Towards a wearable multi-modal seizure detection system in epilepsy: A pilot study

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HIGHLIGHTS

- Wearable EEG, ECG and accelerometry can detect correlates of seizure activity in an epilepsy monitoring unit.
- A support vector machine trained on the multi-modal recordings can detect focal nonmotor and focal tonic seizures.
- Wearable multi-modal monitoring presents new possibilities for personalization in seizure detection algorithm design.

A B S T R A C T

Objective: To explore the possibilities of wearable multi-modal monitoring in epilepsy and to identify effective strategies for seizure-detection.

Methods: Thirty patients with suspected epilepsy admitted to video electroencephalography (EEG) monitoring were equipped with a wearable multi-modal setup capable of continuous recording of electrocardiography (ECG), accelerometry (ACM) and behind-the-ear EEG. A support vector machine (SVM) algorithm was trained for cross-modal automated seizure detection. Visualizations of multi-modal time series data were used to generate ideas for seizure detection strategies.

Results: Three patients had more than five seizures and were eligible for SVM classification. Classification of 47 focal tonic seizures in one patient found a sensitivity of 84% with a false alarm rate (FAR) of 8/24 h. In two patients each with nine focal nonmotor seizures it yielded a sensitivity of 100% and a FAR of 13/24 h and 5/24. Visual comparisons of features were used to identify strategies for seizure detection in future research.

Conclusions: Multi-modal monitoring in epilepsy using wearables is feasible and automatic seizure detection may benefit from multiple modalities when compared to uni-modal EEG.

Significance: This study is unique in exploring a combination of wearable EEG, ECG and ACM and can help inform future research on monitoring of epilepsy.

1. Introduction

Seizure detection in epilepsy can potentially improve seizure documentation, which is a key indicator of disease severity (Bruno et al., 2020; Hoppe et al., 2007), and could be useful in differentiating between seizure types and non-seizure events e.g., psychogenic non-epileptic seizures (PNES). Furthermore, seizure...
A comprehensive analysis of seizure detection is vital in epilepsy (SUDEP) treatment. Beniczky et al. (2016) noted that automatic seizure detection is crucial for diagnosing epilepsy and guiding therapeutic decisions. However, achieving high accuracy in seizure detection is challenging due to the diversity of seizure types and the limitations of current technologies.

2. Methods

2.1. Patients

Consecutive patients admitted to the Epilepsy Monitoring Unit (EMU) at Zealand University Hospital for diagnostic evaluation between 7th of February 2019 and 15th of March 2021 were evaluated for recruitment. The inclusion criteria were: (1) confirmed or clinical suspicion of epilepsy, (2) estimated seizure frequency corresponding to a non-negligible chance of seizure events during the monitoring period and (3) age ≥ 18 years. The study was done in accordance with the Helsinki declaration and approved by the regional ethics committee (SJ-725). All patients gave oral and written informed consent.

2.2. Recordings

The study device setup was wearable, meaning that the patients could move around freely, allowing for out-patient monitoring. The wearable recordings were unsupervised, which prohibited adjustments (e.g., correction of loose electrodes), in an effort to simulate out-patient recordings. The wearable setup consisted of three components: ACM, ECG, and behind-the-ear EEG. Behind-the-ear EEG was recorded using either a portable Enobio 8 (Neuroelectrics, Barcelona, Spain) or a portable TrackIT T4a (Lifelines, London, UK). The EEG amplifier carried in a small bag that could be attached to a belt or worn over the shoulder and concealed under clothing. Cup electrodes were placed bilaterally behind the ear on the upper part of the mastoid process and the reference was placed approximately one cm anterior to Cz. Sampling frequency was 500 Hz or otherwise downsampled to 500 Hz. Patients 1–14 were recorded using the Enobio amplifier, however due to data loss issues, the subsequent were recorded using the TrackIT T4a.

Electrocardiography and sternum ACM was recorded using a wearable one-channel Faros 180 (Bittium, Oulu, Finland) attached by a Bittium FastFix along the sternum with a self-adhesive patch with integrated electrodes. ECG was sampled at a frequency of 500 Hz and ACM at a frequency of 25 Hz. Limb ACM was recorded using two or more SENS Motion (SENS, Copenhagen, Denmark) devices attached with a self-adhesive patch, one posteriorly on the forearm above the wrist, and another on the leg distally to the head of the fibula. SENS ACM data was transmitted via Bluetooth to a smartphone using a custom data management app “Studie APP” (iMotions, Copenhagen, Denmark).

