Contents lists available at ScienceDirect

Seizure: European Journal of Epilepsy

journal homepage: www.elsevier.com/locate/seizure

Tonic-clonic seizure detection using accelerometry-based wearable sensors: A prospective, video-EEG controlled study

Dongni Johansson[a,b,1], Fredrik Ohlsson[c,1], David Krýsl[a,d], Bertil Rydenhag[a,e], Madeleine Czarnecki[c], Niclas Gustafsson[c], Jan Wipenmyr[c], Tomas McKelvey[f], Kristina Malmgren[a,b,*]

[a] Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[b] Department of Neurology, Sahlgrenska University Hospital, Gothenburg, Sweden
[c] RISE Acreo AB, Gothenburg, Sweden
[d] Department of Clinical Neurophysiology, Sahlgrenska University Hospital, Gothenburg, Sweden
[e] Department of Neurosurgery, Sahlgrenska University Hospital, Gothenburg, Sweden
[f] Department of Electrical Engineering, Chalmers University of Technology, Gothenburg, Sweden

ARTICLE INFO

ABSTRACT

Purpose: The aim of this prospective, video-electroencephalography (video-EEG) controlled study was to evaluate the performance of an accelerometry-based wearable system to detect tonic-clonic seizures (TCSs) and to investigate the accuracy of different seizure detection algorithms using separate training and test data sets.
Methods: Seventy-five epilepsy surgery candidates undergoing video-EEG monitoring were included. The patients wore one three-axis accelerometer on each wrist during video-EEG. The accelerometer data was band-pass filtered and reduced using a movement threshold and mapped to a time-frequency feature space representation. Algorithms based on standard binary classifiers combined with a TCS specific event detection layer were developed and trained using the training set. Their performance was evaluated in terms of sensitivity and false positive (FP) rate using the test set.
Results: Thirty-seven available TCSs in 11 patients were recorded and the data was divided into disjoint training (27 TCSs, three patients) and test (10 TCSs, eight patients) data sets. The classification algorithms evaluated were K-nearest-neighbors (KNN), random forest (RF) and a linear kernel support vector machine (SVM). For the TCSs detection performance of the three algorithms in the test set, the highest sensitivity was obtained for KNN (100% sensitivity, 0.05 FP/h) and the lowest FP rate was obtained for RF (90% sensitivity, 0.01 FP/h).
Conclusions: The low FP rate enhances the clinical utility of the detection system for long-term reliable seizure monitoring. It also allows a possible implementation of an automated TCS detection in free-living environment, which could contribute to ascertain seizure frequency and thereby better seizure management.

1. Introduction

Generalized tonic-clonic, as well as focal to bilateral tonic-clonic seizures (TCSs) may lead to traumatic injuries and represent a major risk factor for sudden unexpected death in epilepsy (SUDEP), which, in turn, accounts for 10–50% of all deaths in the epilepsy population [1,2]. High frequency of TCSs is also associated with significant psychosocial disability and quality of life impairment [3,4].

Video-electroencephalography (video-EEG) is the gold standard procedure for the investigation of paroxysmal disorders, but its availability is limited. In day-to-day practice, clinicians base their decisions mainly on patient history and witness accounts. The reliability of such information is, however, hampered by its retrospective nature and the difficulty to recognize all seizures, especially those with impaired awareness and nocturnal seizures (including TCSs) [5]. Seizure detection and accurate measurement of seizure frequency, in outpatient settings, would improve the management of epilepsy and thereby increase patient safety.

Recent advances in accelerometry technology have allowed the development of ambulatory monitoring systems able to detect changes in movement frequency and amplitude associated with motor seizures, and to differentiate these patterns from daily voluntary movements. Accelerometry-based sensors are usually small, portable and easy to use.

With an attractive integrated design, they may fulfil the need of patients with epilepsy to have a better outpatient disease management, while avoiding social stigmatization [6]. Several commercially available devices with proprietary algorithms have been proposed to be effective for TCSs detection, including a wrist watch with built-in accelerometers [7], accelerometry sensors combined with audio recordings [8], or other modalities, such as electrodermal activity [9,10] and heart rate [11].

The sensitivity of TCS detection systems based on accelerometry, possibly combined with additional modalities, is promising. However, false positive rates are an issue and vary depending on the different devices and algorithms used for seizure detection [12,13]. The majority of available seizure detection devices have been developed using training and test data sets from the same patients in the algorithm development phase, which is referred to as inclusion bias [14]. The presence of this bias limits the validity of the proposed algorithm performance due to potential overfitting. Overfitting refers to the model obtaining very good performance in the training set using cross validation for parameter tuning but failing to generalize to a data set containing previously unseen data. Moreover, the evaluation of commercial proprietary algorithm performance is also challenging due to restrictions for health professionals to access raw data. The amount of input from clinicians and clinical data in the algorithm development process varies between these detection devices. In order to obtain a good clinical standard and to match the needs of clinical practice, separate training and test data sets from different patients for the algorithm development and assessment of the performance of seizure-detection algorithms are desirable.

