웨어러블 기기를 이용한 발작의 비-뇌파적 감시

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Non-EEG Seizure Detection Using Wearable Device

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Electroencephalography (EEG) is the gold standard for seizure detection. However, EEG systems are usually expensive and require well-trained technicians for data acquisition. Detection of seizures is important in patients with refractory epilepsy, especially when the seizure is prolonged and unwitnessed. Sudden unexpected death in epilepsy (SUDEP) is an important problem in patients with refractory epilepsy because the risk of SUDEP decreases the quality of life. There are several alternatives to EEG systems that are used to detect seizure-related pathophysiological changes. Measurements of heart rate and heart rate variability can be used to detect seizure-related cardiologic phenomena. Respiratory signals obtained based on respiration rate and respiratory chest and abdominal movements may also be used for seizure detection. Ictal movements can be detected using video analysis or wearable devices, such as accelerometers and gyroscopes. In addition, electrodermal activity (EDA) measurements are currently under investigation as a way to alert others to an ictal period. Although these technologies have limitations, they are affordable and easily wearable. They are thus appropriate for use in patients during daily activity. These devices may be potentially useful to detect the occurrence of unwitnessed seizures, and to increase the quality of life.

Key Words: Seizure, Diagnosis, Quality of life, SUDEP, Electroencephalography

Introduction

Patients with epilepsy have unpredictable seizures. Higher numbers of seizures in these patients are associated with lower quality of life. In addition, more frequent seizures are associated with an increased risk of sudden unexpected death in epilepsy (SUDEP). Preventing seizures is undoubtedly the most important mission in treating epilepsy. Nevertheless, because almost 30% of patients with epilepsy have medically refractory epilepsy, the prediction or even early detection of seizures require urgent attention, as they may decrease seizure burden and seizure-related consequences, such as SUDEP¹⁾.

Electroencephalography (EEG) is the gold standard used to identify seizures because seizures are electrical cerebral phenomena. However, the use of EEG devices during daily life outside of a hospital has several limitations. First, these devices are large, as EEG recordings are usually performed using headsets or electrodes, an attached jack-box, and a full-size computer system. These devices are thus not easy to carry. Second, detection of seizures requires interpretation

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by well-trained experts. Finally, these systems are very expensive. Because of these limitations, there is a need for less expensive versions of seizure alarm systems that are easier to use.

Due to the rapid progress in engineering and technology, novel trials to detect and analyze biological signals have been performed in different medical fields²⁾. There are several current medical studies to investigate the use of commercial products, such as smart watches or fitness trackers. In the field of epilepsy research, there are trials designed to investigate seizure tracking using wearable devices³⁾. Seizure alarms using wearable devices would be easy to use at home, especially for patients with intractable epilepsy. SUDEP management would benefit from using wearable technologies in addition to the traditional gold standard of EEG.

EEG-based seizure detection/prediction

There are several commercial handheld or wearable EEG recording devices^{3,4)}. Because the detection of ictal electrographic signals is the best way to detect seizures, current potential seizure detection devices for daily use rely on these signals. Several reports suggest that it is possible to measure brain electrical activity using wearable device during daily activity⁵⁻⁷⁾. Although various kinds of psychiatric disease are investigated using these devices, no reliable peer-reviewed publications discussing epilepsy treatment are as yet available.

Non-EEG based seizure detection

Many different biological signals are produced that are reflective of the body's condition. Some of these signals can consistently be used to identify pathophysiological conditions. For example, electrocardiography (EKG) is one of the most important diagnostic tools for the detection of myocardial infarction. In the field of epilepsy, several biological signals are potential indicators of peri-ictal conditions. For these signals, sensitivity is slightly more important than specificity, as missing a major seizure is less desirable than producing a false alarm when the goal is to prevent SUDEP.