For reference standard, recordings from the wearable setup were compared with EMU video-EEG recorded using Nicolet (CareFusion, San Diego, USA) system applying the 10–20 system with 25 electrodes and a sampling rate of 1024 Hz. The video-EEG was reviewed by a board-certified clinical neurophysiologist who annotated seizure onset and duration. Because of temporal shift, behind-the-ear EEG was manually synchronized with the EMU-EEG by visually identifying chewing or other characteristic artifacts in both EEGs. The Faros-ECG signal was first manually synchronized with the EMU ECG identified by identifying artifacts, and then an automated cross-correlation based synchronization method was applied on the R-peak time series in order to verify and, if necessary, adjust the synchronization. The limb ACM was synchronized with the sternum ACM by visually identifying characteristic artifacts.

2.3. Seizure detection

2.3.1. EEG preprocessing and features

Feature extraction and visualizations was performed offline using MATLAB version 2019a (Mathworks, Massachusetts, USA). Data was imported using EEGLAB toolbox (Delorme and Makeig, 2004) and custom scripts. Three behind-the-ear channels were used: left-ear to reference, right-ear to reference and a cross channel from the left- to right-ear. For the SVM, the data was segmented into 2-s epochs with 50% overlap before feature extraction. Extracted features were root-mean square, skewness, kurtosis, sample entropy, total band power in the 30–80 Hz band, and total and normalized band power in the following bands: 1–30 Hz, 1–4 Hz, 4–8 Hz, 8–13 Hz, 13–30 Hz. These features were chosen based on previous studies (Boonyakitanont et al., 2020; Greene et al., 2008; Vandecasteele et al., 2020; Zibrandtsen et al., 2020).

For the visualizations, the time-frequency-power plots were made with MATLABs spectrogram function using a short-time Fourier transform. For time-domain plots the unsegmented EEG was filtered with a 1–70 Hz finite impulse response band pass filter and 50 Hz band stop filter. Variance was calculated using a method described elsewhere (Zibrandtsen et al., 2018). Artifact-free and stereotypical seizures were manually chosen for the plots.
2.3.2. Electrocardiography pre-processing and features

R-peaks were detected using the Pan-Tompkins algorithm (Pan and Tompkins, 1985) using R version 4 and the package rsleep (Bouchequet, 2020). The HRV measures Modified Cardiac Sympathetic Index (ModCSI) and Modified Cardiac Sympathetic Index with Slope (ModCSISlope) were calculated as described in (Jeppesen et al., 2014) using a 100 peaks rolling window that was advanced 1 s at a time.

2.3.3. Accelerometry pre-processing and features

The 3-axis accelerometry signal was sampled at 25 Hz by the Faros device. Mean and standard deviation was calculated in non-overlapping 1-s time windows for each of the axes, giving six accelerometry features to be used in the SVM (Kusmakar et al., 2019). Limb ACM was omitted from the SVM due to loss of data.

2.3.4. Support vector Machine

A SVM classifier based on the features extracted from ACM, ECG and EEG data was trained on each patient individually (i.e., patient-specific algorithm) and only on patients with at least five recorded seizures. All seizures from these patients were used in the classifier irrespective of the signal quality and whether ictal changes were visually noticeable in the data. A support vector machine (SVM) with radial basis function kernel was used for classification. The Synthetic Minority Oversampling Technique as implemented in the R package “caret” (Kuhn, 2008) was applied with three resampling iterations to account for class imbalance. The classifier was run several times independently with different subsets of the available features: all modalities, EEG & ECG, ECG & ACM, and only EEG. All features were resampled to 1 Hz. The data for each patient was split into folds, one for each of the seizures, and boundaries between folds corresponded to the middle point between consecutive seizures. Each fold consisted of temporally continuous samples, including seizure and non-seizure data.

Using a leave-one-out cross validation procedure, the algorithm was trained on one fold less than the total number of folds, after setting the random seed for reproducibility. The remaining fold was used as a test set. The classifier returned a prediction (positive / negative for respectively seizure / non-seizure) for each 1 s window sample. Since seizures last at least several seconds, the following post processing was applied to the predictions: if a single sample was predicted as either “seizure” or “non-seizure” while the preceding and subsequent samples belonged to the opposite class, then the prediction was reversed.

