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Modeling Seizure Self-Prediction: An E-Diary Study

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Abstract

Purpose—A subset of patients with epilepsy successfully self-predicted seizures in a paper diary study. We conducted an e-diary study to ensure that prediction precedes seizures, and to characterize the prodromal features and time windows that underlie self-prediction.

Methods—Subjects 18 or older with LRE and ≥3 seizures/month maintained an e-diary, reporting AM/PM data daily, including mood, premonitory symptoms, and all seizures. Self-prediction was rated by, “How likely are you to experience a seizure [time frame]”? Five choices ranged from almost certain (>95% chance) to very unlikely. Relative odds of seizure (OR) within time frames was examined using Poisson models with log normal random effects to adjust for multiple observations.

Key Findings—Nineteen subjects reported 244 eligible seizures. OR for prediction choices within 6hrs was as high as 9.31 (1.92,45.23) for “almost certain”. Prediction was most robust within 6hrs of diary entry, and remained significant up to 12hrs. For 9 best predictors, average sensitivity was 50%. Older age contributed to successful self-prediction, and self-prediction appeared to be driven by mood and premonitory symptoms. In multivariate modeling of seizure occurrence, self-prediction (2.84; 1.68,4.81), favorable change in mood (0.82; 0.67,0.99) and number of premonitory symptoms (1,11; 1.00,1.24) were significant.

Significance—Some persons with epilepsy can self-predict seizures. In these individuals, the odds of a seizure following a positive prediction are high. Predictions were robust, not attributable to recall bias, and were related to self awareness of mood and premonitory features. The 6-hour prediction window is suitable for the development of pre-emptive therapy.

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Dr. Borkowski has nothing to disclose.

Keywords

Seizure prediction; self-prediction; localization-related epilepsy; seizure diary; electronic diary; premonitory symptoms; seizure precipitants

INTRODUCTION

The unpredictability of seizures remains one of the most challenging aspects of epilepsy (Murray 1993, Fisher 2000). Simply knowing when a seizure is coming, may in itself, reduce the burden of unpredictability and improve health related quality of life (Schulze-Bonhage & Buller, 2008). For the most part, efforts to predict seizures have relied on EEG data, although the concept of self-prediction of seizures by persons with epilepsy has been the focus of increasing research and discussion (Spector et al 2000, Lee & No 2005, Schulze-Bonhage et al 2006, Haut et al 2007a, DuBois et al 2010, Dionisio et al 2010). In questionnaire studies, many patients report a "pre-seizure state" characterized by prodromal or premonitory symptoms (Hughes et al 1993, Rajna et al 1997, Lee & No 2005, Schulze-Bonhage et al 2006, Petitmengin et al 2006, Scaramelli et al 2009); more recently, prodromes and seizure self-prediction have been investigated in prospective studies (Haut et al 2007a, Dubois et al 2010, Maiwald et al 2011).

In a paper diary study, we showed that a subset of patients with localization-related epilepsy (LRE) successfully predicted their seizures over a 24 hour window (Haut et al, 2007a). We conceptualize seizure self-prediction as a conscious or subconscious awareness of prodromal features, trigger factors, and possibly unmeasured variables such as state correlates of electrophysiological changes.

To further explore the nature of clinical seizure self-prediction, we conducted an e-diary study that is the basis of the present report. We also included an extensive inventory of trigger factors, premonitory symptoms and measures of mood, expanding our ability to characterize the pre-ictal state. Based on this data, we reported clinical features of the pre-ictal state, demonstrating that mood changes and premonitory features predicted seizure occurrence over 12 hours (Haut et al 2012).

Our primary aim in the present report is to confirm clinical seizure self-prediction utilizing electronic data capture to provide time stamped data collection, reducing the potential for retrospective reporting and recall bias. Furthermore, because of the collection of exposure data twice daily and the time-stamped reporting of seizure onset, we are in a strong position to explore a number of secondary aims, including: define time frames of seizure occurrence following self-prediction; assess self-prediction as an outcome in its own right, independent of accuracy; identify components of self-prediction and ultimately to improve its' accuracy; and finally, determine the separate and joint effect of seizure self-prediction, mood and change in mood, as well as premonitory features on the subsequent occurrence of seizures. Insights into the predictability of seizures could lead to a novel approach to epilepsy treatment, namely preemptive therapy during the pre-ictal state.

