more detrimental. Therefore, the performance measure of sensitivity is relatively more important. However, reducing false positives is also desirable in ambulatory seizure detection devices, especially for everyday use, so this feature is captured by FAR in performance metrics. Some articles also reported specificity, which is the proportion of actual non-seizure cases that are correctly identified, as reflected in table 11. Often, sensitivity is found to be closely related to false alarm rates. Many studies (Poh *et al* 2012, van Andel *et al* 2017) have reported higher false alarm rate if a model was tuned to achieve higher sensitivity. The trade-off between these two metrics needs to be considered based on context, including seizure types and severity and the anticipated actions to respond to the seizure detection. For example, higher sensitivity with a compromise in FAR is acceptable in seizures that are easily ignored, whereas high FAR of low-risk seizures overnight is not desirable in commercial-graded seizure monitoring devices.

Among all collect studies, threshold-based algorithms are not only the most widely used, but also the most common algorithm to have high performance, featuring 12 out of 14 threshold-based models having above 80% sensitivity and 8 out of 13 having below 1 d^{-1} FAR. Among traditional machine learning algorithms, SVM was the most commonly used, and it also had the best performance, with 71% SVM studies having sensitivity over 90% and 60% having FAR under 1 d^{-1} . The few studies using Random Forests ($n = 3$) (please refer to table 5 [8], [24], [28]) and kNN ($n = 2$) (please refer to table 5 [8], [24]) generally achieved good performance (sensitivity above 85% and FAR under 1.2 d^{-1}), whereas the two studies (please refer to table 5 [26], [29]) using CNN and LSTM neural networks had relatively poor performance (sensitivity below 80% and FAR around 10 d^{-1}) tested at all types of seizures. Although one study (please refer to table 5 [30]) did achieve sensitivity around 80%, it failed to retain a low FAR (around 13.63 d^{-1}). However, relatively poor results generated by deep learning algorithms may not necessarily reflect the impertinence of these algorithms in seizure detection/prediction task. The results may not be representative due to the limited number of studies that have tested these techniques and the limited number of training samples used to train these neural networks. Besides, the study implementing LSTM transfer learning algorithm (Nasseri *et al* 2021) was trained on motor seizure data and reported the performance separately on motor seizure dataset and on all types of seizures. Its performance on motor seizures had a much higher sensitivity of 90% with lower FAR 2.45 per day, as compared with the model tested on all types of seizures which reported a sensitivity of 47% and FAR 7.2 per day. The performance variation was also

aligned with the findings from previous literature (Beniczky *et al* 2021). The large variation in the performance may partially be explained by the different extent of manifestations associated with seizure types.

As reflected in table 12, more than half of the studies focused on detecting motor seizures and reported an overall high sensitivity of [73.6%–100%] and low FAR of [0–3.7 d⁻¹]. Among the 16 motor seizure studies, 13 of them involved the detection of GTCS and reported even higher sensitivities above 80% and lower FARs below 2 per day. The most common modality used to detect motor seizures is ACM. The 12 studies that included ACM as single or in multi-modal signals reported many of the highest sensitivities and lowest FARs. Such high performance of ACM is related to its nature of capturing well motions and activities, and motor seizures are characterized mainly by motor symptoms in semiological seizure classifications (Lüders *et al* 1998). However, the studies involving detection of both motor and non-motor seizures had a much larger range of sensitivities and FARs, spanning from 30% to 100% and 0–50 per day respectively. Seven of the 14 mixture studies used single modality and the other 7 used multi-modalities, but there is no significant difference in performance observed across the different modalities. There is only one study (please refer to table 5 [17]) involving only non-motor seizures. The study reported high sensitivity above 80% as well as high FAR between 0.5 and 7.2 per hour, but this result may not be representative due to the limited number of performance metrics included for non-motor seizures. Based on the included articles, motor seizures are generally more likely to be detected with a higher sensitivity and lower false alarm rate, especially for GTCS, which indicates that detections for motor seizure are relatively more mature and well-studied, whereas models for non-motor and mixture seizures detection requires more research to achieve higher performance.

