Predictive factors for controlling seizures using a behavioral approach

DONNA J. ANDREWS & WARREN H. SCHONFELD*

Andrews/Reiter Epilepsy Research Program, Santa Rosa, CA and School of Social Welfare, University of California, Berkeley, CA, USA

Correspondence to Andrews/Reiter Epilepsy Research Program

A behavioral approach using EEG biofeedback for controlling complex-partial seizures has been successful at the Andrews/Reiter Epilepsy Research Program. Records for a random sample of 83 patients with uncontrolled seizures, one third of those receiving care between 1980 and 1985, document that 69 (83%) achieved control by completion of the program. Additional data about initial age of seizure onset, number of years seizures had been uncontrolled and seizure frequency when treatment started were collected to determine whether these factors predicted seizure control. Only frequency was significantly related to whether seizures were controlled when treatment ended. Further study using discriminant analysis showed that earlier onset age and higher seizure frequency were associated with a significantly greater number of treatment sessions required. Thus, these two factors predicted difficulty in controlling seizures, as measured by number of sessions, although onset age did not predict whether control was eventually achieved.

Since even the subgroup achieving the lowest rate of control (i.e., patients having daily seizures when treatment started) had 67% success, these results suggest that a behavioral approach can be useful for many people with currently uncontrolled complex-partial seizures regardless of their characteristics on factors examined in this study.

Key words: complex-partial epilepsy; self-control; behavioral treatment; EEG biofeedback.

INTRODUCTION

Complex-partial epilepsy is a complicated disorder that is often resistant to the present standardized approaches to treatment. It has been suggested that as many as 60% of people with epilepsy still experience seizures despite therapeutic levels of concomitant drug therapy[1]. The drug approach to control seizures generally results in diminished cognitive skills and loss of contact with one's own personality[2]. From this perspective the patients find it difficult, if not impossible, to interact effectively with their environment. This often leads to a failure to achieve normal maturational goals in school and in social and occupational endeavors, which tends to restrict and diminish the quality of life for these individuals. In some cases, drug treatment alters the type and severity of the disorder, creating behavioral problems that never existed before: this is especially true of children with this disorder[3].

These negative outcomes required that a new approach be found to help people with this form of epilepsy; one that does not just rid a patient of the seizures, but more importantly endeavors to understand what precipitates these sporadic events and what beneficial purpose they might be providing for the individual[4-6]. Medical approaches tend to ignore the emotional life of the patient and encourage the patient to do likewise. In so doing important information is overlooked which could have promoted seizure control. Problems, which might easily have been solved early in treatment, become elusive and paradoxical. These unresolved issues tend to overload the coping mechanism and often lead to the seizure state.'

In our approach, we encourage drug mono-therapy at the lowest therapeutic level, because we recognize the importance for the patient to be able to function at his or her highest level of cognitive ability. This facilitates the patients' recognition of subtle cues within themselves and their environment that trigger seizures[5, 6].

The study reported in this paper is intended to determine how successful the approach used at Andrews/Reiter is in controlling seizures and what factors may be helpful in predicting that success.

METHOD

Behavioral treatment approach used at Andrews/Reiter

Beginning in 1980, the Andrews/Reiter (A/R) method started to investigate and identify the psychological and behavioral aspects of seizure potential using a behavior model. Our goals in treatment were to reduce seizure frequency and improve quality of life. The approach to treatment was to identify the pre-seizure warning (aura), identify the triggers (people, situation, emotional or physical state), teach a diaphragmatic breathing technique that would be used when the patient was aware of the aura occurring or that stress was building-up, use electroencephalogram (EEG) biofeedback toward the goal of achieving therapeutic alpha activity (8-12 cps at 50 uV), and reduce medication in cases where it interfered with intellectual and cognitive functioning.

The benefits of operant conditioning using EEG biofeedback are well theorized[1, 7-13, 20]. Further, we began each training session with a diaphragmatic breath, in a Pavlovian attempt to develop a connection between the breath and the production of alpha activity.