METHODS

Subject recruitment

Study inclusion criteria have been reported (Haut et al 2012). Briefly, eligible subjects were ≥18 years old, had focal epilepsy (previously LRE), and reported ≥3 seizures per month. Subjects who reported seizure self-predictive ability and/or awareness of seizure precipitants were preferentially recruited. Subjects with a history of nonepileptic seizures were excluded. The Montefiore Medical Center Institutional Review Board approved the study, and all subjects provided informed consent.

Localization was defined as: temporal, frontal, or extratemporal lobe epilepsy; multifocal epilepsy; focal epilepsy with unknown localization; and generalized epilepsy. Localization was considered unknown in subjects with a history of partial seizures, normal or nonlocalizable EEG and MRI data and no inpatient epilepsy monitoring information.

Data collection

Diary training and data entry: Design of the e-diary has been described (Haut et al 2012). The study utilized a Palm-based electronic Patient Reported Outcome (ePRO) program developed by Symfo (Boston, MA). Subjects accessed a questionnaire in response to preprogrammed alarms. Questions were linked to each other with branching logic. Data were transmitted to a central server that was accessible to the investigators through a secure webportal.

Data were collected twice daily at two fixed intervals scheduled 12 hrs apart (AM and PM), and by patient initiation in relation to seizure or premonitory symptoms. Once data was entered, it was no longer available for editing by the subject (no back-entry). Each diary entry began with a stem question, “How are you feeling right now?” Response options included: not anticipating a seizure; anticipating a seizure; currently experiencing a seizure; recovering from a seizure. When subjects reported “currently experiencing a seizure”, the diary directed them to exit and return to the diary after the seizure concluded. Diary completion was monitored biweekly, and subjects were contacted for diary nonadherence.

Seizure prediction, premonitory symptoms, and precipitants: Seizure self-prediction, potential seizure precipitant and premonitory symptom data were collected during each AM and PM diary entry. Seizure self-prediction was assessed by the following question: How likely are you to experience a seizure [today (AM diary)/in the next 24 hrs (PM diary)? Reponses included: Almost certain (>95% chance); Very likely (75–94% chance); Fairly likely (50–74% chance); Quite unlikely (25–49% chance); Very unlikely (<25% chance).

Data on potential seizure precipitants was collected as previously described (Haut et al 2012). Six items from the mood circumplex (Larsen & Diener 1992) were assessed twice daily on a visual analog scale in response to the questions "how ("happy, sad, relaxed, nervous, lively, bored") are you feeling right now?" Other precipitant data included hours of sleep, menstrual status, alcohol use and medication compliance.

Eighteen premonitory symptoms were chosen based on previously reported symptoms in epilepsy and migraine studies (Hughes et al 1993, Rajna et al 1997, Giffin et al 2003, Schulze-Bonhage et al 2006, Scaremelli et al 2009). Data on these symptoms were collected as, “Are you experiencing any of the following?” followed by multiple choice menus, with an opportunity to add open-ended responses.

Of 22 subjects, 2 (9%) uploaded less than 30 days of diary data and were eliminated from this analysis. Twenty subjects (91%) uploaded >= 90 diary days. One of these subjects, who reported daily seizures, was eliminated from the analysis due to the seizure prediction horizon windows. This left a study sample of 19 subjects.

Statistical analysis—We defined the primary measure of patients’ ability to predict seizures to be the odds ratios associating the individual’s self prediction with the occurrence of a seizure at varying time frames after the prediction averaged over all the patients’ diary reports. Seizure occurrence was modeled as a binary outcome. Odds ratios of seizure occurrence were calculated between individual predictive choices, and also for “positive predictions,” being defined as a response of either “almost certain,” “very likely” or “fairly likely” combined vs. negative predictions (“fairly unlikely” or “very unlikely”). Logit-normal random effects models fit by maximum likelihood were used to estimate the odds ratios. A random intercept took into account individual differences in predictive ability and the repeated within-person measurements across multiple days of diary data. The odds ratio has the interpretation of the ratio of an individual’s odds of seizure for one prediction level divided by the same individual’s odds of seizure at the baseline 'very unlikely' prediction level. Stata versions 11 and 12 (Statacorp) were used for data analyses. In a series of models, we estimated the relative odds of seizure for a given level of prediction over 6, and 12 hours. We also estimated the relative odds of seizure over specified non-overlapping time intervals including 0 to ≤4 hours, 4-≤6 hours, 6-≤12 hours, 12-≤18 hours and 18 to ≤24 hours.

