Multi-Biosignal Analysis for Epileptic Seizure Monitoring

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Persons who suffer from intractable seizures are safer if attended when seizures strike. Consequently, there is a need for wearable devices capable of detecting both convulsive and nonconvulsive seizures in everyday life. We have developed a three-stage seizure detection methodology based on 339 h of data (26 seizures) collected from 10 patients in an epilepsy monitoring unit. Our intent is to develop a wearable system that will detect seizures, alert a caregiver and record the time of seizure in an electronic diary for the patient’s physician. Stage I looks for concurrent activity in heart rate, arterial oxygenation and electrodermal activity, all of which can be monitored by a wrist-worn device and which in combination produce a very low false positive rate. Stage II looks for a specific pattern created by these three biosignals. For the patients whose seizures cannot be detected by Stage II, Stage III detects seizures using limited-channel electroencephalogram (EEG) monitoring with at most three electrodes. Out of 10 patients, Stage I recognized all 11 seizures from seven patients, Stage II detected all 10 seizures from six patients and Stage III detected all of the seizures of two out of the three patients it analyzed.

Keywords: Arterial oxygenation; electrodermal activity; heart rate; limited-channel EEG monitoring; seizure detection; wrist-worn device.

1. Background

Automatic and accurate seizure detection is a challenging goal that offers two benefits. First, a caregiver can be notified, which is important because seizures can lead to injury or other complications including sudden unexpected death in epilepsy (SUDEP). If both patient and caregiver are confident that a detection device will notify the caregiver in the event of a seizure, quality of life will be improved for both parties and secondary effects of seizures (e.g. injury, SUDEP) can be minimized. Second, an electronic diary of seizure events can be created. Such a diary would provide more accurate information for physicians than self-reporting of seizures, which has proven to be inaccurate and unreliable.1–4 In addition, long term use of wearable devices by large
numbers of epileptic patients would provide biosignal data for researchers seeking to better understand long term effects of seizures, and in particular the causes and risk factors of SUDEP.

Electroencephalogram (EEG) is the gold standard for seizure detection, but it is impractical for use in daily life because it requires the use of either a special hat/headset worn in just the right way or sensors implanted in the brain. Neither of these options is convenient, and implanting a device in the brain is inherently invasive and costly. Use of extracerebral signals to detect seizures presents its own set of challenges. These biosignals differ among patients and seizure types; consequently, any given wearable system or device will not be helpful for every patient. We are seeking to develop a system that will be accurate, easy to wear, nonstigmatizing, and helpful for a substantial percentage of epileptic patients.

There are a number of devices on the market designed to detect convulsive seizures using extra-cerebral (nonEEG) signals. Most of these devices employ motion sensors because the convulsive motion is similar from patient to patient, and so is readily identifiable. To the best of our knowledge, however, there is no wearable device available to detect complex partial seizures (CPS), as they are nonconvulsive. Recent work using heart rate (HR) to detect seizures has achieved promising results for patients in epilepsy monitoring units (EMUs), but the authors conceded that there is much room for improvement to their algorithms. In normal daily life, we must expect a greater variation in patient activity, and resulting HR changes greater than those typically found in an EMU.

Based on the literature and our prior experience with wearable sensors, we chose the wrist as the best location for a seizure detection system. This location allows us to monitor several biosignals that are affected by seizures and to embed sensors in an easy to wear, nonstigmatizing wristband. Our approach is novel because, to the best of our knowledge, we are collecting and analyzing more biosignals than anyone since van Buren in the late 1950s. By using today’s wearable devices, we are able to collect these signals less obtrusively than van Buren was able to.

We chose a set of five biosignals which can be monitored at the wrist or for which wrist-based monitoring is currently under development: HR, arterial oxygenation ($\text{SpO}_2$), accelerometry (ACC), electrodermal activity (EDA) and temperature (TEMP). A number of researchers have observed extreme HR changes at the beginning of some types of seizures. Researchers have also found indications that seizures may cause changes in $\text{SpO}_2$ levels. Their findings are supported by studies showing that seizures can cause disruption in patient respiration. A recent study indicates that temporal lobe seizures in particular often cause a temporary cessation in breathing, thereby raising the CO$_2$ level and lowering the O$_2$ level in the patient’s bloodstream. Motion measured by ACC and changes in EDA have been found to effectively indicate the onset of convulsive seizures. Skin TEMP is necessary for proper interpretation of EDA readings. Several seizure sensitive biosignals such as respiration and electromyography cannot be monitored at the wrist and so were not collected in the study, we are reporting here.

2. Data Collection

For our data collection platform, we selected two devices because no device on the market today collects all the signals of interest to us. The Affectiva Q-curve monitors EDA, TEMP and ACC. The Nonin WristOx2 collects HR and $\text{SpO}_2$. Unfortunately, the WristOx2 sensor is housed in a finger cuff because it uses traditional pulse oximetry to collect the patient’s photoplethysmogram. Several companies are working to develop devices capable of reading $\text{SpO}_2$ accurately at the wrist using reflectance oximetry, including Empatica with their E4 wristband, and Samsung with their Gear Smartwatch; but as of this writing, there is no device on the market with that capability. We are proceeding with our research under the assumption that the problem of $\text{SpO}_2$ collection at the wrist will be solved soon. Our immediate goal is to determine the usefulness of $\text{SpO}_2$ for seizure detection.

