Seizure 51 (2017) 180–185

Contents lists available at ScienceDirect

Seizure

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

Review

Seizure self-prediction: Myth or missed opportunity?

Michael Mackay[a,b,c,*], Hector Mahlaba[c], Erika Gavillet[d], Roger G. Whittaker[a,c]

[a] Institute of Neuroscience, Henry Wellcome Building, Newcastle University, Newcastle upon Tyne, NE2 4HH, United Kingdom
[b] School of Computing Science, Urban Sciences Building, Newcastle University, Newcastle upon Tyne, NE4 5TG, United Kingdom
[c] Newcastle upon Tyne Hospitals NHS Foundation Trust, Freeman Hospital, Freeman Road, High Heaton, Newcastle upon Tyne, NE7 7DN, United Kingdom
[d] Newcastle University Library, Newcastle University, Newcastle upon Tyne, NE1 7RU, United Kingdom

ARTICLE INFO

Article history:
Received 1 March 2017
Received in revised form 22 August 2017
Accepted 25 August 2017
Available online xxx

Keywords:
Epilepsy
Seizures
Prodromal symptoms
Review
Systematic
Decision support techniques

ABSTRACT

Purpose: Many patients report being able to predict their own seizures, and yet most seizures appear to strike out of the blue. This inherent contradiction makes the topic of seizure self-prediction controversial as well as difficult to study. Here we review the evidence for whether this ability exists, how many patients are capable of self-prediction and the nature of this capability, and whether this could provide a target for intervention.
Methods: Systematic searches of bibliographic databases including MEDLINE, EMBASE and PsycINFO through OVID were performed to identify relevant papers which were then screened by the study authors for inclusion in the study. 18 papers were selected for inclusion as the focus of this review.
Results: On the basis of two studies, between 17% and 41% of patients demonstrate a significantly greater than chance ability to predict an upcoming seizure in the following 12-h time window. This risk is correlated with self-reported anxiety, stress, sleep deprivation, mood and certain prodromal symptoms. However, there is no evidence for any subjective experience which directly heralds an imminent seizure. Thus, while patients may be aware of seizure risk, and have some ability to predict seizure occurrence over a wide time window, they are unable to subjectively recognise seizure onset in advance.
Conclusion: Utilising subjectively acquired knowledge of seizure risk may provide a widely implementable tool for targeted intervention. The risk fluctuates over a time course appropriate for pharmacotherapy which may improve seizure control and the side-effect profile of anti-epileptic medication.

1. Introduction

For most people with epilepsy seizures appear out of the blue with little or no warning. It is this inherent unpredictability that leads to much of the associated morbidity and social impact. However, it has long been recognised that some patients experience warning symptoms minutes or even hours before a seizure [1]. This is of huge potential benefit as it would allow patients to intervene to prevent the seizure occurring or to mitigate its consequences by taking avoiding action or additional medication. An ability to predict generalised tonic-clonic seizures may help mitigate the risk of SUDEP (Sudden Unexpected Death in Epilepsy). Further study of how patients self-predict seizures could also help understand the underlying neurobiology.

The topic is difficult to study. The majority of studies are based on questionnaires or interviews with patients. These are highly subjective, and produce evidence which is retrospective and largely anecdotal. They give an insight into patient beliefs about their seizures and premonitory symptoms, but little hard evidence to support them. Collecting data on the temporal relationship between symptoms and the occurrence of seizures is even more difficult. Paper diaries of seizures are often poorly maintained and unreliable, and patient recognition and recall of seizures is imprecise [2]. They are also prone to retrospective entry and manipulation. Electronic diaries allow timestamping of data entry, but do not necessarily improve patient compliance and accuracy [3].

The patient population itself is extremely heterogeneous with over 30 different epileptic syndromes and complicated by mimics such as dissociative seizures. Without very large numbers of subjects, subgroup analysis is difficult and patients with different types of epilepsy end up being analysed within the same cohort. Furthermore, the terminology used to describe subjective experiences preceding a seizure, such as prodrome, aura, premonitory

* Corresponding author at: School of Computing Science, Urban Sciences Building, Newcastle University, Newcastle upon Tyne, NE4 5TG, United Kingdom.
E-mail addresses: michael.mackay@ncl.ac.uk (M. Mackay), hector.mahlaba@nuth.nhs.uk (H. Mahlaba), erika.gavillet@newcastle.ac.uk (E. Gavillet), roger.whittaker@newcastle.ac.uk (R.G. Whittaker).

http://dx.doi.org/10.1016/j.seizure.2017.08.011
1059-1311/

symptoms and precipitating factors do not have clear definitions and are often used interchangeably. This has led to very different criteria for categorising premonitory symptoms between studies. For example, some studies simply ask patients about any symptoms noticed prior to a seizure, while other require symptoms to occur at least 30 min prior to a seizure and be semiologically distinct from any usual aura.