The wearITmed project is a non-commercial platform for collaboration between technical experts, medical professionals, researchers and patients aiming to develop an integrated wearable system – a multi-sensor integrated garment – that would be usable in multiple clinical situations, including detection and differentiation of various seizure types, and would allow continuous improvement and adaptation to needs and preferences of patients as well as clinicians [6].

The objective of this video-EEG controlled prospective study was to evaluate the performance of different detection algorithms applicable in the wearITmed prototype accelerometry-based system for TCS detection.

2. Methods

2.1. Participants

This prospective study was conducted with epilepsy surgery candidates > 18 years who underwent scalp or invasive video-EEG recording at the Sahlgrenska University Hospital in Gothenburg, Sweden. Clinical variables were obtained from medical records, seizure-related variables were based on analysis of video-EEG recording, and imaging variables were based on analysis of available magnetic resonance imaging (MRI). The study was conducted in accordance with the Declaration of Helsinki and the study protocol was approved by The Regional ethical review board in Gothenburg, Sweden. Written informed consent was obtained from all participants.

2.2. Study design

During video-EEG monitoring, the patients wore one accelerometry sensor on each wrist. Two types of inertial sensors were used during different phases of data collection (initial phase: in-house developed sensor, RISE Acreo, Sweden; later phase: Shimmer3, Shimmer Research, Ireland). An example of Shimmer3 wrist-worn sensors is shown in Fig. 1. Both sensors measure the acceleration vector components along three orthogonal axes. The measurement range was set to $\pm 3\,g$ (Acreo) or $\pm 8\,g$ (Shimmer3) with a sampling rate of 50 Hz (Acreo) or 102.4 Hz (Shimmer3). The movement data was prospectively continuously collected and stored on a laptop (Acreo) or an SD Memory card (Shimmer3) for later read-out and off-line analysis. At the start of each session, measurements were manually synchronized with the reference time in the video-EEG system by technical experts or by health care professionals who had received special instruction in handling the sensors.

Fig. 1. An example of Shimmer3 wrist-worn sensors.

Timing, duration and clinical type of TCSs (focal vs. generalized vs. unknown onset) recorded during video-EEG monitoring were reviewed and annotated by an experienced epileptologist (DK). The onset and duration of the motor symptoms corresponding to each TCS were estimated from the accelerometer data based on the annotations, with additional consultation and review of the video-EEG recordings in every case where any uncertainties regarding seizure semiology, onset or duration were identified. The seizure onset was manually labelled on the accelerometer data and the epileptologist was blinded to the sensor data during video-EEG inspection and seizure labelling.

The accelerometer measurements from patients with recorded TCSs were divided into two disjoint sets; one training set and one test set. For each measurement in the training set a continuous 24 h period containing all TCSs was selected in order to reduce the data set imbalance and improve model training. This procedure mitigated the tendency of the training process to completely ignore the rare class (seizure) in favor of the dominant one (non-seizure), which results from the penalty of associating every time instance with the dominant class becoming negligible as the imbalance grows sufficiently large. The test set data contained the full measurements except for periods of missing data that were manually identified and removed.

The training set was used for model development and for training the final models, while the test set was reserved exclusively for algorithm evaluation. Inclusion bias was removed from the evaluation results by ensuring that the data recorded for each individual was assigned in its entirety to either the training set or the test set. Only once the method development was completed, including the tuning of all parameters in the algorithms, were the algorithms obtained evaluated on the training set data. The rationale for this practice was to remove the tendency to overestimate the ability to generalize to previously unseen individuals resulting from tuning parameters to optimize performance in the test set.

2.3. Signal processing and feature extraction

Signal processing and algorithm development and evaluation were conducted using MATLAB 2016b (MathWorks, USA). The accelerometry

data was pre-processed using a band-pass filter (with passband 0.25–13 Hz), and a 0.1g movement threshold was applied to remove non-motor epochs. Missing sensor recordings resulting in unphysical interpolated data were automatically identified and removed.

Following pre-processing, a number of features, both in the time domain and the frequency domain, were extracted from the acceleration signal using an overlapping sliding window, whose length varied between 1 s and 10 s depending on the feature. The purpose of extracting features was to condense the raw data into quantities that are sensitive to TCSs and the windowing served to include information at different time scales in the feature set in order to distinguish characteristic seizure

patterns. Previous studies [9,15] have identified several features for seizure detection which were used in this study for algorithm evaluation together with new added features (e.g. signal magnitude area and entropy). Feature values were computed with a 1 s resolution and compiled into a vector representation, and the true class for the corresponding time points (with seizure and non-seizure instances marked as 1 and 0 respectively) was extracted from the seizure records.