Collection of seizure data was done under Institutional Review Board (IRB) protocol at an EMU in Dallas, Texas. EEG collection and seizure annotation were done by our medical consultants using the Natus NeuroWorks EEG platform. The Affectiva and Nonin devices were time synced to the EEG.
Table 1. Patients who provided data for our study.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Gender</th>
<th>Age in years</th>
<th>Years of seizures</th>
<th>Number of seizures captured</th>
<th>Seizure type</th>
<th>Seizure origin (Focus)</th>
<th>Amount (Time) of data captured</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>25</td>
<td>10</td>
<td>1</td>
<td>Secondary GTCS</td>
<td>Nonfocal</td>
<td>16 h, 14 min</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>64</td>
<td>4</td>
<td>1</td>
<td>CPS</td>
<td>Left temporal</td>
<td>11 h, 50 min</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>51</td>
<td>47</td>
<td>2</td>
<td>Secondary GTCS</td>
<td>Left temporal</td>
<td>43 h, 15 min</td>
</tr>
<tr>
<td>9</td>
<td>Female</td>
<td>41</td>
<td>20</td>
<td>3/1</td>
<td>CPS/Sec. GTCS</td>
<td>Left temporal</td>
<td>31 h, 13 min</td>
</tr>
<tr>
<td>10</td>
<td>Male</td>
<td>60</td>
<td>42</td>
<td>4</td>
<td>CPS</td>
<td>Right temporal</td>
<td>54 h, 3 min</td>
</tr>
<tr>
<td>11</td>
<td>Male</td>
<td>40</td>
<td>16</td>
<td>1</td>
<td>CPS</td>
<td>Right temporal</td>
<td>25 h, 21 min</td>
</tr>
<tr>
<td>12</td>
<td>Male</td>
<td>46</td>
<td>12</td>
<td>2</td>
<td>CPS</td>
<td>Frontal</td>
<td>37 h, 24 min</td>
</tr>
<tr>
<td>15</td>
<td>Female</td>
<td>28</td>
<td>23</td>
<td>1</td>
<td>Bilateral tonic</td>
<td>Left frontal</td>
<td>16 h, 4 min</td>
</tr>
<tr>
<td>16</td>
<td>Female</td>
<td>21</td>
<td>9</td>
<td>2</td>
<td>CPS</td>
<td>Right temporal</td>
<td>28 h, 27 min</td>
</tr>
<tr>
<td>18</td>
<td>Female</td>
<td>29</td>
<td>10</td>
<td>1</td>
<td>CPS</td>
<td>Right temporal</td>
<td>30 h, 20 min</td>
</tr>
<tr>
<td>19</td>
<td>Female</td>
<td>35</td>
<td>1</td>
<td>11</td>
<td>CPS</td>
<td>Rt &amp; lt temporal</td>
<td>39 h, 52 min</td>
</tr>
<tr>
<td>20</td>
<td>Male</td>
<td>31</td>
<td>20</td>
<td>1</td>
<td>Primary GTCS</td>
<td>Nonfocal</td>
<td>40 h, 2 min</td>
</tr>
</tbody>
</table>

Note: The other eight patients who enrolled in the study had either (i) no usable data or (ii) no seizures.
algorithm, implemented in MATLAB, is discussed in Sec. 4.

For the remaining patients, we developed three-channel EEG analysis. We discuss this algorithm, implemented in WEKA, in Sec. 5.

Our overall methodology is illustrated in Fig. 1. While the patient is undergoing video EEG (VEEG) monitoring in the EMU, we will collect HR, SpO\textsubscript{2} and EDA using our wristband. The collected data will then be analyzed to determine the patient’s needs:

- If the patient’s seizures produce an HR↑⇒SpO\textsubscript{2}↓⇒EDA↑ pattern in response to seizure, we will send him/her home with the personalized wrist-worn device (Option 1 in Fig. 1).
- If we are unable to attain sufficient accuracy using the wrist-worn device alone (as the cases where the patient’s seizures do not produce the expected HR↑⇒SpO\textsubscript{2}↓⇒EDA↑ pattern), a hybrid system of wristband and three- (or fewer) channel EEG monitoring may be chosen to provide more accurate monitoring (Option 2 in Fig. 1).

We are not yet considering use of limited-channel EEG alone because our early investigation indicates that accurate stand alone limited-channel EEG monitoring requires more than three electrodes. We, therefore, presupposing that the limited EEG data, we will be collecting will not be sufficient for accurately detecting seizures without additional data from extracerebral signals. In this work, we target three or fewer electrodes to communicate with the wristband and leave the option of seizure detection by stand alone limited-channel EEG for future exploration.

4. Analysis of Extracerebral Biosignal Activity

Use of multiple biosignals greatly decreases the false positive rate of our system compared to a system based on only one signal (such as HR). Requiring that the signal changes follow a specific order (pattern) further decreases the false positive rate. The original version of our algorithm was presented at the Seventh International Workshop on Seizure Prediction (IWSP7) and at the 37th Engineering in Medicine and Biology Conference (EMBC 2015). The algorithm was developed on the basis of data from Patients 4, 5 and 10. Our algorithm detected the seven seizures suffered by these three patients with 100% accuracy. The algorithm was then tested using data from Patients 11, 12, 16, 18, 19 and 20. The algorithm was refined on the basis of these test results. The refined algorithm is presented in this section. Original test results and post refinement results are presented in Sec. 6.

4.1. Stage 1: Assessment of biosignal activity

Our first step must be to determine when each signal of interest (HR, SpO\textsubscript{2} and EDA) is active, and when the three signals are concurrently active. This process is accomplished in Stage I (see Fig. 2) and discussed here.

4.1.1. Time series analysis

HR and SpO\textsubscript{2} data is collected at 1 Hz and contains dropouts because the sensor is located in a finger cuff which can be knocked loose by excessive movement. Consequently, it is filtered during processing. The EDA data, collected at either eight or at 32 Hz,
is prefiltered using a 3-s smoothing filter to remove spikes. Each signal is analyzed separately using a 5-s window with 80% overlap. The mean of each window is compared to a moving baseline (i.e. running average), then used to update the baseline. The baseline is constantly updated to accommodate the person’s changing activity and emotional levels. The lengths of the baselines are set by $T_{HR}$, $T_{SpO_2}$ and $T_{EDA}$ (see Fig. 2). If the mean of a window varies from the baseline by a prespecified parameter level ($\Delta_{HR}$, $\Delta_{SpO_2}$, $\Delta_{EDA}$), the time of the window is tagged and recorded. The parameter levels considered are:

- 15%, 20%, 25% and 30% increases for HR, based on Osorio’s finding in Ref. 5 that these four levels are useful for detecting seizures.
- 5%, 7.5%, 10% and 12.5% decreases for SpO$_2$, chosen because apnea is defined as a 4% drop in SpO$_2$ for 8 s or more. Normal SpO$_2$ levels are between 95% and 100%; readings below 90% are low. Consequently, a 5% drop in SpO$_2$ is significant.
- 60%, 80%, 100% and 120% increases for EDA, selected by analysis of the available data. In addition, a threshold for a minimum EDA peak value ($L_{EDA}$) may be set.
Future findings may require modification of some or all parameter levels.