After each sample was classified as either seizure or non-seizure, a minimum seizure duration (MSD) threshold was introduced, defined as the minimum duration in seconds of a positive prediction for it to be considered a seizure. The MSD threshold controls the sensitivity and FAR trade-off, and increasing the value reduced the sensitivity and lowered the FAR. Its value ranged in the interval 5 s to 60 s (with increments of 5 s) when computing the Receiver Operating Characteristic (ROC) of the classifier.

After each positive detection, a refractory period of 2 min was applied, during which any subsequent detections were discarded, to avoid multiple alarms for the same event. To account for small misalignments in the synchronization of the data collection devices, a predicted seizure was considered a correct detection if it occurred from within 60 s from the EEG onset-offset interval.

The classifier was evaluated over each test fold using metrics of sensitivity and false detections expressed as FAR in a 24-h period and aggregated over all the test folds weighted by their time durations.

2.4. Results

We included 30 patients (13 male; age: 19–77 years; median age 43 years). Eighty-two seizures were recorded from ten patients while in the EMU: 29 focal seizures with a temporal lobe onset, 49 focal tonic seizures, three focal seizures evolving to non-convulsive status epilepticus and one focal to bilateral generalized tonic-clonic seizure (Table 1). Three patients had more than five seizures and were therefore eligible for SVM classification. The average recording time from behind-the-ear EEG was 85% of the total EMU admission time (Enobio 74% range: 26–100%; TrackIT 99.6% range: 94–100%) and included 78 (95%) of all seizures. Fig. 1 shows the recording time of each modality for each patient. The main reason for loss of behind-the-ear EEG was due to technical errors. ECG data loss occurred for two patients without seizures due to technical errors. Six SENS ACM recordings containing 58 seizures were lost due to depleted batteries, however ACM from the ECG-device was recorded in all six. For this reason, the SENS ACM data was not included in the SVM. No adverse events were reported following the use of the devices and the devices were generally well tolerated, and all the patients completed their intended monitoring period.

With one exception, all ten patients had one seizure type during the EMU monitoring. Patient 4 had two different types of seizures (Table 1). For each type of seizure in each patient, one seizure was manually selected for time-domain visualizations of the peri-ictal recordings from the wearable ECG, ACM, and behind-the-ear EEG (Supplementary 1). In all cases, seizure onset coincided with electroencephalographic changes, except for patient 6’s focal impaired awareness seizure in which the ictal EEG was masked by EMG activity from the ictal shivering. In the following two subsections we describe the seizures from the three patients with more than five recorded seizures, which were included in the SVM and plot features derived from selected seizures.

2.5. Focal nonmotor seizures

Patient 4 had nine focal nonmotor seizures with a temporal lobe onset and a median duration of 54 s (range: 42–73 s). The semiology included oral automatisms, behavioral arrest, lip smacking and staring. The patient was aware of four out of five seizures that occurred during wakefulness. The EEG during seizures were stereotypical with rhythmic theta and delta activity in the right temporal region (7/9 seizures) and in the right temporal region (2/9). The patient had ictal increase in HR, median peak HR: 110 beats per minute (BPM) range: 93–121 BPM, and prominent changes in HRV reflected in the numerically large ModCSISlope values as illustrated in Fig. 2, visually highlighting possible seizure events.

Comparison of ictal morphology from behind-the-ear EEG and EMU EEG is shown in Fig. 3. Ictal 2–3 Hz activity is visually very similar when comparing behind-the-ear EEG and scalp EEG (Fig. 3-C-D). A prolonged ictal tachycardia, continuing more than 30 s after seizure termination is seen (Fig. 3E). Video recordings of the seizure reveals that the patient is lying still in bed and consequently the ACM recordings only reveal a small post-ictal movement of the right lower leg (Fig. 3F).

Fig. 4 compares ictal time-frequency-power from behind-the-ear EEG and EMU EEG. This shows a similar seizure pattern in both the behind-the-ear EEG recordings and the EMU recordings. The patients’ seizures exhibited stereotypical time-frequency signatures. All patient 4 seizures displayed a consistent stereotypical ictal EEG morphology, however for one seizure it was only apparent on EMU EEG because the behind-the-ear EEG was distorted by movement artifacts.