We previously showed that positive mood items were associated with a decreased risk of seizure while negative mood items had similar magnitudes of effect on seizure probability but in the opposite direction. Accordingly, we combined all six mood measures into a single summary metric; reverse scoring the negative mood items, as previously described (Haut et al 2012). This summary measure was treated as a continuous interval scale predictor, which we refer to as “favorable mood.” In addition, we calculated the change in the value of this mood measure from the corresponding (AM or PM) diary from the previous day, for a summary measure referred to as “favorable change in mood”. Similarly, the number of significant premonitory features reported in a single diary was also used as a continuous interval scale predictor.

RESULTS

The 19 subjects were predominantly female (84%), had a median age of 35 years with mean duration of epilepsy 16.1 years. Median frequency was 3.5 seizures per 30 days. Epilepsy localization was temporal (n=14); frontal (n=1); extratemporal other (n=2) and non-localizable (n=2).

Diaries were completed for a median of 103 days (range 50–151). Subjects provided 1680 AM entries, 1594 PM entries, and reported 258 seizures. Fourteen seizures were excluded: Five occurred as a first diary entry with no preceding diary data; nine occurred >24 hrs after last diary entry due to missed diaries. Thus the analyses presented were performed on of the remaining 244 seizures.

Accuracy of seizure self-prediction by level of predictive certainty (Table 1)

Patient assessments of the likelihood of seizures were distributed as follows across the 3,259 diary reports eligible for analysis: almost certain (15), very likely (77), fairly likely (346), quite unlikely (985), and very unlikely (1851). The OR for seizure occurrence as function of level of self-prediction options is presented over 6 and 12 hour prediction windows (Table 1). For example, the relative odds of seizure occurrence within 12 hours following positive prediction were 5.36 (CI 1.37–21.00) for “almost certain,” and 5.05 (CI 2.46–10.39) for “very likely,” compared to the reference group “very unlikely”. The OR for these response options at 6 hours were even more robust at 9.31 (CI 1.2–45.23) for almost certain and 8.78 (CI 3.84–20.06) for “very likely”, albeit with very large confidence intervals because of the reduced number of events.

Individual self-prediction odds ratios for each participant ranged from 0–16, reflecting heterogeneity in individual predictive ability. Nine of the 19 subjects were able to predict their seizures to a statistically significant degree. In this group of better predictors, the adjusted odds ratio for seizure given positive prediction was 6.44 (3.70–11.25, $p<0.0001$) over 12 hours. The adjusted odds for the group of 10 non-predictors was non-significant.

For self-prediction to usefully identify periods of increased risk for intervention, adequate sensitivity, specificity, positive predictive (PPV) and negative predictive (NPV) values are required. Overall, 7/19 subjects had a sensitivity of 30% or higher. Nearly all of the subjects (16/19) had a specificity of 83% or higher, and most (14/19) had a specificity of at least 90%. Twenty percent of responses of “almost certain” and “fairly certain” were followed by a seizure, while fifteen percent of “very likely” responses were followed by a seizure. Negative diary responses were significantly less likely to be followed by a seizure (4% for quite unlikely and 3% for very unlikely).

For the 9 subjects described above who were best able to predict their seizures, median/mean sensitivity was 50%/34%; median/mean specificity was 95%/92%, median/mean PPV was 16%/23%, and median NPV was 97%/96%.