Our selected extracerebral biosignals take time to settle after a seizure. Hence, a long baseline is needed to detect seizures that are close together. We are currently using a 60s baseline for all three signals ($T_{HR} = T_{SpO_2} = T_{EDA} = 60$). The first and last time of a series of sequential windows which shows a signal change at the selected parameter level is added to a signal activity list and passed to the event search.

The signal activity lists are also exported to Stage III (as shown in Fig. 2) and are used to generate the best-fit list in the event. Stage III is selected for use by the patient during analysis of the data collected in the EMU.

4.1.2. Event search

The event search finds times when all three signals were active, lists them as potential seizure events and passes them to Stage II for comparison with the $HR\uparrow \Rightarrow SpO_2 \downarrow \Rightarrow EDA\uparrow$ seizure pattern. The search methodology is illustrated in Fig. 3. $SpO_2$ is the most stable of the three signals; therefore, for each time the selected $\Delta SpO_2$ was recorded in the $SpO_2$ activity list during the time series analysis step (each $t_{\Delta SpO_2}$ in Fig. 3), the HR and EDA activity lists are searched for matches. If $\Delta HR$ and $\Delta EDA$ are found within the search window (plus or minus 3 min from $t_{\Delta SpO_2}$), all three signals are considered to have been active simultaneously and $t_{\Delta SpO_2}$ represents a potential seizure.

4.2. Stage II: Personalization and pattern recognition

As was mentioned in Sec. 1, biosignal responses to seizure differ from patient to patient. As may be expected, therefore, each patient’s biosignal response to seizure is slightly different within the $HR\uparrow \Rightarrow SpO_2 \downarrow \Rightarrow EDA\uparrow$ pattern as well. Consequently, a personalization (training) phase is required to tune parameters and optimize seizure detection accuracy for each patient.

Biosignal responses to the 10 seizures suffered by six of our patients follow a similar pattern (i.e. the changes occur in a specific order), so we developed and refined Stage II of our algorithm to distinguish those seizures from nonevent events. Implementation of this stage provides a lower false positive rate than does the output from Stage I and corresponds to Option 1 in Fig. 1. Stage II, also shown in Fig. 2, is described in the following two subsections.

4.2.1. Personalization (training)

Personalization (training) is done in the EMU, where EEG-based seizure timing is available. The parameter levels are selected per patient to maximize sensitivity while minimizing the false alarm rate. Parameters are selected by an iterative process through the personalization/training loop shown in Fig. 2. During personalization:

- The multiple $\Delta HR$, $\Delta SpO_2$, $\Delta EDA$ levels are each calculated so that we can determine the appropriate levels for which a patient’s seizures will be distinguished from nonevent events.
- The baseline lengths ($T_{HR}$, $T_{SpO_2}$, $T_{EDA}$) are evaluated and optimized.
- The $P_{EDA}$ values associated with both seizures and nonevent events are compared to allow optimal setting of $L_{EDA}$. Use of $L_{EDA}$ has been added to the original (EMBC) algorithm to reduce the false alarm rates of Patients 11 and 16. We are comfortable requiring a minimum signal value because Cyberonics uses a minimum HR of 100 beats per minute (bpm) in their Aspire seizure detection algorithm.
- Because we are working with signals that do not immediately recover after a seizure — indeed, EDA peaks after the seizure is over (see Fig. 4) — it is difficult to distinguish seizures that are close together. During training, we evaluate how close together an individual’s seizures can be and still be distinguishable based on how quickly his biosignals recover. In our current model, events that occur within 3 min of each other are considered one event.
During the test phase, the parameter values chosen during training are used to evaluate the test data.

Confidence level analysis for Patient 19’s 10 seizures indicates that six to eight seizures should be sufficient for personalizing a system for her. We consider personalization for Patient 19 to be a worst case scenario because her seizures do not produce a distinctively personalized pattern as do the seizures of other patients from whom we captured multiple seizures. Consequently, we think it is reasonable to expect the six to eight seizure requirement found for other patients from whom we captured multiple seizures indicates that six to eight seizures should be sufficient for personalizing a system for her. We consider personalization for Patient 19 to be a worst case requirement for most patients. Personalization is an important issue that needs to be developed in a paper of its own, so it will not be further discussed here.

4.2.2. Seizure pattern search

The methodology of this phase is illustrated in Fig. 3. For each potential seizure event:

- A 30-min event window centered about \( t_{\Delta \text{SpO}_2} \) is selected. A Local SpO2 baseline is calculated using the first 10 min of this window (see Fig. 3).
- \( t_{HR} \), the time HR begins rising, is found within the HR search window.
- \( t_s \), the time SpO2 drops 2% below its local baseline and \( t_r \), the time it returns to halfway between its minimum value and its value at \( t_s \) are found within the SpO2 search window. The value of 2% was empirically selected based on the behavior of SpO2 during the seizures, we captured in our study.
- \( t_{\text{EDA max}} \), the time of the EDA maximum value is found within the EDA search window. The value of the EDA peak (\( P_{\text{EDA}} \)) is also found.

Figure 4 illustrates the HR↑ ⇒ SpO2↓ ⇒ EDA↑ seizure pattern using data from one seizure. The vertical orange lines indicate seizure onset and offset based on EEG. Note the rapid increase in HR (red trace) starting at \( t_{HR} \). This increase is followed by a marked drop in SpO2 (blue trace). After SpO2 begins to recover, the EDA (purple trace) peaks then gradually decreases as it returns to its baseline. It must be noted here that since the EDA peak occurs after the seizure is over, seizure alert will be delayed until EDA’s post SpO2 recovery peak is confirmed. In the case of this seizure, EDA peaks 2 min after seizure onset, so the alert will be delayed by this amount of time. Note that \( t_{\Delta \text{SpO}_2} \) is shown in both Figs. 3 and 4.

As the HR rise is not smooth, the data is windowed to backtrack to the beginning of the rise (\( t_{HR} \) in Fig. 4). The algorithm defines \( t_{HR} \) as the time of the window whose mean is greater than or equal to the means of both chronologically subsequent windows. The size of the window was adjusted so that the time found by the algorithm matched the time found by a visual inspection of the HR curve for each seizure. The original (EMBC 2015) algorithm started the search for \( t_{HR} \) at the event time (\( t_{\Delta \text{SpO}_2} \)). This starting point proved problematic for Patient 11, so the algorithm was modified to start the search for \( t_{HR} \) at \( t_{HR} \) if it occurs chronologically prior to the event time. We consider this modification to be a correction to the algorithm. Since we are searching the HR data, we should have used \( t_{\Delta \text{EDA}} \) as our starting point in the original algorithm. The time of seizure onset, which will be needed for use in a seizure diary, is estimated to be \( t_{HR} \).