In addition, we incorporated a counselor to help the patient to interpret the importance of the aura and the trigger phenomenon. We view these events as demand for appropriate action. With regard to the aura, the action required was limited to taking a deep breath when the individual felt a seizure coming on. When the triggering phenomenon was involved, the action was to determine whether facing the situation or moving away from it would most support the maintenance of their consciousness[14]. In each case, the patients were asked to keep a daily journal record of seizure activity and life situations that seemed to promote seizures, and to record what efforts they employed to avoid the seizure. In the case of a low functioning patient, we had them report this information to their care-provider, who then recorded it in a journal. A full description of the treatment model used in this study is provided in *Taking Control of Your Epilepsy, a* workbook by Reiter *et al.*[5]

Sample section

In 1986 a random sample of 83 people was selected from the population of 250 patients who had been treated prior to September 1985, at the private medical practice in Santa Rosa, CA, where the A/R research program is located. Sampling was conducted by selecting every third case in the file.

Variables

Each person was classified as controlled or uncontrolled, depending on whether they brought their seizures under complete control during the treatment or remained uncontrolled (any seizure activity led to a classification of 'uncontrolled' for the purposes of this study, and there was no distinction made for degree of improvement). In addition information on four other variables was collected, so that the following five variables were available for analysis in this study:

(1) SEIZCON: classification as controlled or uncontrolled at the end of treatment;

(2) ONSETAGE: age when seizures first began;

(3) YRSUNCON: number of years that seizures had been uncontrolled at the time treatment began;

(4) FREQSEIZ: frequency of seizures (number per month) at the time treatment began;

(5) NUMSESS: the number of treatment sessions until treatment was stopped.

Research questions

Three major research questions are addressed in the study.

(1) How effective is this treatment?

(2) Can a prediction equation be developed that will accurately indicate whether aperson entering the A/R treatment program is likely to achieve seizure control and on what factors does the control of seizures depend?

(3)Can the number of sessions needed to achieve seizure control be predicted and on what factors does the number of sessions depend?

Statistical techniques

To explore these questions a variety of statistical techniques were used. Simple univariate descriptive statistics were calculated to summarize each variable; t-tests were used to look at differences in the variable means between the subgroup of people who attained seizure control and the subgroup who did not; and associations between the variables and seizure control were examined by the Chi-square(X^2) test. Multivariate analyses were used to consider the relationships among several variables at the same time. Regression equations were estimated using the number of sessions (NUMSESS) as the dependent variable and the remaining variables as independent variables. In addition, difficulty in achieving seizure control was predicted using discriminant analysis with a dependent variable constructed from both SEIZCON and NUMSESS

RESULTS

Overall seizure control

Total seizure control was achieved by 69 of the 83 people studied, or 83% of the total sample. This is a significant finding.

Summary of variables-univariate

The range, mean and standard deviation (sd) of each of the four study variables is shown in Table 1 for the full sample (n = 83). All of these

Table 1: Summary statistics for predictor variables

Variable	Range		Mean	Sd
	From	To		
ONSETAGE	1	53	16.3	11.8
YRSUNCON	1	42	13.1	10.0
FREQSEIZ	1	600	18.5	68.3
NUMSESS	1	40	11.7	8.0

variables had distributions that were positively skewed. The extreme skewness of the distribution of FREQSEIZ resulted in certain methods of analysis being inappropriate, as described below.

Analysis of relationships

1.Means for subgroup and t-tests

As a first step to determining whether any of the four variables listed in Table 1 might be useful in predicting seizure control, univariate t-tests were conducted to see whether, for each variable, its mean value for those who achieved seizure control differed significantly from its mean value for those who did not achieve control. Table 2 shows the mean and sd for each

variable separately for those who achieved seizure control and those who did not, and the results of the t-test.