Time frame for seizure self-prediction (Table 2)

The odds ratios for overall seizure self-prediction for positive responses (including all 3 positive choices) as estimated from the logit normal models for time intervals ranging from 4 to 24 hours is presented (Table 2). The odds ratios were statistically significant for time intervals up through 12 hours, and were most robust between 4–6 hours, where the odds of experiencing a seizure in the 4–6 hours following a positive response were nearly 7 times greater than the odds of a seizure following a response of “very unlikely.” The OR of seizure occurrence following a positive diary prediction does not achieve statistical significance after 12 hours.

Who successfully predicted seizures?

Duration of epilepsy, seizure frequency and seizure localization were not associated with seizure prediction; however older individuals were better able to predict their seizures. There was a significant association between patient age and self-prediction ability (p=0.041). Every year of age difference increased the odds of successful prediction by 5.23% (odds ratio estimate for interaction 1.0523, 95% CI 1.0020, 1.1052).

Determinants of positive seizure self-prediction independent of accuracy (Figure 1a)

Next, we examined the pre-ictal features related to seizure self-prediction, independent of accuracy. All 6 mood items (happy, relaxed, lively, nervous, sad, and bored) were significantly related to seizure self-prediction. In univariate analysis (Figure 1a, column 1) the “favorable mood” composite score was associated with a reduced risk of a positive seizure prediction (OR=0.21; CI:0.16–0.27), indicating that for each standard deviation increase in favorable mood composite the odds of a positive prediction decreases very substantially. Similarly, a favorable change in mood was associated with a reduction in the relative odds of seizure prediction (OR=0.40; CI:0.33–0.49) (Figure 1a, column 1). However, only favorable mood remains significant when combining both variables in a model.

Similarly, all ten premonitory features that predicted seizure occurrence (blurred vision, light sensitivity, dizziness, feeling emotional, concentration difficulty, hunger/food cravings, noise sensitivity, tired/weary, thirst, difficulty with thoughts) were also associated with seizure self-prediction, and total number of premonitory features was utilized as a composite score for modeling. In univariate analysis, the presence of each additional premonitory symptom nearly tripled the chance of making a seizure self-prediction (Figure 1a, column 1).

Other precipitants, including hours of sleep, menstrual phase, alcohol use and medication compliance, were not associated with reporting a seizure self-prediction. As indicated in Figure 1a, there is variance for seizure prediction not shared by mood and premonitory symptoms; this variance is likely attributable to other unmeasured variables.

In multivariate logistic regression modeling to assess the degree to which self prediction was driven by mood and premonitory symptoms, both mood and premonitory symptoms remained significant (Figure 1a, column 2) in the expected directions. While the significance of the mood variable was modestly attenuated from 0.21 to 0.32 in the multivariate models, the significance of premonitory symptoms remains largely non-attenuated.

Seizure occurrence based on self-prediction, mood and premonitory features (Figure 1b)

We next modeled actual seizure occurrence related to the separate and joint influence of self-prediction, mood and premonitory symptoms. In a series of univariate analyses (Figure 1b, column 1), positive self-prediction was the single strongest predictor of seizures. Favorable mood and favorable change in mood were protective while increased number of premonitory features was a risk factor in these univariate models. Combining the mood variables, only favorable change in mood remained an independent predictor. Combining

favorable change in mood and premonitory symptoms, each remained significant (Figure 1b, column 2).

Multivariate models examining the detailed modeling of seizure occurrence are presented (Webtable). The addition of premonitory features attenuated the odds ratio for self prediction from 3.8 (2.44–5.94) to 2.92 (1.75–4.85) (columns 1,4). In contrast, the addition of favorable change in mood does not substantially influence the OR of self prediction (column 5). In the final model (column 6), variables that remained significant included self-prediction (OR 2.84; 95% CI 1.68–4.81 $p<0.001$), number of premonitory features (1.11 CI 1.00–1.24 $p=0.04$), and favorable change in mood (OR 0.82, CI 0.67,0.99, $p=0.04$), but not favorable mood.

DISCUSSION

This study demonstrates that 9 of 19 (43%) participants with refractory LRE were able to accurately predict their seizures, drawing on awareness of prodromal features such as mood and premonitory symptoms. Self -prediction was more accurate in participants who were more confident in the accuracy of their predictions. For the most confident prediction choices, the odds of seizure increased more than 8 fold compared to times when seizures were thought to be “very unlikely” in unadjusted models. Self-prediction was most robust for prediction windows of 6 hours or less, remaining highly significant over 12 hours but not for longer time frames.