Different signals require the use of different sensors and detection devices. The different biological signals may be categorized as changes in metabolism, heart function, respiratory function, physical movement, and autonomic nervous system. Thanks to considerable improvement in technology, sensor sizes have been reduced, and data collection systems such as smart phones and smart watches are now widely available and affordable^{8,9)}. There are commercially available EEG and non-EEG based wearable devices (Table 1, Fig. 1)

1. Cardiac signals

Heart rhythms can be detected using technologies such as EKG and photoplethysmography (PPG). The types of data from the sensors are heart rate (HR) and heart rate variability. EKG can be used to more precisely detect electrical cardiac activity when compared to PPG. PPG uses light-emitting diodes and optical

Fig. 1. Commercially available wearable devices, (A) Emotive EPOC+, (B) Empatica Embrace, (C) Brain sentinel SPEAC system, (D) Carre technologies Inc. Hexoskin, (E) Qardio Qardiocore, (F) Movisens Movie series, (G) Zephyr, (H) Apple watch, (I) Garmin Fenix 5 series.

Table 1. Commercially Available Wearable Devices

	Name of company	Name of device	Sensors	Website	Comment
A	Emotive	EPOC+	14 channel wireless EEG	https://www.emotiv.com/epoc/	
B	Empatica	Embrace	EDA, Gyroscope, ACM, temperature	https://www.empatica.com/	Realtime seizure alarm
C	Brain Sentinel	SPEAC system	sEMG	http://speacsystem.com/speac-system-seizure-monitor/	Realtime seizure alarm
D	Carre Technologies Inc	Hexoskin	single channel EKG, ACM, respiration	https://www.hexoskin.com/	HR, QRS detection, HRV analysis, step counting, tidal volume measurement, respiration rate
E	Qardio	Qardiocore	single channel EKG, ACM, respiration, temperature	https://www.getqardio.com/	EKG, skin Temperature, HRV, activity tracking, respiratory rate
F	Movisens	Move series	EKG, ACM, EDA	https://www.movisens.com/	
G	Zephyr	Zephyr	EKG, ACM, respiration, temperature,	https://www.zephyranywhere.com/	
H	Apple	Apple Watch	PPG, ACM, gyroscope	https://www.apple.com/	3rd party band expands sensors
I	Garmin	Fenix 5x	GPS, barometer, compass, PPG, ACM	https://www.garmin.com	

EEG, electroencephalography; EDA, electrodermal activity; EMG, electromyography; PPG, photoplethysmography; ACM, accelerometer; HR, heart rate; HRV, heart rate variability; GPS, global positioning system.

sensors to detect hemodynamic changes, as in a saturation monitor use. This technology is commonly used in commercial devices, such as most fitness trackers and smart watches that measure heart rate. These devices include the Samsung Gear series, Apple Watch, and Garmin products. In contrast, EKG recorders are used as patches or in band-aid form in hospitals. Commercial EKG patches are available to monitor patients who have suffered recent myocardial infarctions and are at risk for a recurrence of the attack at home¹⁰. PPG devices are less accurate than EKG devices, but are also less sensitive to motion artifacts.

Peri-ictal HR changes are more noticeable during generalized tonic-clonic seizures, temporal lobe seizures, and frontal lobe seizures because these types of seizures are accompanied by tachycardia, bradycardia, and even asystole^{11,12}. QRS abnormalities, such as QT prolongation may also accompany the above seizures. One study has reported a linear correlation between electrocorticography and EKG during seizure¹³. The automated algorithms used have a seizure detection rate of 90–98% and positive predictive values greater than 50%^{14,15}. In addition to the EKG, combination of other types of signals such as, oxygen saturation, accelerometers (ACMs), and Electrodermal activity (EDA) can increase sensitivity and specificity¹⁶.

Devices monitoring heart signals are ideal for use in wireless systems using smart phone applications and enable the easy collection and processing of data in real-time. Continuous long-term monitoring is important because collecting individualized data patterns during normal activities, such as sleep, resting, and exercise may be important in recognizing sudden peri-ictal HR changes.

2. Respiration

Respiratory abnormalities are thought to be major causes of SUDEP¹⁷. More than one-third of patients with seizure have ictal

central apnea and ictal tachycardia. Changes in respiration rate and oxygen saturation can be used to detect respiratory abnormalities. These abnormalities are usually temporary and reversible, but are at times prolonged and inevitably lethal.