The SpO2 drop occurs so quickly that our algorithm can follow the curve without windowing the data. The bottom of the curve is not always smooth, however, so we search for a lower SpO2 value within 30 s of the apparent bottom and replace it if appropriate. We selected a 30-s search window because in all captured seizures the SpO2 begins recovering within 30 s.

After finding these critical points, we calculate:

\[
\begin{align*}
\tau_{\text{HR}-\text{SpO}_2} & = t_4 - t_{HR} \quad (1) \\
\tau_{\text{SpO}_2-\text{EDA}} & = t_{\text{EDA}} - t_s \quad \text{and} \quad (2) \\
\tau_{\text{EDA}} & = P_{\text{EDA}} - L_{\text{EDA}}. \quad (3)
\end{align*}
\]

In Eq. (1), \( \tau_{\text{HR}-\text{SpO}_2} \) is the time difference between the beginning of the HR rise and the beginning of
the SpO₂ drop, \( t_d \) is the beginning of the SpO₂ drop, and \( t_{HR} \) is the beginning of the HR rise. The value of \( t_{HR} - t_{SpO2} \) will be positive if the HR rise precedes the SpO₂ drop. In Eq. (2), \( t_{SpO2} - t_{EDA} \) is the time difference between the SpO₂ recovery and the EDA peak. \( t_{EDA} \) is the time of the maximum EDA value, and \( t_t \) is the time of the SpO₂ recovery. The value of \( t_{SpO2} - t_{EDA} \) will be positive if the SpO₂ begins its recovery prior to the EDA peak. In Eq. (3), \( t_{EDA} \) is the difference between the maximum value of EDA \( (P_{EDA}) \) and the minimum value recognized as seizure \( (L_{EDA}) \). Hence, if any of these calculations returns a negative number, the pattern for the event does not match the seizure pattern and the event is classified as a nonseizure event.

If there is sufficient data available and all three calculations return positive numbers, the event is classified as a seizure. If the percentage of missing data (caused on occasion by a loose finger cuff) for either the HR (between \( t_{HR} \) and the time of HR recovery) or the SpO₂ (between \( t_d \) and \( t_t \)) is greater than 90%, or if the percentages of missing data for both signals is 80% or more, the event is classified as indeterminate. Our expectation is that the missing data problem will decrease significantly once we are able to collect SpO₂ and HR at the wrist instead of the finger. Nonetheless, we find the “indeterminate” classification to be more useful than forcing these cases into either the seizure or nonseizure category.

5. Stage III: Limited-Channel EEG Analysis

Stages I and II are able to detect the seizures of six out of 10 patients with 100% accuracy. For Patients 12, 18 and 19, we used additional data to detect the seizures corresponding to Option 2 in Fig. 1. All three of these patients suffered CPSs, and none displays a particular automatism during their seizures. Consequently, use of ACC data as proposed by Heldberg et al. is not promising in these cases because there is no specific change in the ACC (either a cessation of movement or a seizure specific movement).

Instead, we are looking at the use of limited-channel EEG analysis for time periods selected from data in the activity lists generated in Stage I and sent to Stage III (see Fig. 2). EEG can be used for diagnosis of a wide range of neurological disorders including autism, major depressive disorder, and attention deficit hyperactivity disorder (ADHD), as well as epilepsy, even though EEG spectral information varies among seizures. By using a limited number of EEG signals instead of the full complement of 21 electrodes, we hope to provide accurate seizure detection while maintaining wearability in nonclinical (i.e. daily life) settings. There are several applications which leverage limited-channel EEG analysis and are reported in the literature. The authors of Ref. 50, for example, used limited-channel EEG for automatic sleep analysis. The authors of Ref. 51 used blind source separation of single-channel EEG in a brain–computer interface.

Because we are looking at the use of no more than three channels of EEG, we believe we can create a device that can be camouflaged with the patient’s hair. The prototype Epitel device has the form factor we envision. It is approximately one inch by one inch by a quarter inch thick. It is to be placed on the scalp by the patient’s epileptologist and records a single channel of EEG for seven days. We are looking to improve upon the Epitel prototype by giving our device the ability to communicate with the wristband and thereby provide feedback to the patient and caregiver on seizure activity. We are not yet considering the use of limited-channel EEG alone because our early investigation indicates that accurate stand alone limited-channel EEG monitoring requires more than three electrodes. We are, therefore, presupposing that the limited EEG data we will be collecting will not be sufficient for accurately detecting seizures without additional data from extracerebral signals.

In this work, we target three- or fewer electrodes to communicate with the wristband and leave the option of seizure detection by stand alone limited-channel EEG for future exploration.

We compare the accuracy of seizure detection using only a few electrodes to the accuracy using the full complement of 21 electrodes in the next three subsections. A discussion of limited-channel EEG analysis of Patients 12, 18 and 19 — the three patients whose seizures could not be detected by Stage II — is provided in Sec. 6.

5.1. Feature extraction and selection

We used frequency domain analysis for our EEG-based epileptic seizure detection as this methodology has been widely investigated and reported in
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Table 2. Comparison of full channel and limited-channel EEG analysis.