Patient 26 had nine focal nonmotor seizures with a temporal lobe onset and a median duration of 45 s (range 10–52 s). The EEG correlates from the EMU EEG were described by the clinical
neurophysiologist as subtle but with an ictal evolution of rhythmic 5–6 Hz activity in the temporal lobe starting 7–10 s after clinical seizure onset. The seizure semiology included behavioral arrest, automatisms, staring, and lip smacking.

2.6. Focal tonic seizures

Patient 19 had 49 nocturnal stereotypical focal tonic seizures with a frontal lobe onset and a median duration of 35 s (range 6–44 s), 47 of which were recorded using the wearable EEG device. The ictal EEG activity was masked by muscle activity on the behind-the-ear EEG. In the wearable recordings, all seizures showed a visible ictal change in variance of the EMG signal and/or a marked change in ModCSISlope (Fig. 5). Video recordings reveal a short awakening following some of the seizures, and a corresponding minor increase in the mean magnitude on the ACM is observed. The seizures were stereotypical with high amplitude, high frequency EMG oscillations and ictal tachycardia up to 100BPM (Fig. 6).

Table 1
Characteristics of patients with recorded seizures.

| ID | Sex & Age | ASM | Semiology | Electroencephalographic onset | Known Seizure types* | Seizures recorded (study EEG / EMU EEG) | Primary ictal EMU EEG findings** |
|----|-----------|-----|-----------|-------------------------------|----------------------|--------------------------------------|----------------------------------|
| 1  | F 32      | LEV, LTG | Auras and oral automatisms | Multi-focal. Right and left temporal region. | FIA | 2/3*** | Generalized 2–3 Hz spikes and polyspikes |
| 4  | F 55      | LEV   | Auras and oral automatisms | Multi-focal. Right and left temporal region. | FIA & FA | 9/9 | Rhythmic 5 Hz activity |
| 6  | F 39      | LEV   | Automatisms and behavioural arrest. | Left temporal region | FIA | 2/2 | Rhythmic 3 Hz activity |
| 19 | F 23      | LEV   | Nocturnal tonic posturing | Frontal region | FIA | 47/49 | Rhythmic 4–5 Hz activity in the right frontal region |
| 22 | F 44      | LEV   | Behavioural arrest and automatisms | Right temporal region | FA | 3/3 | Rhythmic 5–6 Hz activity |
| 24 | F 42      | LTG, LEV | Déjà vu and Auras | Right fronto-temporal region | FA | 2/2 | Rhythmic 5–6 Hz activity |
| 26 | M 29      | VAL, LEV | Impaired awareness and automatisms. Rarely FBTC. | Left temporal region | FIA & FBTC | 9/9 | Rhythmic 5–6 Hz activity |
| 28 | M 23      | LAC, LEV | Impaired awareness and déja vu. | Left temporal region | FIA & FBTC | 1/1 | High amplitude rhythmic 3–4 Hz activity |
| 29 | F 56      | LTG   | Shivering and automatisms | Right temporal region | FA | 3/3 | Rhythmic 6–7 Hz activity |
| 30 | F 42      | LTG   | Déjà vu and dizziness | Left temporal region | FA & FIA | 1/1 | Rhythmic 13 Hz activity evolving to 7 Hz and later to 5–4 Hz activity |

*If more than one seizure type, the highlighted seizure type was recorded in the EMU. ** As described by a board-certified clinical neurophysiologist blinded to the study recordings. ***Three distinct seizures progressing to non-convulsive status epilepticus.

Abbreviations. ASM, Anti-seizure medication; EMU, Epilepsy monitoring unit; LEV, Levetiracetam; LTG, Lamotrigine; VAL, Valproate; LAC, Lacosamide; FIA, Focal impaired awareness seizure; FA, Focal aware seizure; FBTC, Focal to bilateral tonic clonic seizure; GTC, Generalized tonic clonic seizure.