1) Respiratory belts and nasal air flow detection

Abdominal or chest belts sense movements of the widening chest wall during respiration. Nasal thermistors detect temperature changes produced by respiratory airflow. These devices are commonly used in polysomnography to detect sleep apnea. Ictal apnea can be easily captured using the same devices.

2) Oxygen saturation

Medical-grade oxygen saturation monitors are very expensive. However, there are many other less-expensive oxygen saturation monitors. Some oxygen saturation sensors can be accessed wirelessly using a smart phone. This enables the device to alarm the caregiver if the patient is in a hypoxic condition. For example, portable oximeters with Bluetooth connectivity approved by the Food and Drug Administration of the United States are sold for around 200 to 400 USD in the market.

3. Motion detection using video and motion sensors

Changes in movement are the most noticeable changes during seizures. The vast majority of movements during seizures are rhythmic and repetitive movements comprising kicking, reaching, jerking, or a combination of the above. Nevertheless, many types of seizures, including absence seizures and atonic seizures, have negative symptoms. Clearly, motion detection techniques are designed to detect positive symptoms. In this sense, recognition of ictal movements as distinct from non-epileptic movements would be required for a gold standard technique.

1) Video

Video analysis can be easily adopted in clinical settings because it does not require contact. In addition, large amounts of data can be collected based on video-EEG measurements. Automated motion tracking of short video clips from ictal video-EEG showed more than 90% of sensitivity and specificity for focal motor seizure^{18,19}. However, during daily activity, the patient may be invisible, as when he or she is under a blanket. Adding infrared cameras or even thermographic cameras to video monitoring devices may thus improve seizure detection, although the addition of such devices increases cost without improving detection resolution. There is not real-time video analysis for seizure detection currently available.

2) Motion sensors

Almost all new smart phones have ACMs, gyroscopes, and magnetometers, which are very sensitive and can be used to analyze motion patterns. Most fitness trackers, activity trackers, and smart watches also have the abovementioned sensors and can send motion data to smart phones. ACMs can be used to detect seizures²⁰⁻²⁴, although the sensitivities of these devices are highly dependent on seizure type. Specifically, they have been reported to have a sensitivity close to 100% and a 50% positive predictive value for GTC seizures²⁴. In contrast, they have been reported to have a sensitivity of 16-34% for other types of seizure²³.

4. Electrodermal activity (EDA)

Autonomic nervous function is dramatically altered in the perictal period. Autonomic changes affect skin perfusion and perspiration, which are parameters that can be measured based on changes in electrical signals. As a result, EDA or galvanic skin response is considered as an indicator of physiological arousal followed by the activation of sympathetic nervous system. Sweat on the skin leads to changes in electrical resistance or EDA during

seizures^{16,25}. In fact, a considerable increase in the amplitude of electrical resistance of greater than 30-fold has been reported during GTC seizures²⁵. Several studies have reported the coexistence of seizure and EDA markers^{8,9,25}. There is one commercial product that mainly focuses on seizure detection based on EDA parameters^{25,26}.

Discussion

1. Seizure detection for SUDEP prevention

The remarkable physiological changes during seizure include sympathetic activation, which leads to increases in heart rate, blood pressure, respiratory rate, etc. These phenomena are followed by parasympathetic activation, which can decrease heart rate and blood pressure²⁷. The known risk factors for SUDEP are generalized tonic-clonic (GTC) seizures, male sex, age at seizure onset, epilepsy duration, and seizure frequency²⁸. In addition, coexistence of intellectual disability and central nervous system lesions can increase the risk of SUDEP, especially in children with epilepsy. SUDEP may occur during sleep or during daytime. Early detection of seizure may enable early intervention to stop seizure. Accurate estimation of seizure burden including unwitnessed seizures can attribute to establish better treatment plan.