The entire signal processing and feature calculation step was designed to accommodate varying sampling frequencies, so that the feature sets computed for the two sensor types (Acreo and Shimmer3) could be treated identically in the subsequent analysis.
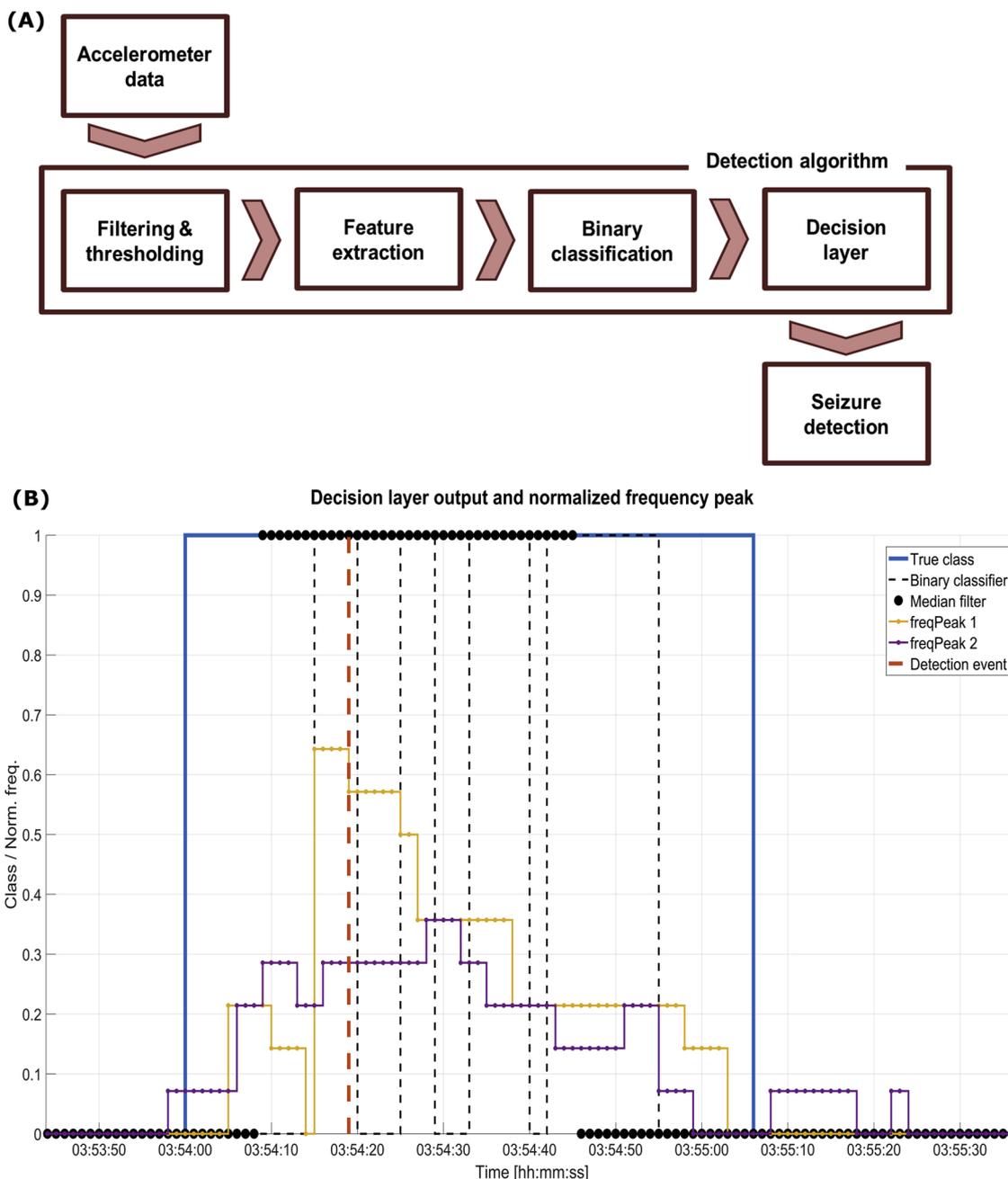

Fig. 2. (A) Schematic illustration of the seizure detection algorithm. The three different algorithms evaluated differ in the feature set derived from accelerometer data, the binary classifier used, and the parameters of the decision layer. (B) Illustration of the operation of the decision layer for a time sequence containing a seizure, recorded for patient ID 7 in the training set, during model development. The true class (solid blue) and the output from the binary classifier (dashed black) are shown together with the intermediate decision layer median filter output (black asterisk), the frequency peak features for the two sensors (yellow and violet point-dotted) used in the veto and the final decision layer output detection (dashed red). The median filter serves to smooth the binary classifier output and suppress intermittent misclassifications to reduce the false positive rate. The subsequent threshold and veto requires simultaneously a sufficient number of consecutive time instances classified as seizure and a sufficiently high frequency peak in both sensors in order to generate a detection event (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

2.4. Algorithm design and evaluation

The seizure detection algorithm design was based on a binary classifier taking the feature vector as input and predicting the class of each 1 s interval as seizure (1) or non-seizure (0). Since the task at hand was detection of seizure events, rather than correctly classifying each time instance, the output from the binary classifier was processed using a decision layer, combining a modified median filter with a subsequent threshold for consecutive seizure classifications. In addition, a veto could optionally be applied based on a feature specific thresholding. If all conditions were fulfilled, the decision layer generated a detection event and resumed analysis after a 120 s delay to avoid generating multiple detections for a single seizure. The algorithm and the application of the decision layer are schematically illustrated in Fig. 2.