In addition, studies using different modalities varied in performance as well. Generally, studies based on modality such as ECG and ACM tend to have higher sensitivity and low FAR, probably due to the reliability of ECG signals and the close relation between movement and motor seizures. The sensitivity and FAR of studies using EMG and non-invasive EEG signals alone had very wide ranges, indicating that their performances are probably more related to the algorithms used to process these signals. PPG signals are usually used in combination with other modalities such as ACM to achieve best performance. The study that used PPG signal alone (Vandecasteele *et al* 2017) had worse-than-chance sensitivity and high FAR, whereas performance got greatly improved in Arends, *et al*'s multimodality study using both ACM and PPG. Another commonly used multimodality pair is ACM and EDA. All three studies based on ACM-EDA combined signals had sensitivity above 80% and either FAR below 1 d⁻¹ or specificity above 90%. Although no study was included that used EDA as single modality, EDA was commonly used in multimodality studies: 7 out of the 9 multimodality studies included EDA as one of the bio-signals. Some modalities are more applicable to certain types of seizures and the above data may be confounded by fact where some seizures are easier to detect. For instance, ACM might outperform other signals, potentially attributed by the fact that it is commonly applied for detecting motor seizures which intrinsically are easier to detect than non-motor seizures.

4.5. Recommendations

There exists some variability across different studies in terms of classifying seizure types. The ambiguity and inconsistency in naming convention and seizure classification make it difficult to group the studies by its targeted seizures and learn about the common modality being used for a specific seizure type. For instance, some studies may choose to divide the recorded seizures as convulsive and non-convulsive, while others categorize the seizures based on its onset, focal versus generalized or even brain region (e.g. temporal lobe epilepsy). The two different dichotomy systems impose complexity in developing seizure specific classifiers. In addition, we also noticed some inconsistency among these studies in reporting performance metrics. One study may choose to report only accuracy of their algorithm, others may use AUC, FAR, making it infeasible to generate a reliable, comprehensive evaluations towards these algorithms. One guideline (Luo *et al* 2016) for employing machine learning models in biomedical data helps to avoid the above issues by listing out minimum performance metrics required to report: sensitivity, specificity, positive predictive value, negative predictive value, AUC for classification task. A more standardized seizure types and performance metrics used by the studies would be useful in assessing and validating the models' performances for a particular seizure type. Finally, increasing use of machine learning techniques to detect seizure in ambulatory settings also calls for the research community to jointly invest in developing a common dataset that can be used to benchmark different algorithms, ensure reproducibility, and advance the field in a measurable and transparent way. Given the potential number of patients the technology will touch, it is imperative that future studies follow a rigorous approach to develop algorithms and report results.

4.6. Limitation

This scoping review presents a systematic mapping of the current feasible systems (device + algorithm) for seizure monitoring in an ambulatory environment. The essential information was extracted from the selected

articles and recorded in table format to answer the proposed research questions. One limitation of this study is the lack of critical evaluation of results in the collected articles as the scoping review does not perform any quality appraisal instead provides comprehensive knowledge for the current field. Despite that, we performed systematic search strategy based on the keywords and utilized the related review papers to identify any pertinent records, there is still a potential omission of relevant studies. Studies published in other languages were excluded, and only the peer-reviewed articles were considered in our case, which may limit our understanding in what has been achieved in this area and confine our analysis only in those scientific reported journals.

5. Conclusion

To the best of our knowledge, this scoping review is the first to summarize research activities regarding wearable devices for seizure monitoring purpose by capturing a comprehensive list of data elements covering device brands and modalities, extracted feature characteristics, algorithms, and performances. Based on the studies we reviewed, non-cerebral physiological signals acquired by wearable devices have exhibited promising results in detecting or even forecasting seizure occurrences, especially for detecting motor seizures (GTCS, FTBTC). However, further research is needed to refine the signal analysis techniques and decision algorithms for accurately detecting non-convulsive seizures and reducing FAR for motor seizures. With the emerging trend of using various deep learning algorithms to process data from wearable devices, performance that has been achieved using traditional machine learning methods is poised to be further boosted. Ultimately, the integration of machine learning and wearable devices offers a great alternative option of long-term continuous seizure monitoring under ambulatory settings. Towards such a goal, we anticipate a growing number of studies in this field.

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