These results confirm and extend findings from our previous paper diary study with nightly measures (Haut et al 2007a). The present report is more robust and informative because the electronic diary format provides time stamping, because exposures were captured twice daily and because we included detailed inventories of mood and premonitory features. We also show that elements of the prodromal state play a large role in seizure self-prediction and ultimately, in accurate modeling of seizure occurrence.

Identifying the elements that contribute to seizure self-prediction offers the possibility of both understanding and improving self-prediction (Figure 1a). The most significant variables associated with self-prediction were favorable mood and number of reported premonitory features. As both of these elements are relatively easy for patients to attend to and record, this observation offers the promise of improved self-prediction with use of education and training.

Mood and stress are reported to be among the strongest seizure precipitants in both questionnaire and prospective diary studies (Neugebauer et al 1994, Spector et al 2000, Nakken et al 2005, Haut et al 2007b, Sperling et al 2008, Haut et al 2012). In this e-diary study, current mood and not change in mood influenced self-prediction in multivariate models, while change in mood was associated with actual seizure occurrence. Training patients to be more aware of mood change from one day to the next might improve their ability to self-predict seizures accurately and yield more powerful models of seizure probability (Figure 1b).

Premonitory symptoms make a strong contribution to self-prediction, which similarly offers opportunities to train patients on their own symptoms. Of note, premonitory features have been examined in a number of studies to date with conflicting results (Schulze-Bonhage et al 2006, Maiwald et al 2011, Haut et al 2012), as was discussed in a recent review (Schulze-Bonhage & Haut, 2011).

In the modeling of seizure occurrence, self-prediction, favorable change in mood and premonitory features remain independent predictors (Figure 1b). The OR for the associations in multivariate modeling suggest that self-prediction and premonitory symptoms both contribute to accurately assessing the probability of seizure occurrence.

Significant seizure self-prediction has been similarly reported in the inpatient epilepsy monitoring setting (DuBois et al 2010). Developing seizure self-prediction and seizure occurrence models may have important clinical implications. If “at risk” seizure states can be identified, interventions can range from taking precautionary measures to the actual use of pre-emptive therapies. Pre-emptive treatment will rely on robust modeling of seizure probability, of which seizure self-prediction may be a significant contributor. There is no evidence-based approach for pre-emptive therapy in adult epilepsy, although in practice clinicians may prescribe oral benzodiazepines for use in certain settings. If clinically based seizure prediction becomes more robust, candidate pre-emptive treatments might include short-term use of benzodiazepines, or even supplemental anti-epileptic medications. The association between mood and prediction suggests the possibility of utilizing a behavioral intervention during periods of increased seizure risk. In fact, a randomized controlled e-diary trial of a behavioral intervention is currently being conducted (Polak et al 2012).

As in other studies (Haut et al 2007a, DuBois et al 2010), predictive ability was not uniformly distributed among patients. The current cohort was enriched with subjects who described perceived self-predictive ability and/or awareness of precipitants, and almost 50% of the subjects demonstrated significant self- prediction. This percentage is much higher than in our previous study where 21% of the subjects were significant predictors. Here, older age was associated with better predictive ability, in contrast to our prior study where younger patients were better predictors (Haut et al 2007a). DuBois et al (2010) reported that subjects with a longer duration of epilepsy were better at predicting “no-seizure” days. The current findings support the concept that longer experience with seizures is associated with more accurate prediction. DuBois et al (2010) also found that higher seizure rates were associated with better prediction which was not the case in our current study. This disparity may well relate to differences between outpatient and inpatient seizure frequencies.

Is self-prediction and seizure modeling ready for clinical use? Seizure self-prediction has a very high specificity (Haut et al 2007a, Dubois et al 2010), reflecting the accuracy of negative predictions. Successful negative prediction is important for pre-emption; if the intervention carries any risk, this will limit unnecessary treatment. A clinically relevant pre-emptive therapy also requires high sensitivity. In the group of predictors, median sensitivity and specificity were 50% and 95%. These numbers, while sufficient for a behavioral intervention, will not support a pre-emptive pharmacologic trial, but may be improved with training.