During the model development phase [16], the training set data was used to evaluate several different binary classifiers, optimize the feature

Table 1
The demographics and clinical characteristics of all participants in this study.

	Participants n = 75
Age[a], years	35 (18–77)
Female (n [%])	47 (63)
Epilepsy duration, years	17 (2–70)
Number of AEDs	2 (0–4)
AED ≥3 (n [%])	26 (35)
History of TCSs	61 (81)
Types of seizures (n [%])[b]	
Focal onset	59 (79)
Generalized onset	4 (5)
Unknown onset	12 (16)
SOZ[c] location (if focal)	
Temporal	32 (43)
Frontal	11 (15)
Occipital	3 (4)
Parietal	3 (4)
TPO	4 (5)
Unknown	6 (8)
SOZ[c] side (if focal)	
Left	25 (33)
Right	25 (33)
Bilateral	9 (12)
Type of video-EEG (n [%])[d]	
Scalp	67 (89)
Invasive	10 (13)
Video-EEG duration, days	7 (2–16)
History of nocturnal seizures (n [%])	59 (79)
History of febrile seizures (n [%])	11(15)
History of status epilepticus (n [%])	15 (20)
History of aura (n [%])[e]	58 (77)
Somatosensory	17 (23)
Epigastric	23 (31)
Cephalic	18 (24)
Others[f]	15 (20)
Oroalimentary automatisms (n [%])	38 (51)
Gestural automatisms (n [%])	37 (49)
MR lesion (n [%])	20 (27)

Data are presented as median (range) unless otherwise specified.
TCSs, tonic-clonic seizures; video-EEG, video-electroencephalography; AED, antiepileptic drug; SOZ, seizure-onset zone; TPO, temporo-parieto-occipital junction; MR, magnetic resonance.
   [a] Age in years at the time of video-EEG monitoring.
   [b] Classification according to the new classification of seizures by the International League Against Epilepsy 2017. [27].
   [c] Seizure-onset zone based on the whole electroclinical syndrome.
   [d] Two patients were conducted vide-EEG monitoring in separate distances.
   [e] Classification according to semiological seizure classification. [28].
   [f] Others: visual aura (n = 8), auditory aura (n = 3), olfactory aura (n = 4), gustatory aura (n = 2). One patient had history of both visual and gustatory auras. One patient had history of both visual and auditory auras.

set for each classifier and tune the parameters of both the classification algorithms and the decision layer used for event detection using cross-validation. The training set performance of the algorithms in patient-specific (training and testing on the same individual) and patient-general (training and testing on different individuals) settings was evaluated together with their robustness against false positives during normal activities characterized by high frequency and/or large amplitude movements, which could be mistaken for seizure activity (playing badminton, tooth brushing and dishwashing).

The models and decision layer parameters yielding the best performance in the model development [16] were selected for further optimization and the final algorithms trained using the full training set. Only after the selected algorithms were finalized were they evaluated on the test set data in order to obtain an unbiased estimate of their performance.

A detection was considered to be a true positive (TP) if the time window contributing to the detection, the length of which was given by the sum of the median filter length and the seizure detection threshold, contained at least one time instance labelled as a seizure. Otherwise the detection was considered to be a false positive (FP). Seizures which generated no detection events were considered to be false negatives (FN). In order to obtain a conservative estimate of the performance the following procedure was applied in case a detection with no contribution from a time instance labelled as seizure occurred within 120 s before an actual seizure; a FP was considered to be detected and the algorithm was reset at the start of the seizure. Only if the algorithm then also generated a detection which received contribution from a time instance labelled as seizure was a TP also recorded.

3. Results

Seventy-five patients (median age 35 years, range 18–77 years, 63% female) were enrolled in the study. The demographic and clinical characteristics of all patients are presented in Table 1 and individual characteristics and demographic data in Supplementary Table 1. Sixty-one of them had a history of TCSs. During the sensor monitoring, a total of approximately 8933 h accelerometer data was recorded. The mean recording time was 121 h per patient (median 104, range 4–264 h). Thirty-seven TCSs in 11 patients were recorded by the accelerometry sensors. All seizures in the study are symmetric in the sense that they involve clear convulsive manifestations in both arms.

Sensor recordings containing TCSs were divided into a training set, consisting of 96 h of data and containing 27 TCSs in three patients, and a test set consisting of 570 h of data and containing 10 TCSs in eight patients. The clinical characteristics and seizure occurrence for the patients in both sets are presented in Table 2.

3.1. Missing data and non-adherence to wrist-worn sensors

Of 64 TCSs in 19 patients detected by video-EEG, 12 TCSs occurred when patients had no sensors on, 10 TCSs in three patients occurred after sensors were removed due to discomfort and five TCSs were unrecorded by sensors due to technical errors. A total of 1952 h missing data (22%) was noted in 29 patients with an average of 65 h (range 10–144) per patient. Missing data attributable to technical errors was 71%, and unknown reasons (e.g. sensors were not started correctly) were attributable to 29% of the missing data. The percentage of individual missing data and non-adherence for sensor recording are presented in Supplementary Fig. 1.