Fig. 1. Overview of seizure count and monitoring duration for each modality for all patients. Duration is indicated by horizontal bars and the colors indicate different modalities. Missing accelerometry (ACM) refers to the dedicated SENS ACM device. Missing electrocardiography (ECG) includes sternum ACM from the ECG device. Total electroencephalography (EEG) duration for each patient is shown to the right with device coverage percentage in the parentheses. PNES: psychogenic non-epileptic seizure.
2.7. SVM classification results

Receiver operating characteristic curves for all MSD threshold values (5–60 s) were drawn for the three patients (Fig. 7). In the first patient with focal nonmotor seizures (patient 4), EEG and ECG yielded a sensitivity of 100% and a FAR of 13/24 h with a 40 s MSD threshold. Across most of the MSD thresholds, the combination of EEG and ECG achieved the highest sensitivity, followed...
by all modalities (sensitivity of 75% and FAR of 19/24 h for MSD 30 s) and only EEG. In comparison the combination of ECG and sternum ACM performed poorly with a sensitivity up to 67% and FAR of 48/24 h (for MSD 35 s). The difference may in part be due to the lack of ictal movement, which can cause sternum ACM data to be less predictive of seizures. In the second patient with focal nonmotor seizures (patient 26) EEG and the combination of EEG and ECG with an MSD threshold of 35 s both yielded 100% sensitivity and a FAR of 7/24 h and 5/24 h respectively. For both a 25 s and 35 s MSD threshold, the combination of EEG and ECG both achieved a sensitivity of 100%, but the addition of ECG improved the FAR when compared to only-EEG (Fig. 7). This compares to patient 4 where the addition of ECG both improved the sensitivity and FAR, as sensitivity of 100% and a FAR below 20/24 h could only be achieved with the combination of EEG and ECG. The combination of sternum ACM and ECG yielded a lower sensitivity and a high FAR, as an MSD threshold of 25 s yielded a sensitivity of 78% and FAR of 40/24 h. All modalities and an MSD threshold of 35 s and 40 s yielded identical results with the lowest FAR of 1/24 h but with a sensitivity of 33%.

For the patient with focal tonic seizures (patient 19) all modalities and a 15 s threshold yielded a sensitivity of 91% and FAR of 20/24 h, while a 25 s threshold yielded a sensitivity of 84% and FAR of 8/24 h (Fig. 7). Combining all modalities led to better sensitivity and FAR trade-offs across all MSD thresholds, when compared to any other combination of modalities. Increasing values

**Fig. 5.** Nineteen-hour interval with 11 focal tonic seizures from patient 19. Seizures are indicated with a red dot. A&B) Electroencephalography (EEG) variance (channel: left ear – right ear) and heart rate variability (HRV) fluctuate in synchrony during seizure events. Note that most non-ictal fluctuations in either variance or HRV are not synchronized. C) Accelerometry shows movement after some of the seizures. *Represents the seizure shown in the time-domain in Fig. 6. Mean Mag: mean magnitude. CSI100 × slope: cardiac sympathetic index 100 (sliding window of 100 R-R intervals) with slope.

**Fig. 6.** Time–domain plots from patient 19 of the seizure marked with * in Fig. 5. A.) Behind-the-ear electroencephalography (EEG) (channel: left ear – right ear) during a tonic frontal lobe seizure showing an electromyography-signal. B.) Epilepsy monitoring unit (EMU) EEG (channel: T9-T10) during the same seizure with a similar signal. C) Ictal tachycardia with a heart rate (HR) increase from ~ 50 beats per minute (BPM) to a maximum of 100 BPM 15 s after seizure termination.
of the MSD threshold yielded lower sensitivity and improved FAR, as expected.

3. Discussion

The development of seizure detection devices and algorithms is a gradual process, starting with in-patient proof-of-concept studies scaling to multicenter and in-field validation studies. According to a commonly used tiered classification system (Beniczky and Ryvlin, 2018), this is an exploratory phase 1 study. We demonstrate that wearable ECG, ACM, and behind-the-ear EEG in combination can detect ictal changes and we describe how this varies by modality and seizure type. Supplementary 1 demonstrates the ictal changes in the wearable recordings from various seizure types. However, the complexity of multi-modal sensor data analysis, illustrated in Supplementary 1, is a good example of how machine learning tools, such as SVM, can discover multi-dimensional patterns and test a binary classification scheme for seizure vs. non-seizure aimed towards automatic seizure detection. Comparatively, manual visual analysis becomes inefficient not only because of the amount of data but also because human visual attention becomes increasingly strained by having to follow different types of recordings simultaneously.

