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Predicting the Outcome of Surgery in Patients with Medically Refractory Temporal Lobe Epilepsy – Artificial Neural Networks Model

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Abstract: ***Background and Aims:** To use an artificial neural networks (ANN) model based entirely on presurgical clinical and investigation variables for predicting postoperative surgical outcome for patients who underwent surgery for medically refractory temporal lobe epilepsy (TLE), and at the same time to compare with binary logistic regression model (BLR) using the Engel outcome.*
***Methods**: The subjects included were 115 patients with temporal lobe epilepsy who underwent surgery and had at least 1 year post surgery follow up. Initially 17 presurgical variables were coded on binary scale and depending on p value (<0.05) with logistic regression forward selection 3 predictors were selected namely: imaging (MRI), partial seizures with secondary generalization and seizure frequency for developing the models. Outcome was assessed using ANN and BLR according to Engel outcome classifications on binary scale. **Results**: The 115 datasets of the patients were used for classification by BLR and ANN methods for predicting the Engel outcome. BLR model sensitivity 80 %, specificity 85 % and that of ANN Sensitivity 80 % specificity 85 %, however the ROC area under curve for BLR is 0 .703 and ANN is 0.732.The ANN model the ROC area under curve is higher compared to BLR model. **Conclusions**: Using artificial neural networks, prediction models were developed to predict the outcome of surgery in patients with refractory temporal lobe epilepsy by using simple pre-operative clinical and investigation parameters. The ANN classifier performed better than BLR classifier.*

Keywords: Epilepsy Surgery, Prediction, Artificial Neural Networks and Binary logistic regression

1. Introduction

Anterior temporal lobectomy (ATL) is the procedure most frequently performed at epilepsy surgery centers for patients with medically refractory seizure disorders. The majority of ATL patients demonstrate improvement after surgery in clinical, psychological, and social measures. However, a significant percentage from 10% to 30% may fail to obtain a meaningful improvement in seizure frequency, may develop post-operative neurological deficits, or both [1-3].Moreover, there are significant risks inherent in the invasive surgical procedures [4].

To avoid negative outcomes from surgical therapy, the patient usually is processed through an intensive clinical and technological protocol. The guiding principle throughout this evaluation is that of data convergence: a number of different tests are conducted which should yield data that are consistent in pointing to a single area of brain responsible for generation of seizures. Furthermore, it must be possible to excise that area of brain safely.

Preoperative and surgical protocols vary from center to center. Different weight is given to results obtained from individual tests, such as the intracarotid amytal procedure (IAT), neuroimaging studies, and electrophysiologic evaluation [5-7].

When test results are not convergent, the risk of surgical failure is higher, yet the weight that should be given to divergent test results in the decision for or against surgery is unclear (8). Clinicians probably are influenced as much by their own past experience as by published empirical data.

The intensive evaluation of patients for surgical therapy can be expensive. This upfront cost is justified when the medical and financial cost of intractable epilepsy is examined over the lifetime of the patient [9,l0]. Refinements in epilepsy surgery have made it possible for certain groups of patients to undergo less invasive and less expensive evaluation [11]. However, external financial pressures will be felt at all institutions, and the challenge will be to use expensive technologies effectively without compromising patient care. Outcomes will have to be measured. Justification of all procedures will have to be based on empirical data.

Artificial neural networks (ANNs) are computer models composed of parallel, nonlinear computational elements ("neurons") arranged in highly interconnected layers with a structure that mimics biologic neural networks. The ANN can be trained with data from cases that have a known outcome. The network can evaluate the input data, recognize any pattern that may be present, and apply this knowledge to the evaluation of unknown cases. In the analysis of data sets, ANNs have the advantage of relative insensitivity to noise while having the ability to discover patterns that may not be apparent to human observers. Recently, there has been widespread interest in using ANNs for an extraordinary range of problem domains, in areas as diverse as finance, physics, engineering, geology, and medicine. In areas where there are

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problems of classification, prediction, or control, ANNs are being introduced [12].

Jim Grisby et al [13] have studied the prediction outcome of anterior temporal epilepsy using simulates neural networks and was found to be significantly superior to discriminant analysis.

In this study, we proposed to develop an ANN with Multilayer perceptron(MLP) model based entirely on preoperative clinical parameters and investigations for predicting postoperative surgical outcomes for patients who are undergoing anterior temporal lobectomy for refractory epilepsy using Engels outcome classification as endpoints and comparing with binary logistic regression(BLR)analysis.

2. Material and Methods

After Institutional ethical and research committee clearance the data sets were recorded for 115 patient who underwent anterior temporal lobectomy for refractory epilepsy. The following data was recorded and transformed into binary data in the following manner.

