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Towards accurate prediction of epileptic seizures: A review

Elie Bou Assi [a,*], Dang K. Nguyen [b], Sandy Rihana [c], Mohamad Sawan [a]

[a] Polystim Neurotech Lab, Institute of Biomedical Engineering, Polytechnique Montreal, Montreal, QC, Canada
[b] University of Montreal Hospital Center (CHUM), University of Montreal, Montreal, QC, Canada
[c] Biomedical Engineering Department, Holy Spirit University of Kaslik (USEK), Jounieh, Lebanon

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ABSTRACT

Recent research has investigated the possibility of predicting epileptic seizures. Intervention before the onset of seizure manifestations could be envisioned with accurate seizure forecasting. Although efforts for better prediction have been made, the translation of current approaches to clinical applications is still not possible. While early findings have been optimistic, the absence of statistical validation and reproducibility has raised doubts about the existence of a preictal state. Analysis and algorithmic studies are providing evidence that transition to the ictal state is not random, with build-up leading to seizures. We have reviewed the general framework of reliable algorithmic seizure prediction studies, discussing each component of the whole block diagram. We have explored steps along the pathway, from signal acquisition to adequate performance evaluation that should be taken into account in the design of an efficient seizure advisory/intervention system. The present review has established that there is potential for improvement and optimization in the seizure prediction framework. New databases, higher sampling frequencies, adequate preprocessing, electrode selection, and machine-learning considerations are all elements of the prediction scheme that should be assessed to achieve more realistic, better-than-chance performances.

Contents

* Corresponding author at: Polystim Neurotech Lab (polystim.org), Institute of Biomedical Engineering, Polytechnique Montreal (polymtl.ca) 2900, boul. Édouard–Montpetit, Université de Montréal Campus, 2500, Chemin de Polytechnique Montréal, Québec, H3T 1J4 Room M5306, Lassonde Building, Canada.
E-mail address: elie.bou-assi@polymtl.ca (E. Bou Assi).

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1. Introduction

Epilepsy is a prevalent chronic condition characterized by recurrent seizures. Long-term drug therapy is the major form of treatment, to which ~30% of epileptic patients are refractory [1]. Epilepsy surgery is recommended after medication failure and when seizures are confined to one area of the brain where tissue can be safely removed. Unfortunately, complete seizure control remains elusive [2]. In temporal lobe epilepsy surgeries, the probability of becoming seizure-free is ~75% in lesional cases and only 50% in nonlesional cases [3], whereas in frontal lobe epilepsy surgeries, the probability of becoming seizure-free is 60% in lesional cases and merely 35% in nonlesional cases. The most obvious explanation of surgical failure is inaccurate localization or characterization of foci due to limitations of current tools, such as magnetic resonance imaging, single photon emission computed tomography/positron emission tomography scans, and surface or intracranial electroencephalographic (EEG) recordings [4]. Work in the last few years has suggested that network connectivity is at the center of epilepsy [5–9], i.e., a more complex 'epileptic network' concept has replaced the classical, simplistic notion of a single epileptic focus. In the 'epileptic network', the synchronized activity of 'nodes' with increased excitability (or decreased inhibition) is involved in the generation of pathological spikes or seizures, and vulnerability to epileptiform activity in any one part is influenced by activity elsewhere in the network.

Because of their unpredictable nature, uncontrolled seizures represent a major personal handicap and source of worry for patients. In addition, persistent seizures constitute a considerable burden on healthcare resources, accounting for a high number of disability days or unemployment and low annual income [10,11]. Some difficulties and challenges faced in the treatment of drug-refractory patients can be overcome by algorithms able to anticipate seizures. Seizure detection and prediction algorithms have been proposed in an attempt to deliver therapies during times of high seizure likelihood [12]. It has been recently demonstrated that seizures are more likely to be controlled by means of closed-loop stimulations as compared to open loop strategies [13]. Although detection algorithms are currently better in terms of sensitivity (SS) and specificity (SP) than prediction algorithms, the activation of seizure-aborting interventions (such as focal cooling, electrical stimulation or release of anticonvulsants) after electrical seizure onset means that patients could already have disabling clinical manifestations [14].