In the two patients with focal nonmotor seizures (patient 4 and patient 26), the combination of EEG and ECG detected all seizures with a lower FAR compared to other modality combinations (patient 4: sensitivity 100% and FAR: 13/24 h & patient 26: sensitivity 100% and FAR 5/24 h). Two previous studies used only behind-the-ear EEG recorded with the same clinical EEG amplifier as the reference full scalp EEG. In the first study, a non-patient specific seizure detection algorithm achieved a median sensitivity of 94.5% and FAR of 0.49/24 h using a patient specific algorithm on 182 mostly focal seizures with a temporal lobe onset (Vandecasteele et al., 2020). In patient 19 with focal tonic seizures, we achieved a sensitivity of 91% and FAR of 20/24 h. In comparison, a previous study combined HR and ACM in a bracelet for the automatic detection of generalized tonic seizures (with a duration > 30 s) and found a median detection rate of 0.89 (Arends et al., 2018).

In a world of imperfect seizure detection, the sensitivity vs false alarm trade off might favor high sensitivity at a cost of more false detections, considering a system that identifies epochs for later manual review. Consequently, depending on the purpose of the monitoring, a singular threshold for unacceptably high false alarm rate is not meaningful. If the purpose is quantification of seizures over time, high sensitivity is preferable and identified epochs can be subsequently re-evaluated manually.

Some commercial systems are designed for this purpose (Duun-Henriksen et al., 2020). Focusing on high detection sensitivities using non-wearable behind-the-ear EEG and ECG has yielded a mean sensitivity of up to 92% with a FAR of 44.4/24 h. Consequently, leaving approximately two data epochs per hour for manual review (Vandecasteele et al., 2021). Semi-automatic review of behind-the-ear EEG for the detection of absences seizures decreased the review time from 1–2 h to 5–10 min while improving the accuracy (Swinnen et al., 2021). However, a low FAR is important in the development of automatic real-time seizure alarming devices, as false detections can lead to unnecessary distress for the patients and caregivers (Bruno et al., 2020). In the present study a high sensitivity (>90%) was achieved in all three patients with a FAR of up to 20/24 h. Multiple daily false alarms,
as presented in this study, would probably be unacceptable for seizure alarming purposes, especially in patients with infrequent seizures.

For seizure quantification purposes, a semi-automatic approach would require tools for improving the manual review of both the entire recordings and for the automatically identified epochs. We explored how visualizations of the time series data can facilitate manual review of long-term recordings. This feature selection varies with the seizure types. For example, a detection strategy based on visual inspection of windowed variance-estimates previously used for GTCS detection (Zibrandtsen et al., 2018) can be used for the identification of tonic seizures or the tonic phase of tonic-clonic seizures. Combining it with HRV measures as in Fig. 5 could improve the manual review of long-term monitoring of tonic seizures.

Focal seizures with temporal lobe onset exhibit spatio-temporal frequency patterns, “signatures”, that are highly stereotypical within individuals (Weisdorf et al., 2020, Zibrandtsen et al., 2017) and that can be visually and quantitatively analyzed through time-frequency analysis of behind-the-ear EEG. Likewise, ictal tachycardia varies between individuals with epilepsy and this can be used as additional information both for manual review and for individualized seizure detection algorithms (De Cooman et al., 2020, Jeppesen et al., 2020). Once detected, its occurrence conforms to seizure stereotypy and is predictive for future episodes of ictal tachycardia (Smith et al., 1989, van Elmpt et al., 2006, Zijlmans et al., 2002). Absence of tachycardia is also useful in an individualized algorithm for the same reason. This represents an opportunity to improve seizure detection efficacy by including ECG derived patient specific seizure signatures as a feature.

Personalization of detection algorithms has shown to decrease the FAR in an unimodal ECG-based study (De Cooman et al., 2020) and improve sensitivity and FAR in a unimodal behind-the-ear EEG study (Vandecasteele et al., 2020). Conceivably it may also improve the performance of a multi-modality setup.

The impact of a multi-modal approach upon the FAR has differed in previous studies, showing a decrease (Milosevic et al., 2016) and an increase (Fürbass et al., 2017, van Andel et al., 2017). In one study, a detection was marked as a seizure if either ACM or HR was above a threshold which may explain the increased FAR (van Andel et al., 2017). We found that the combination of ECG and EEG improved the SVM performances, when compared to unimodal EEG, indicating that an inherently multimodal classifier is a better approach when combining modalities (Vandecasteele et al., 2021).