3.2. Algorithm development

During the model development stage [16] the decision layer parameters were tuned and the detection performance was found to improve with the application of a veto threshold for the frequency peak feature, which contains information regarding the frequency range containing the maximum energy. The three binary classifiers performing best, both in terms of sensitivity and false positive rate, during

Table 2
Clinical characteristics of patients with tonic-clonic seizures (TCSs) detected by both accelerometry sensors and video-EEG monitoring.

ID	Age[a] /Gender	Age at onset	Number of AEDs	TC seizure onset[b]	SOZ[c] location (if focal)	SOZ[c] side (if focal)	Number of TCSs detected with video-EEG	Available Number of TCSs for development/ evaluation[d]	Number of TCSs detected with sensors[e]
Training set									
7[f]	25/M	13	2	Focal	TPO	Left	12	11[g]	11
							12	12	12
48[h]	29/F	1	2	Focal	Temporal	Left	2	2	2
55	41/M	23	4	Focal	Parietal	Right	2	2	2
Test set									
19	27/F	13	2	Focal	Temporal	Right	1	1	1
35	46/M	15	3	Focal	Temporal	Left	2	2	2
47	34/M	6.5	3	Focal	Unknown (Temporal?)	Unknown (Right?)	4	1	1
59	40/F	35	3	Generalized	NA	NA	3	1	1
66	36/M	14	3	Focal	Temporal	Unknown	2	2	2
68	26/M	21	2	Focal	Temporal	Left	3	1	1
74	25/F	10	3	Focal	Temporal	Left	1	1	1
93	25/F	7	2	Generalized	NA	NA	1	1	1

M, male; F, female; AEDs, antiepileptic drugs; TCSs, tonic-clonic seizures; SOZ, seizure-onset zone; video-EEG, video-electroencephalography; TPO, temporo-parieto-occipital junction; NA, not applicable.

[a] Age in years at the time of video-EEG monitoring.
[b] Classification according to the new classification of seizures by the International League Against Epilepsy 2017. [27].
[c] Seizure-onset zone based on the whole electroclinical syndrome.
[d] Five unrecorded TCSs occurred when sensors were not worn (ID 47 and ID 68). Two TCSs were unavailable due to technical errors (ID 59).
[e] At least one of the algorithms in development or evaluation detected TCSs.
[f] Video-EEG monitoring was conducted twice at separate instances.
[g] One atypical tonic-clonic seizure was excluded from the training set.
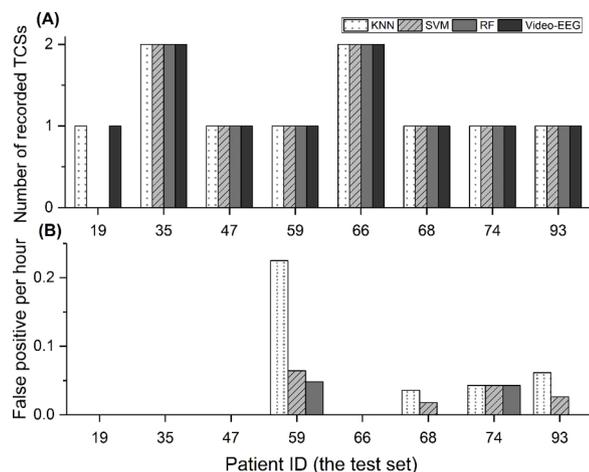[h] The patient wore the sensors on the upper arms.

Fig. 3. Performance of the three classification algorithms in tonic-clonic seizure detection in each individual of the test set. (A) Number of tonic-clonic seizures detected by the three classification algorithms. (B) The average false positive rate per hour in each of the three classification algorithms. KNN, K-Nearest Neighbors; SVM, Support Vector Machine; RF, Random Forest; video-EEG, video-electroencephalography.

the model development stage were K-Nearest Neighbors (KNN) with 5 neighbors, Support Vector Machine (SVM) with linear kernel and Random Forest (RF) with 30 trees. The feature sets used for each classifier were also optimized, and the optimal sets were in all cases found to contain features related to the acceleration magnitude and standard deviation as well as the signal entropy and the energy content in various frequency bands. In addition, the frequency peak feature described above was used in one optimal set.

Based on the development results [16], the classification algorithms based on the KNN, SVM and RF methods were selected for further development. The decision layer parameters and the veto threshold level were further optimized individually for each of the three selected classification algorithms using the training set data, and three final detection

algorithms were trained using the complete training set. The training performance, obtained by evaluating the models obtained on the training set itself, was perfect (100% sensitivity and 0 FPs) for all three algorithms.