2. Limitations

However, there is still a long way for these technologies to go. First, there is no large qualified studies in epileptology yet. Although many studies suggest the potential benefits, they were conducted only for the carefully selected small number of population. Second, the commercially available devices are limited in epilepsy medicine. Because the best result of these devices is basically less than that of EEG, the studies are mainly focusing to alarm seizure with blind to EEG. So, the commercial devices

Table 2. Comparison of the Sensors and Seizure Detection

Sensors	Seizure type	Sensitivity	Advantage	Disadvantages
EEG	All types	Overall 74-99%	Gold standard	Less sensitive to mesial temporal onset
ECoG	All types	Overall 80-99%	Gold standard	Invasive
EMG	Motor seizure only	Upper body 95-100% Lower limb 53-57%	Good for tonic seizure	Only detect motor seizure, electrode could detach
EKG	GTCS, Focal seizure, secondarily generalized seizures	Tonic seizure 50% Focal seizure 70-99%	Easy to detect, high signal to noise ratio	Only detect with HR change, HR changes from daily activities
EDA	GTCS, dyscognitive seizure	GTCS 100% Dyscognitive seizure 86%	Easy to detect	Vulnerable to motion artifact
ACM	Motor seizure only	GTCS 87-100% Myoclonic seizure 0-80%	Easy to detect, good sensibility	Only detect motor seizure
Video	Motor seizure only	Hyper-motor seizure 93-100%	No discomfort	Only detect motor seizure, limited to cover area

Electroencephalography (EEG), Electrocorticography (ECoG), electromyography (EMG), Electrocardiography (EKG), electrodermal activity (EDA), accelerometer (ACM), heart rate (HR), generalized tonic clonic seizures (GTCS)

focus on larger market, such as individuals with cardiac disease, or even professional sports trainers. Third, seizure types decide the usability. The devices can detect easily GTCS, however they are almost useless for the other types of seizure, such as focal behavioral changes (Table 2).

Conclusion

The detection of seizures is a major issue in the management of epilepsy. However, detecting every seizure is not only technically difficult, but also time-consuming for caregivers. Better techniques for the recognition of seizures that are easy to perform on a daily basis are required to reduce the risk of SUDEP. Portable devices are good alternatives to EEG monitoring. Although these devices are far less accurate than EEG, they enable the continuous collection of data over 24 hours. Nevertheless, using a single approach is not an appropriate solution for seizure monitoring. There are many commercial products with various kinds of sensors which is not currently focusing seizure detection. Several commercial products combine more than two different types of signals to recognize ictal patterns²⁶⁾. These signals include HR, EDA, and data from ACMS. Combining data from such devices in the future would enable detection of seizures using wearable medical devices. These devices may be ultimately used for epilepsy treatment.

요약

뇌파는 발작을 발견하는 최선의 방법이다. 하지만 뇌파기는 대체로 고가이며 뇌파데이터를 기록하는 데 잘 훈련된 인력이 필요하다. 발작을 감시하는 것은 난치성 뇌전증 환자에게 중요하며, 목격자가 없거나 발작이 길어지는 경우 특히 그렇다. 뇌전증에서 돌발성 사망(SUDEP)은 난치성 뇌전증 환자에게 중요한 문제이며, 돌발성 사망의 위험은 삶의 질을 떨어뜨리기 때문이다. 뇌파 이외에 발작을 감지하기 위한 병태생리학적 변화를 감지하는 여러 대체 기술들이 연구되어 왔다. 심박과 심박 변이도는 발작과 관련한 심혈관계 현상을 이용한다. 호흡수와 호흡운동이 또한 이용될 수 있다. 발작기의 움직임은 영상분석을 통해서 혹은 가속도센서, 회전계(자이로스코프) 등을 통해서 감지할 수 있다. 또한 피부전도도가 발작기를 알려주는데 연구되고 있다. 이러한 기술들은 각각 한계가 있다. 하지만 이 기술들은 가격이 저렴하며 환자들이 매일 착용하고 사용하는 것이 간편하다. 이러한 장점을 통해 목격자 없는 발작을 발견하는데 유용할 수 있으며 삶의 질을 높이는 데에 도움을 줄 수 있을 것이다.

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