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Seizure origin</th>
<th>EEG channels used</th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>Accuracy</th>
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<tbody>
<tr>
<td>9</td>
<td>Left temporal lobe</td>
<td>All 21</td>
<td>1.000</td>
<td>0.971</td>
<td>0.971</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T5, C4, P3</td>
<td>1.000</td>
<td>0.981</td>
<td>0.980</td>
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<tr>
<td>12</td>
<td>Frontal lobe</td>
<td>All 21</td>
<td>0.994</td>
<td>0.974</td>
<td>0.974</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pz, O2, Cz</td>
<td>0.994</td>
<td>0.979</td>
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<tr>
<td>18</td>
<td>Right temporal lobe</td>
<td>All 21</td>
<td>1.000</td>
<td>0.964</td>
<td>0.963</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F8, F7, A2</td>
<td>1.000</td>
<td>0.974</td>
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</tr>
<tr>
<td>19</td>
<td>Right and left temporal lobe</td>
<td>All 21</td>
<td>0.988</td>
<td>0.976</td>
<td>0.975</td>
</tr>
<tr>
<td></td>
<td></td>
<td>A1, F7, Fz</td>
<td>0.977</td>
<td>0.961</td>
<td>0.961</td>
</tr>
</tbody>
</table>

the literature. References 53–55 are all examples of this methodology. We calculated the power spectrum density of the EEG signal per window per channel and used the results as spectral features to classify each window as seizure or nonseizure. We used 10-s windows with no overlap. Our sampling frequency was 200 Hz. We applied a Fourier transform to each window and divided the result into five frequency bands: (a) delta (0.1–4 Hz), (b) theta (4–8 Hz), (c) alpha (8–12 Hz), (d) beta (12–30 Hz), and (e) low-gamma (30–70 Hz). Note that for each frequency band, power is averaged over its corresponding frequency range. In order to provide a fair comparison among all windows, we normalized the averaged spectral power (ASP) of each window by dividing it by the total spectral power of the window. Five normalized average spectral power (NASP) features calculated for each of 21 channels generates a total of 105 features/dimensions for our EEG data set.

Since, our goal is to use a limited number of electrodes to detect seizures, we ranked all 105 features by their information gain (IG) and selected the best three electrodes for each subject. Table 2 lists the three electrodes chosen for each patient based on his or her EEG data in the order of their IG. The use of three electrodes at this time was a purely empirical choice. Use of different numbers of electrodes can be further investigated as another personalization metric.

5.2. Automated seizure detection

We used a k-nearest neighbor classifier (KNN) with \( k = 1 \) neighbor. For each patient, we selected 30 min of known nonseizure data that was at least 1 h from the nearest seizure as that patient’s no-target class. For this group of patients, seizure duration varies from 20 s to 120 s. As each patient spends relatively little time seizing, the data set is not balanced. In order to visually compare limited (i.e., three)-channel detection with full (21)-channel detection, we projected our feature subset (explained in Sec. 5.1) into a two-dimensional plane using principal component analysis (PCA) to achieve dimension reduction.

5.3. Comparison of 21-channel and three-channel EEG seizure recognition accuracy

Figure 5 shows a two-dimensional feature projection for (a) 21-channel and (b) three-channel EEG spectral analysis for one subject (Patient 18). PC1 and PC2 represent the first and second principal components.
Fig. 6. NASP of a 10 s window for a seizure in multiple frequency bands (Patient 18). (a) delta, (b) theta, (c) alpha, (d) beta and (e) low-gammas.

Fig. 7. NASP of a 10 s window for a nonseizure event in multiple bands (Patient 18). (a) delta, (b) theta, (c) alpha, (d) beta and (e) low-gammas.

components, respectively. They illustrate that when using only the best three channels, most windows are still visually distinguishable as either seizure or nonseizure.

Figures 6 and 7 represent the brain spatial-spectral map color coded by the NASP values of multiple frequency bands in both seizure and nonseizure events for the same patient. These figures not only illustrate the frequency information, they visualize brain spatial pattern during seizure and nonseizure events. The spectral power of nonseizure events is distributed primarily in low frequency bands (i.e. delta). The high frequency features (i.e. beta and low-gammas) are critical as they are present primarily during seizure. In addition, we can observe the intensity of each channel at different frequency bands in these figures. In this case, the channels belonging to the temporal lobes have relatively higher NASP values. These higher values indicate that this patient’s seizures originate from the temporal lobes. Therefore, the temporal lobes are the most informative channels (i.e. have the highest IG) and are the best candidates for implementation of ambulatory seizure monitoring using three-channel EEG.

Table 2 shows the accuracy of seizure detection using three-channel EEG analysis by comparing it with full-channel analysis. It can be seen that the nonrelevant electrodes are no longer injecting noise and skewed data. Our results mean that each patient’s best three channels are good candidates for integration into wearable devices for seizure detection.

6. Results

Results are presented for each of the stages in our algorithm to demonstrate the improved detection accuracy provided by each successive stage.

6.1. Evaluation of stage I

Table 3 summarizes the results of our Stage I multisignal analysis by seizure. Of the 26 analyzable seizures, 23 were CPS — the seizure type, we are most interested in detecting, two were secondarily GTCS and one was a primary GTCS. Patient 12’s two CPSs are of frontal lobe origin. The other 21 CPSs and the secondarily generalized seizures were all of temporal lobe origin.

All of the seizures captured in our study show at least a 15% increase in HR. In addition to the HR increase, 19 of the 26 seizures show an SpO₂ drop of at least 5% and 19 show an EDA increase of 60% or more.

Of the 26 seizures, 15 show changes at or above our established thresholds in all three signals. That all three of the GTCSs show changes in all three signals is not surprising based on the literature and
Table 3. Results of Stage 1 multi-extracerebral biosignal analysis.

<table>
<thead>
<tr>
<th></th>
<th>Recorded by biosensors</th>
<th>HR↑</th>
<th>HR↑ +SPO2↓</th>
<th>HR↑ +EDA↑</th>
<th>HR↑ +SPO2↓ +EDA↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPS&lt;sup&gt;a&lt;/sup&gt;</td>
<td>23</td>
<td>16</td>
<td>16</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Secondary GTCS&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Primary GTCS&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total Seizures (Total)</td>
<td>25</td>
<td>26</td>
<td>19</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>False Positives</td>
<td>—</td>
<td>1201</td>
<td>265</td>
<td>92</td>
<td>13</td>
</tr>
<tr>
<td>False Negatives</td>
<td>—</td>
<td>0</td>
<td>7</td>
<td>7</td>
<td>11</td>
</tr>
</tbody>
</table>

<sup>a</sup>CPS: A seizure that involves only part of the brain (usually the temporal or the frontal lobe) and that alters consciousness or awareness. It may be accompanied by automatism.<sup>60</sup>

<sup>b</sup>Generalized Seizure: A seizure involving the whole brain. It may involve alterations of alertness or awareness, as during absence or CPS, or tonic (stiffening)–clonic (rhythmic jerking of an extremity or of the whole body) movements of both sides of the body.<sup>60</sup>

<sup>c</sup>GTCS: During the tonic phase, the patient’s body goes rigid, during the clonic stage, the body convulses. A primary GTCS involves the entire brain from the beginning of the seizure, whereas a secondary GTCS evolves from a CPS to involve the entire brain.<sup>60</sup>

the fact that GTCSs are more severe than CPSs. It makes sense that the biosignal response to a GTCS would be more pronounced in all respects than the response to a CPS.