3.3. Detection algorithm evaluation

The performance of the three algorithms in the test set is shown in Fig. 3 and Supplementary Table 2. When evaluated on the test set, the KNN detection algorithm correctly detected all 10 TCSs with 26 FPs generated for the 570 h of data (100% sensitivity, 0.05 FP/h, 1.2 FP/24 h). The SVM algorithm detected 9 out of 10 TCSs with 11 FPs (90% sensitivity, 0.02 FP/h, 0.48 FP/24 h), while the lowest false positive rate was obtained for the RF algorithm which also detected 9 out of 10 TCSs and only generated 6 FPs (90% sensitivity, 0.01 FP/h, 0.24 FP/24 h). Examples of TP and FP detection events generated by the detection algorithms are shown in Fig. 4.

4. Discussion

To our knowledge, this study is the first to systematically evaluate the performance of different classification algorithms for TCS detection while using separate data sets to avoid inclusion bias. All three algorithms evaluated had a high sensitivity to detect TCSs (SVM and RF sensitivity 90%, KNN 100% sensitivity). The lowest false positive rate was obtained for the RF algorithm (0.01 FP/h, 0.24 FP/24 h) and achieved solely by using the accelerometry-based system. Notably, the patients had no movement restrictions during video-EEG recording.

There are three sensor-based devices reporting comparable sensitivity (above 90%) for TCSs detection. The reported detection sensitivity for a commercially available wrist-worn device (SmartWatch, Smart Monitor, USA) ranges from 31% to 92% [8,17,18] and one of the studies reported 204 false events in 40 patients with eight TCSs [17]. Another accelerometry-based single wrist-worn sensor device (Epi-Care Free, Danish Care, Denmark) detected 9 out 22 TCSs (sensitivity 41%, FP 0.15/24 h) in one study [19], and in another study identified 35 out of 39 TCSs in 20 patients (sensitivity 90%, FP 0.2/24 h) [7]. However, in that study patients were instructed to refrain from performing certain
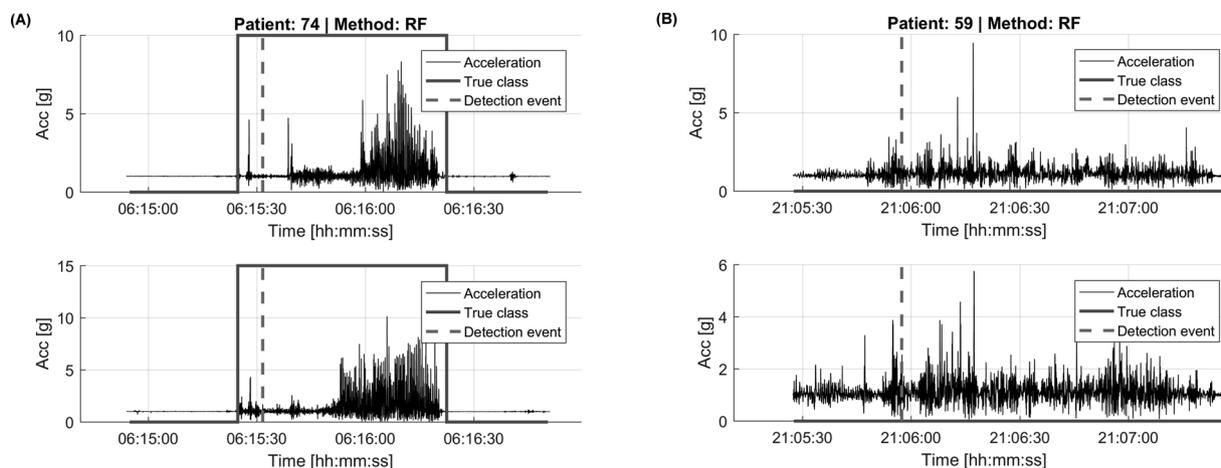
Fig. 4. Examples of detection events in the test set generated by the RF algorithm; top and bottom graphs show acceleration magnitude (black) and renormalized true classification (solid grey) as functions of time for the two sensors. (A) Example of a TP event for patient ID 74 with estimated start of seizure indicated by the dashed line. (B) Example of a FP event in patient ID 59 indicated by the dashed line. RF, Random Forest; TP, true positive; FP, false positive.

repetitive daily movements that could be misclassified as seizures (such as brushing teeth with the hand that had a sensor attached) [7]. A multimodal system (Empatica Embrace, USA) based on both accelerometry and electrodermal activity detected 15 out 16 TCSs in seven patients in one study and 52 out of 55 TCSs in 22 patients in another study (sensitivity around 95%, false alarms 0.2/24 h) [9,10]. However, inclusion bias was, to some extent, found to be present in those studies [14]. Consequently, in comparison with other studies, our results achieved comparable sensitivity and FP rate using only one modality, without inclusion bias and without any movement restrictions in the algorithm development and evaluation.

A variation in the number of FPs was noted between individuals in relation to heterogeneous motor phenomena of TCSs in this study, similar to other seizure detection devices [20–22]. Two individuals (ID 59 and 93) with generalized onset TCSs generated a higher false positive rate in the KNN algorithm than in the other two algorithms, and generally high false positive rates when compared to patients with focal onset TCSs. On visual inspection of the accelerometer data, patient (ID 59) showed a long period with high frequency movements to which 30–50% of the FPs in each of the three algorithms was attributed (Fig. 3). In another patient (ID 74), a focal bilateral clonic seizure with preserved awareness caused a movement pattern which was difficult to distinguish from TCSs, and generated a FP in all the three algorithms. Individualization of the algorithms for included individuals before application of the seizure detection system could potentially further decrease the false positive rates and consequently improve the clinical relevance of the results.