These tests show no evidence of significant differences in sample means for the two subgroups. Since the assumption of normality required for the t-test may not hold for any of the variables shown in Table 2, and definitely was violated by the distribution of FREQSEIZ, and since the sample size for the uncontrolled subgroup was small, it was decided to use the non-parametic Chi-square test to examine further the existence of any relationship between these variables and SEIZCON.

2.Measures of association

Each of the four variables was rescaled to a dichotomous variable so that it could be analyzed against SEIZCON in the form of a 2x2 contingency table. With the exception of FREQSEIZ, none showed a significant association with SEIZCON at the 0.05 level. There was a significant relationship between FREQSEIZ at the 0.05 level (x 2 = 4.7, 1 df), as displayed in Table 3.

From Table 3, it can be seen that about 90% of those people with five or fewer seizures per month at the time treatment began ended up controlling their seizures, whereas only 72% of those with six or more seizures at the start achieved seizure control. This is a significant difference from a statistical point of view. However, the table shows more than the association between frequency of seizures and seizure control. Even for the subgroup with higher seizure frequency, almost three-quarters ended treatment with seizure control.

The results of the t-tests and X2 tests suggest that the whole variable that significantly related to whether seizure control was achieved was the frequency or seizures at the start of treatment. However, these tests only take into account a single independent variable at a time. More sophisticated methodology is required to obtain a full picture of the relationships.

Table 2: Tests for differences by seizure control

Variable	**Subgroup**	**n**	**Mean**	**sd**	**t-statistic**	**P-value**
ONSETAGE	Controlled	69	17.2	11..8	1.67(81 df)	*NS*
	Uncontrolled	14	11.5	11.5		
YIISUNCON	Controlled	69	12.4	10.0	1.52(8t(if)	*NS*
	Uncontrolled	14	16.5	9.9		
FREQSEIZ	Controlled	69	10.7	21.9		
	Uncontrolled	14	57.1	158.0		
NUMSESS	Controlled	69	11.4	8.1	0.13(81 df)	*NS*
	Uncontrolled	14	13.2	7.7		

NS Indicates not significant at the 0.05

level ** Indicates that departures from the necessary assumptions of equal variances and normality of distributions in each subgroup were too extreme to warrant performing the t-test

Table 3: Relationship between seizure control and frequency

SEIZCON	FREQSEIZ				
	1 to 5 seizures		**6 or more seizures**		**Total**
	n	(%)	n	(%)	
Controlled	46	(90.2)	23	(71.9)	69
Uncontrolled	5	(9.8)		(28.1)	14
Total	51	(100%)	32	(100%)	83

3. Multivariate analysis of variance and discriminant analysis

Use of these multivariate techniques requires that the non-dichotomous variables be normally distributed and have equal covariance matrices for the subgroups being analyzed. These assumptions are not met by the existing data set with sample size 83. However, by the removal of a single outlier, the case for which FREQSEIZ has the value 600, the remaining data set of n = 82 cases is more suitable for analysis. Treating the one case as an outlier seems justified since the person with the next highest number of seizures per month had only 120 at the start of treatment.

The remaining analyses are performed on the group of n = 82 people, 69 of whom were controlled at the end of treatment and 13 of whom were not. (The person with 600 seizures per month did not achieve seizure control.) Table 4 shows the means for the four variables whose means were previously calculated, both for the total sample and for the subgroup separately.

Table 4: Means for predictor variables with subgroups

Variable	Subgroup	n	Mean
ONSETAGE	Controlled	69	17.2
	Uncontrolled	13	12.3
	Total	82	16.5
YRSUNCON	Controlled	69	12.4
	Uncontrolled	13	17.6
	Total	82	13.1
FREQSEIZ	Controlled	69	10.7
	Uncontrolled	13	15.4
	Total	82	11.4
NUMSESS	Controlled	69	11.4
	Uncontrolled	13	14.0
	Total	82	11.8

Notice that only the variable FREQSEIZ has substantially different means than before, this is due to the deletion of the outlier.