Of the seven CPSs that did not produce a 5% drop in SpO<sub>2</sub>, one was from Patient 9 (a 3% drop), two were from Patient 12 (no response), and the other four were from Patient 19 (two produced 4% drops, two produced no response). All seven of the CPSs that do not show a 60% or greater increase from baseline in EDA belong to Patient 19. Data from Patients 12 and 19 was analyzed using limited-channel EEG in Stage III since their seizures did not produce tri-signal responses.

Patient 9’s data, on the other hand, could not be further analyzed. This patient’s biosignal responses generally depart from baseline, sometimes even by the required amount, but do not stay elevated/depressed long enough for our algorithm to recognize the change. Consequently, her seizures were not even placed on the event list in Stage I and indicate the need for a more versatile Stage I methodology.

Patient 9’s EDA responses raise a concern for us about the effect of at least some antiepileptic drugs (AEDs) on this biosignal. Although, we captured complete biosignal data from only two of Patient 9’s seizures, we captured EDA responses to four seizures, three CPSs and one secondary GTCS. She had an EDA response to her GTCS of over 9 microsiemens (µS). Her responses to her CPSs were, in chronological order, 2.5, 0.7 and 0.2 µS. She resumed taking her AEDs about 8 h before the second CPS and 14 h before the third CPS. One possibility is that the AEDs may have adversely affected her EDA response to the last two CPSs. We did capture EDA responses to seizure from other patients who were either back on AEDs or had just entered the EMU and so still had AEDs in their systems when they had their seizures. Consequently, we do not have enough data to make an overall assessment about the effects of AEDs on EDA response.

6.2. Evaluation of stage II

We begin by presenting seizure detection results by patient both before and after algorithm refinement in Table 4. It can be seen clearly that the algorithm either catches all of a patient’s seizures or none of them. Hence, we consider our most important result to be that the algorithm works with 100% accuracy for six out of 10 patients. Note also that our initial test of the algorithm using data from the later patients (Patients 11, 12, 16, 18–20) shows that it was able to recognize seizures from two of the new patients (Patients 16 and 20) but that the false positive rate was high. After refining the algorithm (see Sec. 4.2.2), we are able to catch Patient 11’s seizure and eliminate the false positives from Patients 11 and 16. Our algorithm now detects all seizures for three of our six new patients, giving it an overall
Table 4. Results of algorithm testing and refinement.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Number of seizures analyzed</th>
<th>Results of testing initial algorithm</th>
<th>Post refinement results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number of seizures detected</td>
<td>Number of false positives</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>Data from these patients used</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>for initial algorithm development</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>Data used for initial development</td>
<td>4</td>
</tr>
<tr>
<td>11</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>16</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>18</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>19</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 5. Analysis of data from six patients whose seizures produce an HR↑ ⇒ SpO₂↓ ⇒ EDA↑ biosignal pattern.

<table>
<thead>
<tr>
<th>Class</th>
<th>Results without personalization</th>
<th>Results with personalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure</td>
<td>10 (100%)</td>
<td>10/10 (100%)</td>
</tr>
<tr>
<td>Nonseizure</td>
<td>3</td>
<td>6/11 (73%)</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>0</td>
<td>0/2 (0%)</td>
</tr>
</tbody>
</table>

Sensitivity: 10/10 (100%) 8/11 (73%) 9/9 (100%)

Specificity: 10/10 (100%) 6/11 (55%) 9/9 (100%)

Accuracy: 18/21 (86%) 16/16 (100%) 19/19 (100%)

The nonpersonalized parameter levels for the results shown in Table 5 are: ΔHR = 15%, ΔSpO₂ = −5%, ΔEDA = 60%, LEDA = 0. The algorithm detected all 10 seizures suffered by the six patients whose seizures produced the expected biosignal pattern. It also identified an additional 11 possible seizure events. Two of these events were classified as indeterminate (for lack of sufficient data), six were classified as nonseizure events, and three were classified as seizures. Two of these three were nonseizure events and therefore are false positives. The third event occurred while the patient was off EEG and video, so its actual classification is unknown.

6.2.1. Personalization for improved accuracy

Use of personalization within our algorithm provides improved accuracy in seizure detection because each patient’s biosignal response to seizure takes on a unique variation. Patient 10 has very large SpO₂ drops during seizure; consequently, we can change his ΔSpO₂ from −5% to −10%. Patient 16 experienced two nonseizure events that follow the HR↑ ⇒ SpO₂↓ ⇒ EDA↑ seizure pattern, but in which the peak EDA value was very small — less than 0.25 µS — compared to a seizure response of 1.85 µS. Her LEDA was raised from 0 to 0.5 µS to distinguish these nonseizure events from seizures. Following this personalization step, the number of events detected drops to 19 — 10 seizures plus nine additional events. Eight of these nine events are classified as nonseizure events and the ninth is indeterminate because of excessive missing HR and SpO₂ data.

6.2.2. Additional EMU data and nonEMU data

Because our data set is so small, we decided to analyze the additional biosignal data available to us (even though there were no seizures included in the data) to find out how many false positives we might find. We had an additional 32 h of data from Patients 1 and 15 which we analyzed.
Table 6. Comparison of Stage II results (using a three biosignal pattern and 202 h of data) to detection using heart rate alone.