Our study has certain limitations. Our primary outcome measure is the occurrence of self-reported seizures as recorded using an electronic diary. This approach is vulnerable to errors of both under-reporting or over-reporting of seizures (Neugebauer 1989, Blum et al 1996, Tatum et al 2001, Hoppe et al 2007, Cook et al 2013).

The accuracy of self-reported seizures is a concern, as recently reported in a long-term study using implanted electrodes, where disparities between reports of seizures in patient diaries and electrographic seizure patterns on EEG reached statistical significant in almost a third of subjects (Cook et al 2013). Though this area requires additional attention, continuous EEG monitoring is rarely available. As a consequence, we will continue to rely on self-report both in clinical trials and clinical practice for the foreseeable future. However, unless errors in seizure reporting are associated with the exposures of interest, we would expect our reported associations to get stronger with perfect reporting of seizure occurrence.

Another challenge in a seizure self-prediction study is that patients may be predicting a seizure during their aura, reporting the “ictal” and not “pre-ictal” state. Again, absent EEG monitoring, this possibility cannot be completely ruled out. However, the most accurate prediction window of this study was 4–6 hours after a self-prediction, whereas a reported seizure would be expected to follow an aura report by minutes. Finally, although the number of subjects is modest we had over 3 thousand diary days and almost 250 seizures. The positive results support our feeling that the sample size is appropriate to confirm seizure self-prediction using electronic data capture.

There remains modeling evidence that as yet unmeasured variables are contributing to seizure self-prediction. These variables may represent other biological phenomenon that patients recognize as heralding a seizure, for example self-awareness of electrophysiological changes. A follow up study that includes continuous EEG monitoring, while logistically challenging, would likely clarify the phenomenon of self-prediction even further.

Our data confirms our previous findings that seizure self-prediction is possible for a subgroup of patients with epilepsy, and that in these individuals, the odds of a seizure following a positive prediction is high. While these findings may only be generalizable to patients who report either self-predictive ability or awareness of seizure precipitants to their clinicians, prevalence studies indicate that this may be a substantial subgroup. Improvement in predictive ability will be necessary for a planned pre-emptive trial; this may be accomplished with education and training individuals on their own data, focusing on features of the prodromal state such as premonitory symptoms, and change in mood. Ultimately, quantitative EEG analysis may also be utilized in combination with self-prediction, to enhance the effectiveness of both techniques. We anticipate that this work may represent a step towards a new paradigm of treatment, namely pre-emptive therapy for epilepsy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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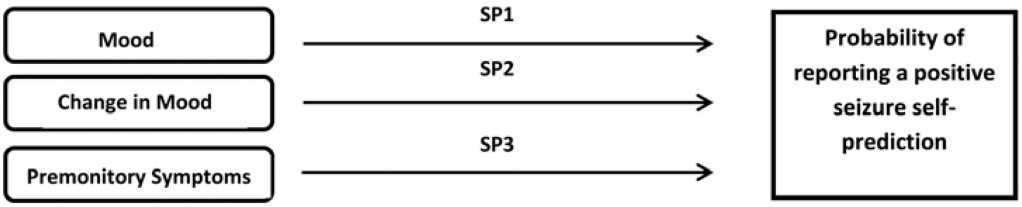
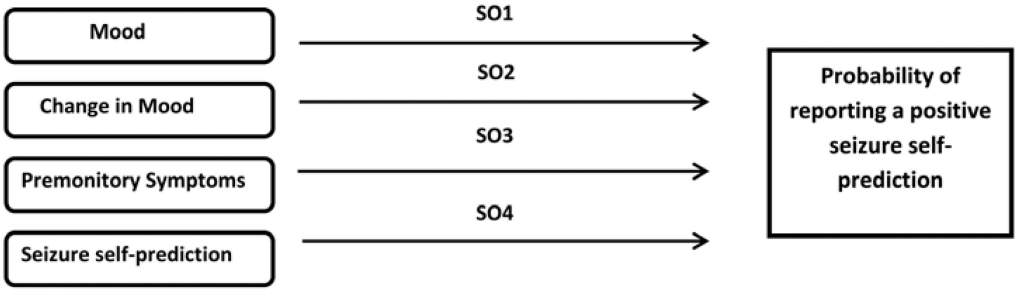
The influence of mood, change in mood and premonitory features on self-predicting a seizure: Results from random effects logistic regression models.