However, multiple modalities may be excessive for patients with only convulsive seizures or known prominent ictal tachycardia, for whom one or two selected non-EEG modalities may be sufficient (Beniczky et al., 2021, Van de Vel et al., 2016). In this study, the lack of ictal rhythmic motor activity (e.g. clonic or myoclonic phases) across all three patients, may explain why the combination of sternum ACM and ECG yielded lower sensitivity and higher FAR when compared to the other modality combinations. Previous studies on ACM based convulsive seizure detection relies upon the ictal rhythmic motor activity (Arends et al., 2018) and is often measured on the limbs were the oscillations may be larger, which conceivably adds value to the SVM based seizure detection. We find that the combination of EEG and ECG may suffice for the detection of focal seizures without prominent motor activity. However, in the patient with focal tonic seizures, all modalities did achieve slightly higher sensitivity and lower FAR when compared to the combination of EEG and ECG (Fig. 7). In patient validation of a multi-modal setup, as performed in this study, may help personalize the choice of modalities suitable for long-term out-patient monitoring. For instance, our results suggest that EEG and ECG may suffice for the detection of focal nonmotor seizures in patient 4 and 26.

Besides considering appropriate modalities and sensor types, patient’s willingness to wear visible electrodes and the required monitoring time must also be taken into consideration. In interviews reported elsewhere (Beck et al., 2020), the patients included in this study disclosed that they were willing to use the devices provided the experience was reassuring and that the reality of their seizure events could be validated. All included patients completed their in-patient monitoring period. Wearables and skin-electrodes may be accepted by the patients for a short monitoring period, but implanted subcutaneous devices may be needed for longer recordings, i.e. months or years, allowing for long-term monitoring of treatment efficacy (Weisdorf et al., 2020). Implanted subcutaneous devices are less cumbersome than wearable multi-sensor systems, however their invasive single-use nature may lead to implant related complications and they are unsuitable for shorter monitoring periods (Duun-Henriksen et al., 2020). Long-term seizure monitoring may provide advances in seizure diagnostics, given the extended temporal EEG resolution. However, video-EEG remains the gold standard providing records of ictal semiology, real-time testing of seizure awareness and a larger spatial EEG resolution. Future seizure detection research should preferably be done in a phase-3 multi-center setup with video-EEG as a reference standard and an online-seizure detection algorithm (Beniczky and Ryvlin, 2018). However, the wearables are designed for out-patient monitoring, and a smaller out-patient trial can provide knowledge on signal quality, adverse events, patient experience and compliance, which are important variables when planning a costly phase-3 trial. In this study the wearable recordings were unsupervised to simulate a long-term out-patient recording and to approximate the recording quality from inconsistently maintained electrodes. Future large-scale studies are needed to improve the detection algorithm and should evaluate whether the patient-important outcomes (e.g. clinical decision making, morbidity, patient acceptability or quality of life) can justify the cost and the patients trouble from using these devices.

3.1. Limitations

This study is limited by the number of patients with seizures, total number of seizures and the inter-patient heterogeneity in seizure type. Only three patients had enough seizures to allow for SVM testing, and the results on focal tonic seizures were from one patient, which reduces the generalizability. However, the results are comparable to previous studies on automatic seizure detection (Gu et al., 2017; Vandecasteele et al., 2021, 2020). Previous studies on convulsive seizures have used limb worn ACM, but this was only recorded from one of the three of our patients with more than five seizures and therefore omitted from the SVM. Visual inspection of limb ACM recordings compared to axial ACM appears to have larger fluctuations and it’s possible that the contribution of ACM to the SVM classification accuracy would have been better if we could have used limb ACM.

4. Conclusion

We explored the value of a dedicated wearable offline multimodal seizure detection system for the long-term detection of focal seizures, both automatically and through manual review. An SVM based automatic seizure detection algorithm using different multi-modal combinations of EEG, ECG and ACM yielded improved sensitivity and FAR when compared to uni-modal EEG. Visualizations of ictal EEG and ECG derived features can supplement the manual data review of long-term recordings by providing an overview of seizure suspicious epochs in the recorded data.
Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clinph.2022.01.005.

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