<table>
<thead>
<tr>
<th></th>
<th>Without personalization</th>
<th>With personalization</th>
<th>Lowerest settings</th>
<th>Highest settings</th>
<th>Secondaryly generalized seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Worst case)</td>
<td>(Best case)</td>
<td>(Worst case)</td>
<td>(Best case)</td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100%</td>
<td>100%</td>
<td>n/a</td>
<td>n/a</td>
<td>88.66%</td>
</tr>
<tr>
<td>Specificity</td>
<td>73%</td>
<td>100%</td>
<td>n/a</td>
<td>n/a</td>
<td>90%</td>
</tr>
<tr>
<td>Accuracy</td>
<td>86%</td>
<td>100%</td>
<td>98.33%</td>
<td>88.33%</td>
<td></td>
</tr>
<tr>
<td>Potential False positive</td>
<td>0.015/h</td>
<td>0.000/h</td>
<td>9.5/h</td>
<td>1.1/h</td>
<td>n/a</td>
</tr>
</tbody>
</table>

using our default parameter values ($\Delta \text{HR} = 15\%$, $\Delta \text{SpO$_2$} = -5\%$, $\Delta \text{EDA} = 60\%$, $L_{\text{EDA}} = 0$). The algorithm found three nonseizure events which it incorrectly classified as seizures.

We also had data we had collected from 37 volunteers in our laboratory under University of Texas at Dallas IRB approval. Approximately, 40 min of data was collected from each volunteer for a total of over 26 h. Each volunteer followed the same routine, in which he/she alternately relaxed and performed three predesigned tasks. The first of the three tasks was a physical stress, the second was a cognitive stress and the third was an emotional stress.\(^61,62\)

Our algorithm found no potential false alarms produced by either the cognitive or emotional stresses on any of our 37 volunteers. Under physical stress, however, four patients exhibited sufficient change in all three biosignals to generate an event. In two cases, the events were classified as nonseizure and in the other two as seizures. It is possible that all the subjects in this study would have produced sufficient biosignal activity to generate an event if they had been sufficiently stressed during the physical activity. It is not clear, however, that all would have produced a seizure-like biosignal response pattern; nor do we have enough data to determine the level of physical stress — with respect to the individual’s physical condition — required to generate such a response.

6.2.3. Discussion of stage II results

Combining all our data, we have 397 h of data collected, 10 seizures detected (all the seizures from six patients), 16 not detected (all the seizures from four patients) and nine false positives. Because no one else has looked at the same set of signals that we have looked at, we have no direct comparison for our results. We have previously mentioned efforts to detect seizures using HR alone and have argued that use of multiple biosignals will provide superior results. Consequently, in Table 6, we compare the results of our analysis of the six patients whose seizures produce the tri-signal pattern expected by our algorithm to results based on HR analysis alone. Osorio’s results are comparable to the results we found using HR alone. (Our settings are between his, as is our HR only false positive rate from Table 3 — 1201 false positives/339 h = 3.5 false positives/h.\(^4\))

Osorio’s research was sponsored by Cyberonics, the company that developed VNS for use in controlling seizure activity, so it appears that the company developed their new Aspire system at least partly on the basis of Osorio’s work. Traditional VNS therapy consists of 30 s of electrical stimulation to the vagus nerve every 5 min. The wearer can initiate additional stimulation with a magnet if he senses the onset of a seizure. However, patients are unable to use the magnet if they do not have auras to warn them of seizure onset, are asleep, or are disabled by the seizure. The Aspire’s automatic stimulation mode activates the system when it detects an abrupt increase in HR. First year clinical trials of the Aspire found a reduction in both frequency and severity of seizures, and improvement in recovery from seizures. Results of first year clinical trials in both Europe and the United States were presented at the 2015 American Epilepsy Society (AES) meeting.

Dr. Pegah Afra from the University of Utah presented results from one of the United States Aspire trials. After personalization, the system is able to
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distinguish the difference between an HR increase caused by seizure onset and an increase caused by physical activity with very high accuracy. As a result, the automatic stimulation mode rarely false alarms, although it is unclear what is meant by “rarely.” Cyberonics has access to epileptic patients across the United States and Europe and so has access to a large data base to aid them in their study of the differences between these two causes of HR increase.\textsuperscript{53, 64}

In addition, since the Aspire is implanted under the skin in the chest area, it may be reading more than just HR for use in its algorithm.\textsuperscript{37, 65–67}

Our methodology is not comparable to the one used by Behbahani’s group as they used data mining techniques and features extracted from both HR time and frequency domains. They include only day-time seizures that are at least 5 h apart.\textsuperscript{13}

6.3. Evaluation of stage III

We have demonstrated that limited-channel EEG analysis is as accurate as full-channel EEG analysis for differentiating seizures from nonseizure events based on a small sample of the data from each of the four patients listed in Table 2 (see Sec. 5.1). We now examine its effectiveness in detecting seizures that Stage II cannot detect. We have three candidates for Stage III analysis: Patients 12, 18 and 19. A discussion of each follows. The results of our Stage III analysis of three seizures and five nonseizure events from Patients 12 and 18 is summarized in Table 7. The overall detection accuracy per patient is shown in Table 8. Table 8 is divided into two sections by a horizontal line. The four patients listed above the line were the patients in our original data set. The six patients listed below the line provided data for testing and refinement. See Table 4 for more details.

Table 7. Results of stage three spectral analysis on Patients 12 and 18 (three seizures).

<table>
<thead>
<tr>
<th>Class</th>
<th>Seizure</th>
<th>Nonseizure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Nonseizure</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Specificity</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Accuracy</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

6.3.1. Analysis of patient 12

Patient 12 is an excellent candidate for Stage III analysis because both of his seizures produced significant increases in HR and EDA, but no change in SpO\textsubscript{2}. (Patient 12’s seizures originated from his frontal lobes. A recent study found that seizures that affect only the frontal lobes do not disrupt respiration and so will not affect SpO\textsubscript{2} levels.\textsuperscript{22}) Evaluation of the signal activity lists from Stage I show that in 35 h of data, there were 19 occasions on which HR and EDA were concurrently active at 15% and 60%, respectively. Two of these occasions were the patient’s two seizures. The other 17 were false positives. In order to decrease our high false alarm rate (0.5/h), we turned to limited-channel EEG analysis.

The HR and EDA data are one channel each and are collected at a much lower frequency (1 Hz and 32 Hz, respectively) than EEG, which is collected at 200 Hz. Consequently, use of the HR↑ + EDA↑ activity lists prescreens the data so that only the EEG for times on this list needs to be analyzed. We have 9 h of EEG data for Patient 12 per IRB protocol restrictions. These 9 h include the two seizures and five of the false alarms.