Predictor variable	Univariate analysis	Multivariate modeling
Favorable current mood **(SP1)**	**0.21** (0.16-0.27 p<0.001)	**0.32** (0.22,0.46 p<0.001)
Favorable change in mood **(SP2)**	**0.40** (0.33,0.49 p<0.001)	0.91 (0.61,1.20 p=0.49)
Increased number of premonitory symptoms **(SP3)**	**2.88** (2.48-3.35 <0.001)	(2.08,2.82 p<0.001)

b. The influence of mood, change in mood, premonitory features and seizure-self prediction on seizure occurrence: Results from random effects logistic regression models.



Predictor variable	Univariate analysis	Multivariate modeling
Favorable current mood **(SO1)**	**0.75** (0.61-0.91 p<0.004)	1.04 (0.81-1.33 P=0.75)
Favorable change in mood **(SO2)**	**0.71** (0.59-0.86 p<0.001)	**0.82** (0.67-0.99 p=0.038)
Increased number of premonitory symptoms **(SO3)**	**1.24** (1.13-1.35 p<0.001)	**1.11** (1.00-1.24 p=0.04)
Seizure self-prediction (SO4)	**3.8** (2.44-5.94 p<0.001)	**2.84** (1.68-4.81 p<0.001)

Figure 1.

(a) The direct effect of variables on the probability of self-predicting a seizure is denoted by SPI (mood), SP2 (change in mood), and SP3 (premonitory features). The relative odds of seizure self-prediction as a function of each of these factors is shown for univariate models and after multivariate adjustment. Multivariate models are adjusted for all the factors shown. (b) The direct effect of variables on the probability of seizure occurrence is denoted by SOI (mood), SO2 (change in mood), SO3 (premonitory features), and seizure self-prediction (SO4). The relative odds of seizure occurrence as a function of each of these factors is

shown for univariate models and after multivariate adjustment below. Multivariate models are adjusted for all the factors shown.

Table 1

Relative odds of seizure by level of self-prediction at 6 and 12 hours

Patient reported likelihood of seizures (Self-prediction	Odds Ratio of seizure within time window compared to reference group "very unlikely"	95% Confidence Interval	P value
6 hour time window			
Almost Certain	**9.31**	1.92,45.23	0.006
Very likely	**8.78**	3.84,20.06	<0.001
Fairly likely	**4.68**	2.53,8.63	<0.001
Quite unlikely	**1.20**	0.65,2.20	NS
Very unlikely	1.0	reference	---
12 hour time window			
Almost Certain	**5.36**	1.37,21.00	0.016
Very likely	**5.05**	2.46,10.39	<0.001
Fairly likely	**4.15**	2.51,6.85	<0.001
Quite unlikely	**1.34**	0.87,2.08	NS
Very unlikely	1.0	reference	---

Odds Ratios of seizure occurrence within 6 or 12 hours following specific prediction choices. Each choice is compared to the reference group "very unlikely".

Table 2

Predictive accuracy of seizure self-prediction* for seizure occurrence over various non-overlapping time intervals.

Time frame from diary entry to seizure	Odds Ratio of seizure for positive prediction compared to reference group "very unlikely "	95% Confidence Interval	P value
<4 hours	**4.02**	2.14,7.54	<0.001
4–<6 hours	**6.72**	2.48,18.2	<0.001
6–<12 hours	**2.81**	1.54,5.13	<0.001
12–<18 hours	0.99	0.43,2.27	0.10
18–24 hours	0.88	0.38,2.07	0.77

Odds Ratios of seizure occurrence within specified time frames following a positive prediction (almost certain, very likely, fairly likely)*, compared to the reference group "very unlikely".