A multivariate analysis of variance was performed to determine whether the variables above have significantly different means for the 69 people who achieved control and the 13 who did not. Their differences are not significant**,** based on a value of 0.975 for Wilks' lambda (with 4 and 77 df). Although the distributions of the variables are skewed, this analysis is robust to departures from normality. The assumption of equal co-variance matrices is satisfied (based on Box's M test). The results of the preceding analysis imply that the four variables considered together are not useful to discriminate between those people who achieved seizure control and those who did not.

In considering the lack of success in predicting seizure control using the above approach, two issues are worth notice. First, there are differences in the means of the variables for the two subgroups being examined, though not significant differences. One fact, which may contribute to the lack of statistical significance, is the fact that the uncontrolled subgroup is small, with only 13 people. If the two subgroups were of more equal size, there would be a better chance of observing significant differences. Second, although seizure control is obviously important, there may be other ways of considering the whole issue of benefit from treatment. We might consider the difficulty experienced in controlling seizures rather than the outcome of achieving control or not. In other words, perhaps some variable other the SEIZCON might be a more

useful way of dividing the entire sample into two more equally sized sub-groups which differ in regard to difficulty of achieving control.Following this line of thought, we defined a new variable, EASCONT, which takes into account both seizure control and number of sessions, in the following manner:

EASECONT = 1 if seizure control was achieved in 12 or fewer sessions;

EASECONT = 2 if seizure control required more than 12 sessions or was not achieved.

(The number of sessions used for the dividing point was 12, since this was close to the mean.) Thus, EASECONT is a dichotomous variable, which divides the entire sample into two subgroups, one (with 50 subjects) which had greater ease in achieving seizure control and one (with 32 subjects) which had more difficulty (as measured by number of sessions) or did not achieve control when discriminant analysis was used to predict EASECONT from the three independent variables ONSETAGE, YRSUNCON and FREQSEIZ, the three variables taken together predict ease of achieving seizure control, in that they significantly distinguish between the two subgroups of people defined by EASECONT (Wilks' lambda = 0.867 with 3 and 78 df, P = 0. 0 1).

The sub-group which achieved seizure control with greater ease had a later mean onset age (19.7 years compared with 11.4), fewer mean years of uncontrolled seizures (11.4 years compared with 15.9), and a lower mean frequency of seizures (8.5 compared with 15.9).

4. Multiple regression

To complete the investigation of what factors affect the control of seizures, we looked at whether ONSETAGE, YRSUNCON and FREQSEIZ were significantly related to NUMSESS, using a multiple linear regression model. Since the third major research question deals with predicting the number of sessions needed to achieve seizure control, this analysis was restricted only to the subgroup of 69 people who achieved seizure control. The overall regression was significant at the 0.05 level (F = 3.34 with 3 and 65 df, P =0.025). However with the multiple R-square = 0.133, the model shows only weak explanatory power. Furthermore, only the age of onset and frequency of seizures were useful predictors of the number of sessions.

CONCLUSIONS

The high percentage of seizure control (83%) among the entire sample clearly indicates that the approach used is successful in controlling seizures by the end of treatment. Even people having daily seizures when treatment started, who were the patients with the lowest

rate of control, had 67% success. These results suggest that a behavioral approach can be useful for many people with currently uncontrolled complex-partial seizures regardless of their characteristics or the factors examined in this study.

A corollary of the high success rate for all kinds of patients is that none of the factors is strongly predictive of success. With respect to predicting seizure control, the only factor significantly related to achieving control was frequency of seizures. People who were experiencing fewer seizures when they began treatment had a higher percentage achieving control.

For those people achieving control, both frequency of seizures and age of onset affected the number of sessions. Fewer seizures and lateronset age were associated with fewer sessions. Even though these relationships were statistically significant, the ability to predict number of sessions is poor.

In general, seizures can be controlled more easily using a behavioral approach in those people with a later age of seizure onset, fewer years of uncontrolled seizures, and less frequent seizures.