Using limited-channel EEG analysis with three electrodes, we analyzed a 2 min segment of the Patient 12 EEG data from 1 min before to 1 min after each of the seven possible seizure times on the HR↑ + EDA↑ activity list. Each of these two minute segments includes 12–10 s windows. We classified each window using the model we trained in Sec. 5.1 and 5.2. We classified a segment as a seizure if more than 50% of its segments were classified as seizure. By this assessment, all five nonseizure events and both seizures were classified correctly, giving us a Stage III classification accuracy of 100% for Patient 12.

6.3.2. Analysis of patient 18

Our biosensors captured a single seizure from Patient 18. This seizure produced sufficient activity in HR, SpO\textsubscript{2} and EDA to make the event list in stage I. The pattern produced by the three signals does not match the pattern expected by Stage II, however, this data set was also analyzed by Stage III. Patient 18 provided over 30 h of data during which time there were no other events that could be misinterpreted as seizures. Our limited-channel EEG analysis correctly
Table 8. Summary of seizure detection accuracy by patient.

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Data collected</th>
<th>Number and types of seizures</th>
<th>Stage used for detection</th>
<th>Detection accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>11 h, 50 min</td>
<td>1-CPS</td>
<td>Stage II</td>
<td>100</td>
</tr>
<tr>
<td>5</td>
<td>43 h, 15 min</td>
<td>2-secondary GTCS</td>
<td>Stage II</td>
<td>100</td>
</tr>
<tr>
<td>9</td>
<td>31 hr, 15 min</td>
<td>3-CPS, 1-secondary GTCS(a)</td>
<td>None(b)</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>54 h, 3 min</td>
<td>4-CPS</td>
<td>Stage II</td>
<td>100</td>
</tr>
<tr>
<td>11</td>
<td>25 h, 21 min</td>
<td>1-CPS</td>
<td>Stage II</td>
<td>100</td>
</tr>
<tr>
<td>12</td>
<td>35 h, 24 min</td>
<td>2-CPS</td>
<td>Stage III</td>
<td>100</td>
</tr>
<tr>
<td>16</td>
<td>28 h, 27 min</td>
<td>1-CPS</td>
<td>Stage II</td>
<td>100</td>
</tr>
<tr>
<td>18</td>
<td>30 h, 20 min</td>
<td>1-CPS</td>
<td>Stage III</td>
<td>100</td>
</tr>
<tr>
<td>19</td>
<td>39 h, 52 min</td>
<td>7-CPS</td>
<td>None(c)</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>40 h, 2 min</td>
<td>1-primary GTCS</td>
<td>Stage II</td>
<td>100</td>
</tr>
</tbody>
</table>

\(a\) We captured complete biosignal data for this patient’s CPSs but not for her GTCS, which is therefore excluded from this survey.

\(b\) As this patient’s data could not be properly evaluated by Stage I, we need to improve the methodology for this stage.

\(c\) We hypothesize that our difficulty in detecting this patient’s seizures is at least partly caused by the fact that she is young, healthy and has newly developed seizures (about a year). Consequently, her biosignal responses to seizure are erratic.

We identified the seizure as such, so our detection accuracy for Patient 18 is 100%.

6.3.3. Analysis of patient 19

Ten seizures from Patient 19 were included in our analysis. Of these, only two produced significant activity in all three biosignals. In one case, the EDA began to rise several minutes prior to seizure onset and was not captured by our algorithm’s search technique. In the other case, the seizure was recognized by the algorithm as an event, but did not display the pattern expected in Stage II. Consequently, this data set was also analyzed by Stage III. Eight out of 10 seizures produced sufficient HR and SpO\(_2\) activity to be included in the HR↑⇒SpO\(_2\)↓⇒EDA↑ seizure pattern. However, only two produced sufficient HR and EDA activity to be included in the HR↑⇒EDA↑ activity list. The HR↑⇒SpO\(_2\)↓ list was used to pre-screen the data for EEG analysis. Unfortunately, as is shown in Table 8, efforts to distinguish the seizures from nonseizure events in the prescreen list using limited-channel EEG was unsuccessful. We are not yet certain why, but do have some thoughts about possible causes. This patient’s biosignal responses to seizure were erratic. We had four patients in addition to Patient 19 from whom we captured multiple seizures. In each of those four cases, the biosignal response to a given patient’s seizures had an individualized pattern that was distinguishable from the other patients’ patterns. Patient 19 in her biosignal responses to seizure followed no clear pattern which was unique. Patient 19 is fairly young, apparently healthy, and has had seizures for about one year. Her seizures appear to be relatively mild and most are short — often 30 s or less. As we are unable to correlate even the lengths of the seizures to the strength of their biosignal response, we hypothesize that this patient has not yet suffered sufficient damage from her seizures to have developed an individualized pattern. If our hypothesis is correct, monitoring of extracerebral biosignals may prove to be quite insightful for analyzing the types and severity of damage caused by seizures over long periods of time.

7. Conclusions and Future Work

The HR↑ ⇒ SpO\(_2\)↓ ⇒ EDA↑ seizure pattern has been observed in six out of 10 epileptic patients whose data were collected in the EMU. Seizures from two of the remaining four patients were detectible using three-channel EEG on data preprocessed by a search for concurrent activity in HR, SpO\(_2\), EDA or a subset of these signals. Overall, we were able to detect seizures of eight out of 10 patients. We need to collect data from epileptic patients in daily life to take into account the effects of factors such as lifestyle, daily activities, medication, etc. Our methodology is never expected to be as accurate as seizure...
detection using implanted electrodes, and will not be helpful to all epileptic patients. However, once fully developed and implemented, it will provide a non-invasive, relatively inexpensive option for detecting seizures for the purposes of providing feedback to patients and caregivers and of providing a seizure diary for use by physicians. It will also record biosignal responses to seizure for use in studying the long-term effects of seizures and may provide clues to the causes and risk factors of SUDEP.

While the results of our clinical study and data analytics are overall very promising, we have observed that some patients exhibit erratic biosignal responses (perhaps because of newly developed seizures), or responses that are not suitable for detection using a change from baseline methodology. These cases require additional analysis and the development of a more sophisticated methodology. Our future work will include: (i) development of a more versatile biosignal activity recognition algorithm (Stage I), (ii) further development and refinement of limited-channel EEG analysis (Stage III) to include the possibility of seizure detection using limited-channel EEG on its own, and (iii) implementation of the hybrid wrist-worn and limited-channel EEG analysis in a unified and embedded system platform.

Acknowledgments
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