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Real-time detection of epileptic seizures in animal models using reservoir computing

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Summary In recent years, an increasing number of studies have investigated the effects of closed-loop anti-epileptic treatments. Most of the current research still is very labour intensive: real-time treatment is manually triggered and conclusions can only be drawn after multiple days of manual review and annotation of the electroencephalogram (EEG). In this paper we propose a technique based on reservoir computing (RC) to automatically and in real-time detect epileptic seizures in the intra-cranial EEG (iEEG) of epileptic rats in order to immediately trigger seizure treatment.

The performance of the system is evaluated in two different seizure types: absence seizures from genetic absence epilepsy rats from Strasbourg (GAERS) and limbic seizures from post status epilepticus (PSE) rats. The dataset consists of 452 hours iEEG from 23 GAERS and 2083 hours iEEG from 22 PSE rats.

In the default set-up the system detects 0.09 and 0.13 false positives per seizure and misses 0.07 and 0.005 events per seizure for GAERS and PSE rats respectively. It achieves an average detection delay below 1 s in GAERS and less than 10 s in the PSE data. This detection delay and the number of missed seizures can be further decreased when a higher false positive rate is allowed.

Our method outperforms state-of-the-art detection techniques and only a few parameters require optimization on a limited training set. It is therefore suited for automatic seizure detection based on iEEG and may serve as a useful tool for epilepsy researchers. The technique avoids the time-consuming manual review and annotation of EEG and can be incorporated in a closed-loop treatment strategy.

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Introduction

Interictal and ictal EEG from patients with epilepsy is characterised by typical patterns that are usually visually detected for diagnostic purposes. In a research setting the EEG is often used to evaluate therapeutic efficacy. In this case, in humans and especially in animal research settings, many hours of EEG require manual review and analysis. Automated seizure detection decreases the workload and may also be more reliable compared to hours of visual analysis.

Many (Buteneers et al., 2010; Van Hese et al., 2009; Nandan et al., 2010; Westerhuis et al., 1996; White et al., 2006; Haas et al., 2007) automated seizure detection programs, based on various techniques are available. Only a few of them allow real-time seizure detection (Nandan et al., 2010; Haas et al., 2007). The advantage of accurate real-time seizure detection is the potential to incorporate this detection into a so called closed-loop system that allows immediate triggering of an intervention at the time of seizure occurrence including fast working anti-epileptic drugs, Deep Brain Stimulation (DBS) (Waterschoot et al., 2006; Wyckhuys et al., 2010), Vagus Nerve Stimulation (VNS) (Boon et al., 2001), etc.

In recent years machine learning in general and more specifically artificial neural networks are more commonly used to build seizure detection algorithms. Reservoir computing (RC) is a recurrent neural network (RNN) training technique which has been shown to achieve state-of-the-art performance for annotating EEG (Buteneers et al., 2010). It keeps the performance of regular RNNs but reduces the training time dramatically (Lukoševičius and Jaeger, 2009). For seizure detection RC has the advantage that it is a learned non-linear dynamical system which is opposed to the mostly linear classification techniques used in literature. This paper improves the annotation accuracy of Buteneers et al. (2010) and extends it with the ability to detect the seizures with a low latency. To investigate the accuracy of RC to detect epileptiform discharges in real-time, we apply it to the EEG of genetic absence epilepsy rats from Strasbourg (GAERS) and post status epilepticus (PSE) rats.

GAERS and PSE rats are well known and widely used models for human absence and temporal-lobe epilepsy respectively (Danober et al., 1998). The EEG is characterised by very stereotyped ictal epileptiform discharges shown in Figs. 1 and 2. The models have a very good electroclinical correlation and the animals have a high seizure frequency. For these reasons they are a useful model for drug screening and the application of seizure detection algorithms.

Materials

This study compares several methods for epileptic seizure detection on two different seizure types: absence seizures from GAERS and limbic seizures from PSE rats. In both cases, the EEG was recorded with a custom-built amplifier. Afterwards it was subsampled to 200Hz before being evaluated by experienced encephalographers.

The complete dataset consists of 454 hours of data from GAERS and 2083 hours of data from PSE rats. For GAERS the training set, 5.75 hours in total, consists of the first 15 minutes of EEG per rat that contained at least 90 seconds of ictal EEG. The training set for the PSE data, 44 hours of data, consists of the first 10 seizures of each rat in the dataset combined with about 5 minutes of pre-ictal and post-ictal EEG. The rest of the data following the training data was used for testing.

Genetic absence epilepsy rats from Strasbourg

GAERS are a strain of Wistar rats that all exhibit spontaneous absence seizures characterised by paroxysmal unresponsiveness to environmental stimuli and cessation of ongoing activity. These absence seizures, which are displayed as synchronous spike and wave discharges (SWDs) on the EEG, occur mostly when the animal is in a state of quiet wakefulness. However, they are rare during periods of active arousal and sleep. The number of seizures and their duration increase with age, until it reaches a maximum at about 6 months. The EEG of SWDs shows a fundamental frequency in the range of 7—12 Hz and several harmonics (see Fig. 1), an amplitude varying from 300 to 1000 μV and a duration from 0.5 to 120 s.

Dataset A was made during a study to evaluate the effect of acute and non-acute high (130 Hz) and middle high (60 Hz) frequency DBS on the occurrence of SWDs (Waterschoot et al., 2006). The rats from dataset B were part of a study to evaluate the effect of long-term VNS.

All EEG fragments were visually reviewed, the data contaminated with stimulation artefacts was removed, one EEG channel was selected and all present SWDs with a minimum seizure length of 0.5 s were marked by an experienced encephalographer. These annotations were used as the 'gold standard' in this study. From study A, 64.5 hours of single-channel depth EEG-data recorded in the anterodorsal thalamus from 12 different rats was used. 23% of the total time contained the 3468 seizures which lasted on average 15 s. Study B yielded 390 hours of single-channel scalp EEG-data recorded over the frontoparietal cortex from 11 rats. A total number of 6183 seizures made up 4.5% of the data and lasted 10 s on average. Each of the seizures lasted between 0.5 and 110 s.

Post status epilepticus rats

Kainic acid is a potent central nervous stimulant, isolated from the seaweed digenea simplex. This excitotoxic product is an agonist of a subclass of ionotropic glutamate receptors and a systemic injection in healthy rats triggers a cascade of molecular and cellular events eventually leading to status epilepticus, followed by a period of gradual increase in seizure frequency, which eventually stabilizes. Finally, rats display spontaneous, secondary generalized limbic seizures which resemble those seen in temporal-lobe epilepsy patients (Baraban, 2009).

During annotation, spontaneous EEG seizures were recognized against background by their large amplitude (more than 3 times baseline amplitude), high-frequency EEG activity ($\geq$5 Hz), with characteristic high temporal correlation and progression of spike frequency. Fig. 2 shows an example of a limbic seizure.

Dataset C was made during a study to evaluate the effect of long-term high frequency (130 Hz) and Poisson distributed