False alarms are a potential barrier for the use of wearable sensors in seizure detection [5]. A majority of patients would nonetheless accept false alarms as long as they are fewer in number than the correct predictions [23]. Twenty-five percent false positive alarms (i.e. 1 FP for every 3 TP) has been reported as acceptable from most patients and caregivers [24]. Since the expected rate is dependent on seizure frequency in a given individual, it cannot be directly translated into a FP/h rate of the detection algorithm. This 25% acceptable rate can however, given the performance of the algorithm, be used to identify the subgroup of patients with sufficient seizure frequency to find the detection device acceptable.

Different strategies have been suggested to decrease FPs, such as the use of multimodal systems and patient-specific algorithms [9,25]. Multimodal systems are promising, but give rise to other concerns, such as higher demand on data handling and processing and increased power consumption. A trade-off may be needed between minimizing the FP rate while still maintaining the technical feasibility to enable the use of wearable sensors in long-term seizure monitoring outside the hospital environment.

A discrepancy between the numbers of TCSs recorded by video-EEG and by the accelerometry sensors was noted. Unrecorded seizures by the accelerometry sensors were mainly attributable to missing data and non-adherence to sensors. A relatively high percentage of missing data (22%) was noted in the study, which is in accordance with other studies using wearable sensors [13]. Technical issues with the sensors included battery failure, memory card or data storage problems, and failed synchronization between sensors. The advantage of access to raw sensor data in the in-house developed system allows an investigation of reasons causing missed seizures in the algorithms. Even though the overall adherence rate in this study was high (96%), three out of 75 patients reported discomfort caused by the sensors and removed them after approximately two to three days of monitoring, resulting in 10 unrecorded TCSs. This emphasizes the importance of a comfortable, patient-centered design for wearable seizure detection devices, which may increase the motivation for wearing them [6,26].

The study population was heterogeneous regarding the type of TCSs, as well as lateralization and localization of seizure onset in focal-onset TCSs. There were no TCSs recorded by the sensors that were not registered by video-EEG, which underlines the role of video-EEG as gold standard for studies evaluating sensor performance. Bilateral sensors were used instead of a single wrist sensor. This may allow for a comparison between upper limb movements at the onset and offset of TCSs with regard to the side of movement, movement frequency and amplitude. This information may also be helpful while classifying the type of TCS, as well as give hints about the lateralization of the seizure onset and can be useful for generating TCS evolution patterns once data from a larger group is collected. The use of bilateral sensors can also be useful for improving TCSs detection performances in cases such as when one arm is constrained (e.g. the rhythmic arm movement is constrained by nurses or other people or availability of limited space during the seizures) or when the motor manifestation is unclear as to which wrist is predominant.

The strengths of the present study are that separate training and test data sets were used for algorithm development and evaluation, that the evaluated algorithms can detect TCSs during video-EEG monitoring with high sensitivity and a low FP rate, relative to comparable studies using only one sensor modality, and this was obtained without imposing any movement restrictions. In fact, the FP rate was also comparable to that obtained in state-of-the art multimodal systems [10,11]. The ability to obtain such a low FP rate using only one modality, implies that power consumption can be reduced compared to multimodal system, which in turn increases the expected battery life time and therefore the clinical utility of the proposed accelerometry-based system in long-term use for TCS detection. The weaknesses of the study include that the number of TCSs, the number of individuals with

recorded TCSs, and the total number of hours of recorded data in the test set were all relatively low. The stability of the performance under generalization to larger populations was therefore difficult to assess.

The next stage in the development of an integrated multimodal sensors garment will hopefully further increase the precision in detecting TCSs, as well as allow detection of other types of seizures, while still remaining easy to use for the patients. In conjunction with this work, the issue of computational expense for the candidate methods (KNN, SVM and RF) in a future real-time application will also be investigated. A close collaboration between technical experts, health professionals and patients is essential to develop an appealing, comfortable, adaptable, reliable and technically feasible wearable seizure detection device.

5. Conclusions

The low false positive rate achieved in the present study, with a single modality used, no inclusion bias and no restrictions on movements during the sensor monitoring, provides a possible implementation for a long-term reliable seizure monitoring in free-living environment to enable better seizure management. The collaborative in-house development of such systems allows for an improved design of detection algorithms that, in turn, affects the overall performance of the device.

Conflict of interest statement

FO and JW are employees of RISE Acreo AB. At the time of their contribution MC and NG were MSs students at RISE Acreo AB. The remaining authors have no conflicts of interest.