The current study leaves many unanswered questions and suggests both the need and potential value of further research. More detail about the personal and health characteristics of the patient sample would enable other potential predictive factors to be investigated. In other words, more research is required to determine why this approach works and to identify which variables are most important in measuring an individual's potential for achieving success.

It is important to note that we continue to follow those who completed treatment to determine how long the successful results achieved last after sessions have ended. The results of this longitudinal study will be presented in a subsequent report when the last ones treated achieve 10 years post-treatment (1995). Ultimately, a randomized clinical trial study may be required to confirm the benefits of a behavioral approach.

APPENDIX: VARIABLE

1. SEIZCON-Classification as controlled or uncontrolled at the end of treatment.

2. ONSETAGE-Age when seizures first began.

3. YRSUNCON-Number of years that seizures had been uncontrolled at the time treatment began.

4. FREQSEIZ-Frequency of seizures (number per month) at the time treatment began.

5. NUMSESS-The number of treatment sessions until treatment was stopped.

REFERENCES

1. Sterman, M.B., MacDonald, L.R. and Stone, R.K. Biofeedback training of the sensorimotor EEG rhythm in man. Epilepsia 1974; 15: 395-416.

2. Baart, E., Difficult epilepsy cases: a psychodynamic point of view. In: *Advances in Epileptology: Proceedings of the XIth Epilepsy International Symposium.*. New York, Raven Press, 1980.

3. Taylor, D.C. and McKinlay, J. When not to treat epilepsy with drugs. *Developmental Medicine and Child Neurology* 1984; **25:** 822-833.

4. Dahl, J. Behavior therapy in the treatment of epilepsy: an application of applied relaxation. Scandinavian *Journal of Behavior Therapy* 1988; **17:** 139-153.

5. Reiter, J.M., Andrews, D. and Janis, C. *Taking Control of Your Epilepsy.* (Available from Andrews-Reiter Epilepsy Research Program) Santa Rosa, CA, USA, 1987.

6. Richard, A. and Reiter, J.M. *Epilepsy A New Approach,* New Jersey, Prentice Hall, 1990.

7. Finley, W.W., Smith, H.A. and Etherton, M.D. Reduction of seizures and normalization of the EEG in **a** severe epileptic following sensorimotor biofeedback training preliminary study. *Biological Psychology* 1975; 2:189-203.

8. Lubar, J.F. and Bahler, W.W. Behavioral management of epileptic seizures following EEG biofeedback training of the sensorimotor rhythm. *Biofeedback and Self Regulation* 1976; 1: 77-104.

9. Sterman, M.B., McDonald, L.N. and MacDonald, L.R., Effects of central cortical

EEG biofeedback training on seizure incidence in poorly controlled epileptics. Epi*lepsia* 1978; 19: 207-222.

10. Kuhlman, W.N. EEG feedback training for epileptic patients: Clinical and electroencephalographic analy*sis. Electroencephalography* and Clinical *Neurophysiology* 1978; 45: 699-710.

11. Kuhlman, W.N. and Kaplan, B.J. Clinical applications of EEG training. In: *Clinical Applications of Biofeedback: Appraisal and Status* (Eds, Gatchel and Price). New York, Pergamon, 1979: pp. 65-93.

12. Olton, D.S. and NoonBerg, A.R. Epilepsy. In: *Biofeedback: Clinical Applications in Behavioral Medicine.* New Jersey, Prentice Hall, 1980: pp. 242-283.

13. Yates, A.J. Voluntary control of the electrical activity of the brain, In: *Biofeedback and the Modification of Behavior*. New York, Plenum, 1980: pp. 268-324.

14. Reiter, J.M., Lambert, R.D., Andrews, D., Kasti, A. and Cobb, T. Complex-partial epilepsy: A therapeutic model of behavioral management and EEG biofeedback. *Self-control in Epilepsy 1990;* 1: 27-38.

15. Wyler, A.R., Robbins, C.A. and Dodrill, C.B. EEG operant conditioning for control of epilepsy. *Epilepsia* 1979; 20:279-286.