Recent research has been mainly oriented towards the prediction of epileptic seizures much in advance to allow intervention before seizures start. To date, very interesting reviews of seizure prediction have been published [14,15], but none has been specifically dedicated to classification methods in an algorithmic seizure prediction framework. We start by presenting basic conventions and considerations for reliable seizure prediction. Various seizure prediction approaches adopted by the epilepsy research community are discussed while paying special attention to algorithmic studies because of their applicability in seizure advisory/intervention implantable devices. The basics, history, and advancements in algorithmic studies are detailed in a block-by-block fashion. We have reviewed state-of-the-art achievements in each block, highlighting signal processing methods that have contributed to progress and yielded realistic evidence in the field. Several acquisition modalities are covered, focusing on intracranial (iEEG) and/or scalp EEG recordings. The algorithmic studies reviewed are based on personal and international databases as well as long-term recordings with ambulatory devices. Feature extraction covers linear and nonlinear methods with both univariate and multivariate approaches. Prominent feature selection techniques, classifiers as well as regularization functions are compared. The discussion section emphasizes current issues and required considerations with analyses of the progress made in each block. The review ends by identifying future prospects in the field and challenges that still need to be overcome.

2. Epileptic seizure prediction – state-of-the-art

2.1. Basic conventions in seizure prediction studies

Seizure detection employs algorithms that aim to detect seizure onset. Seizure prediction looks at the possibility of forecasting seizure occurrence and is therefore intended for fulfillment much earlier than detection. This review focuses solely on algorithmic seizure prediction studies. Published works were selected to cover different signal processing strategies proposed in a seizure forecasting framework. When several studies using similar processing approaches were found, only those adhering to the recommendation for reliable seizure prediction were selected [14]. Studies proposing novel methods, but not adhering to the reliable forecasting recommendations, were discussed, highlighting potential pitfalls.

Numerous investigations have demonstrated gradual transition between interictal (in-between) and ictal (during) seizure states, known as the preictal state [15]. Thus, seizure prediction can be considered as early detection of the preictal state. Some recent studies have added the notion of intervention time (IT) or seizure horizon [16]. IT, assumed to lie between the end of the preictal period and seizure onset, should ensure enough time for intervention and help to distinguish seizure prediction from simple seizure detection. Fig. 1 presents 5-channels iEEG recordings illustrating typical brain states.

2.2. Different approaches to seizure prediction

Seizure prediction is an active research topic dating back to the 1970s. In a detailed review on the predictability of epileptic seizures, Mormann et al. [14] presented a chronological overview of seizure prediction studies and their findings. Early approaches searched for precursors from scalp EEG with linear methods, such as autoregressive modeling [17,18]. Then, studies suggesting the possibility of preictal phenomena started emerging. The latter – generally based on nonlinear dynamics [19] – were, however, limited to investigations of the preictal state, without taking the normal brain state into account. They were followed by proof-of-principle and controlled studies on predictability that tackled the issue of specificity by making comparisons between preictal and interictal states. Although these early findings were optimistic, the absence of statistical validation and reproducibility was a major constraint in the development of clinical devices. They led to a phase that Mormann et al. [14] called "the rise of skepticism", during which studies based on extensive databases revealed poorer performance than earlier ones. It highlighted the need for statistical validation and long-term multi-day EEG recordings made possible at the turn of the millennium due to booming mass storage capability. Current seizure prediction approaches can be grouped into 2 main categories: analytical/statistical and algorithmic. Since the main goal of prediction studies is seizure control, it can be achieved by implementing algorithms able to track the preictal state. Accurate seizure-prediction algorithms may open possibilities for on-demand, EEG-triggered interventions once the preictal state is detected. Below, we review algorithm-based studies in a methodological manner, discussing each component of the whole block diagram.