Given the lack of consensus and the potential benefit to patients we performed a review of the published literature seeking to answer the following questions: Can patients truly predict their seizures? If so, what proportion of patients are capable of doing so, on the basis of what information, and could this be used for interventional therapies?

2. Methods

Our search strategy is detailed in Table 1. Concept one and three terms are searched as keywords, while concept 2 terms are searched as subject headings. Concept four and five are used to narrow down results to exclude papers using EEG for seizure prediction; and look for papers studying human seizure prediction since 1980.

Searches were run on the MEDLINE, EMBASE and PsycINFO databases through OVID in December 2014 by EG. We used all five concepts in all searches, and subject headings were used without subheadings. The search of the MEDLINE database used focussed subject headings and returned 233 results. The searches of EMBASE and PsycINFO used unfocussed subject headings and returned 523 and 180 results respectively, giving a total of 936 papers. Removal of duplicate results returned 661 papers for screening. Review author HM screened the titles and abstracts of all identified studies for inclusion resulting in the retrieval of 17 full-text papers. Full-text study reports were then independently screened by review authors MM and HM for inclusion and all papers were considered suitable for inclusion. Reference lists of primary studies and review articles were checked for additional references resulting in one further paper considered suitable for inclusion. A total of 18 papers comprised the focus of this review.

We have excluded reflex epilepsies from this review, as these epilepsies are defined by the reliable triggering of seizures by a known stimulant. Therefore the central question of this review; whether patients are able to predict their own seizures, is redundant in these populations. Additionally, consideration of this population of patients does not contribute anything to the analysis of seizure self-prediction by the general epilepsy population, and would indeed confound the results.

Within the appraised literature the terminology used was somewhat inconsistent; however most authors regarded prodromes as symptoms which may occur hours to minutes before a seizure. They were considered to be non-ictal, but their cause is unknown. Triggers, or precipitating factors, were external factors which exposure to, or experience of, may precipitate a seizure. Premonitory symptoms referred to any prodromal symptoms or precipitating factors which the patient believed had, or which could be shown to have, predictive ability for seizure risk. Due to the heterogeneity in study design, definitions and outcomes, a meta-analysis of data was not considered possible. However, in most studies there was a clear distinction made between precipitating factors and prodromes, albeit with slightly differing definitions in terms of temporal relationship to an ensuing seizure, and hence we divided the analysis into these two broad categories.

3. Results

Any discussion about seizure self-prediction confronts two contradictory viewpoints. One the one hand, epilepsy is characterised by the spontaneous and seemingly random occurrence of seizures. Indeed, it is this aspect that causes such a profound effect on patients' quality of life and leads to many of the legal restrictions placed on patients. At the same time, as long as there has been epilepsy there has been the concept that seizures can be provoked or triggered, and that they may be preceded by warning signs or symptoms. The evidence presented herein supports the conclusion that some patients do indeed have a degree of awareness of their underlying seizure risk. The series of studies by Haut et al. show that a subgroup of patients is able to utilise information gained from self-recognition of factors such as anxiety and stress to inform the perceived risk of impending seizures. This predictive ability peaks at 4–6 h prior to a seizure and is seen in 17–41% of patients [7–10].

The evidence for patient awareness of the precise timing of an upcoming seizure is limited to anecdotal reporting by patients. While studies looking at the timing of prodromes find mixed evidence as to whether they are related to seizures, they do not find any close temporal link, on the order of minutes, or with high positive predictive value. The study by Maiwald et al. suggests that many patients may be identifying prodromal symptoms retrospectively. Studies by *Haut* et al. also asked patients about prodromal symptoms and found a number of these symptoms were related to increased seizure risk in the following epoch. Taken together the evidence suggests that what patients are reporting as prodromes are more appropriately interpreted as representing increased seizure risk, but are not heralding an imminent seizure.

There is significant overlap in the nature of the symptoms described as prodromes and those described as precipitating

Table 1
Search grid used to plan search strategy.

Concept 1: Sensation	Concept 2: Disease	Concept 3: Species	Concept 4: EXCLUDE	Concept 5: INCLUDE
Prodrom*	Epilepsy	Self*	EEG	human
Premonit*	Epileptic			1980-current
Predict*	Seizure			
Anticipat*	Ictus			
Warn*	Fit			
Pre-ictal	Episode			
Preictal	Event			
Pre-seizure	Paroxysm			
Preseizure	Convulsion			
Precipit*				
Impend*				
Presag*				
Aura*				
Trigger*				