Acknowledgements

References

[1] Shorvon S, Tomson T. Sudden unexpected death in epilepsy. Lancet 2011;378:2028–38.
[2] Lawn ND, Bamlet WR, Radhakrishnan K, et al. Injuries due to seizures in persons with epilepsy: a population-based study. Neurology 2004;63:1565–70.
[3] Baker GA, Jacoby A, Buck D, et al. Quality of life of people with epilepsy: a European study. Epilepsia 1997;38:353–62.
[4] Schneider-von Podewils F, Gasse C, Geithner J, et al. Clinical predictors of the long-term social outcome and quality of life in juvenile myoclonic epilepsy: 20-65 years of follow-up. Epilepsia 2014;55:322–30.
[5] Elger CE, Hoppe C. Diagnostic challenges in epilepsy: seizure under-reporting and seizure detection. Lancet Neurol 2018;17:279–88.
[6] Ozanne A, Johansson D, Hallgren Graneheim U, et al. Wearables in epilepsy and Parkinson's disease-A focus group study. Acta Neurol Scand 2017.
[7] Beniczky S, Polster T, Kjaer TW, et al. Detection of generalized tonic-clonic seizures by a wireless wrist accelerometer: a prospective, multicenter study. Epilepsia 2013;54:e58–61.
[8] Velez M, Fisher RS, Bartlett V, et al. Tracking generalized tonic-clonic seizures with a wrist accelerometer linked to an online database. Seizure 2016;39:13–8.
[9] Poh MZ, Loddenkemper T, Reinsberger C, et al. Convulsive seizure detection using a wrist-worn electrodermal activity and accelerometry biosensor. Epilepsia 2012;53:e93–7.
[10] Onorati F, Regalia G, Caborni C, et al. Multicenter clinical assessment of improved wearable multimodal convulsive seizure detectors. Epilepsia 2017;58:1870–9.
[11] van Andel J, Ungureanu C, Arends J, et al. Multimodal, automated detection of nocturnal motor seizures at home: Is a reliable seizure detector feasible? Epilepsia Open 2017;2:424–31.
[12] Jory C, Shankar R, Coker D, et al. Safe and sound? A systematic literature review of seizure detection methods for personal use. Seizure 2016;36:4–15.
[13] Johansson D, Malmgren K, Alt Murphy M. Wearable sensors for clinical applications in epilepsy, Parkinson's disease, and stroke: a mixed-methods systematic review. J Neurol 2018.
[14] Leijten FSS. Multimodal seizure detection: a review. Epilepsia 2018;59:42–7.
[15] Nijsen TAR, Arends J, Cluitmans P. Automated detection of tonic seizures using 3-D accelerometry. IFMBE Proceedings 2008;22:188–91.
[16] Czarnecki M, Gustafsson N. Machine learning for detection of epileptic seizures, 2015: ex - Institutionen för signaler och system, Chalmers tekniska högskola, no: EX028/2015 Accessed February 28, 2018 http://publications.lib.chalmers.se/records/fulltext/219371/219371.pdf.
[17] Lockman J, Fisher RS, Olson DM. Detection of seizure-like movements using a wrist accelerometer. Epilepsy Behav 2011;20:638–41.
[18] Patterson AL, Mudigoudar B, Fulton S, et al. SmartWatch by SmartMonitor: assessment of seizure detection efficacy for various seizure types in children, a large prospective single-center study. Pediatr Neurol 2015;53:309–11.
[19] Van de Vel A, Verhaert K, Ceulemans B. Critical evaluation of four different seizure detection systems tested on one patient with focal and generalized tonic and clonic seizures. Epilepsy Behav 2014;37:91–4.
[20] Conradsen I, Beniczky S, Wolf P, et al. Seizure onset detection based on a Uni- or multi-modal intelligent seizure acquisition (UISA/MISA) system. Conf Proc IEEE Eng Med Biol Soc 2010:3269–72. 2010.
[21] Gu Y, Cleeren E, Dan J, et al. Comparison between scalp EEG and behind-the-Ear EEG for development of a wearable seizure detection system for patients with focal epilepsy. Sensors (Basel) 2017:18.
[22] Beniczky S, Conradsen I, Henning O, et al. Automated real-time detection of tonic-clonic seizures using a wearable EMG device. Neurology 2018;90:e428–34.
[23] Schulze-Bonhage A, Sales F, Wagner K, et al. Views of patients with epilepsy on seizure prediction devices. Epilepsy Behav 2010;18:388–96.
[24] Tovar Quiroga DF, Britton JW, Wirrell EC. Patient and caregiver view on seizure detection devices: a survey study. Seizure 2016;41:179–81.
[25] Cuppens K, Karsmakers P, Van de Vel A, et al. Accelerometry-based home monitoring for detection of nocturnal hypermotor seizures based on novelty detection. IEEE J Biomed Health Inform 2014;18:1026–33.
[26] Patel AD, Moss R, Rust SW, et al. Patient-centered design criteria for wearable seizure detection devices. Epilepsy Behav 2016;64:116–21.
[27] Fisher RS. The New Classification of Seizures by the International League Against Epilepsy 2017. Curr Neurol Neurosci Rep 2017(17):48.
[28] Luders H, Acharya J, Baumgartner C, et al. Semiological seizure classification. Epilepsia 1998;39:1006–13.