Age <20 as ‘0’ and ≥20 as ‘1’,female as ‘0’ and male as ‘1’, duration <10 years as ‘0’and ≥ 10 as ‘1’,history of febrile convulsions absent ‘0’ and present as ‘1’,childhood insult absent as ‘0’and present as ‘1’,aura absent as ‘0’and present as ‘1’,types of epilepsy CPS (Complex Partial Seizures) generalized as ‘0’ and CPS as ‘1’,IQ below normal as ‘0’ and above normal as ‘1’, delay in development of child as ‘0’ and normal development as ‘1’.history of status epilepsy development absent as ‘0’ and present as ‘1’,number of antiepileptic drugs<3as ‘0’ and ≥3as ‘1’,present antiepileptic drugs <3as ‘0’ and ≥3 as ‘1’,family history of epilepsy absent as ‘0’ and present as ‘1’,seizure frequency <7 as ‘0’ and >7as ‘1’,psychiatric illness absent as ‘0’ and present as ‘1’,MRI normal as’0’and medial temporal sclerosis as ‘1’, ectal EEG IA as ‘1’ and others as ‘0’. The Engel outcome was measured and Type I taken as ‘1’ and type II, III and VI as ‘0’ on Binary scale..

Table 1: Predictor variables for outcome of epilepsy surgery

S.No	*Variable*	*P value*
1	Age	0.5005
2	Sex	0.2918
3	Duration	0.2154
4	History of febrile convulsions	0.5389
5	Symptomatic Neurological insult	0.3910
6	Aura	0.5948
7	Partial Seizures	0.0331*
8	IQ	0.5198
9	Delay in development of child	0.4105
10	History of status epilepsy	0.2139
11	Past antiepileptic drugs	0.2997
12	Present antiepileptic drugs	0.3979
13	Family history of epilepsy	0.1950
14	Seizure frequency	0.0406*
15	Psychiatric illness	0.6188
16	MRI	0.0001*
17	Ectal EEG	0.8591

* Indicates significant P Value (< 0.05)

Initially all the 17 variables were analyzed and ranking was done by using the Tanagra datamining software [14]with logistic regression forward selection with P value of < 0.05. The 3 variables were selected depending upon their importance and ‘P” value, namely MRI Imaging , Complex partial seizures and seizure frequency score for Engel outcome model .The data sets were classified by multilayer perception (MLP) neural networks and binary regression analysis (BLR)with Tanagra software. The MLP architecture consisted of one hidden layer with 4 neurons in it. The learning rate 0.1000, max iterations 1000, and with error rate threshold was 0.010. These computations were performed on Pentium(R) IV CPU with 3.10 GHz.

Table1: MLP architecture of ANN model

Architecture	*ANN Model*
Neurons in the hidden layer	4
Learning rate	1.00
Max iteration	1000
Error rate threshold	0.0100
Error rate	0.1913

The performance of ANN and BLR were evaluated by calculating the area under the curve (AUC) of ROC curve and the other assessment parameters like sensitivity, and specificity for the both modules

3. Results

The study population included 115 patients with temporal epilepsy. The age range was 7-51 (mean 27·1) years. There were 64 males and 51 females. The age of onset of epilepsy was 1-39 (mean 11·9) years. The duration of epilepsy was 2-36 (mean 15·4) years. Febrile convulsions were noted in 52 (45·2%) patients and 51 (44·3%) had aura before the seizure. The partial seizure with secondary generalization was noted in 48 (41·7%).

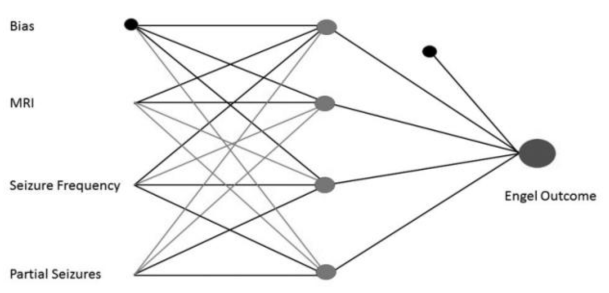

Figure 1: Architecture of Ann with MLP with 4 hidden nodes

The IQ was below 70 in 11 (9·6%) and normal in the rest. Five (4·3%) patients has history suggestive of status epilepticus and 33 (28·7%) had family history of epilepsy. The number of AED failed prior to surgery was 2 to 9 (mean 4·77). At the time of surgery the average number of AED being used was 2·66 (range 2-7). The seizures were infrequent in 20 (17·4%) and very frequent (weekly to daily seizures) in 95 (82·6%). At the time of last follow up 74

(64·3%) were totally seizure free and 42 (36·5%) were totally off the AED.

The 115 datasets were used for training with ANN and also for BLR. The ANN learning characteristics were shown in table 1. BLR model sensitivity 80 %, specificity 85 % and that of ANN Sensitivity 80 % specificity 85 %, however the ROC area under curve for BLR is 0 .703 and ANN is 0.732. (Table.5).The ANN model the ROC area under curve is slightly more compared to BLR model.

Table 4: Comparison of BLR and ANN models

Model	*Area of ROC*	*Sensitivity*	*Specificity*
BLR	0.703	80.20	85.71
ANN	0.732	80.20	85.71

4. Discussion

Predicting outcome is useful in health care financing, as the cost of treatment is increasing day by day. The use of simulated neural networks for predicting outcome of epilepsy surgery for making the cost effectiveness decision in the patient management is quite useful. The logistic regression model is widely used in medical filled ,however the use of datamining methods like ANN given an advantage over BLR, because of development of active learning process inculcated in datamining techniques. In this present study both the outcome classifications were studied.

In our study, we constructed an ANN models that estimated the outcome end points after epilepsy surgery. A neural computational models have the potential to meet several important roles, such as assisting clinical decision making, facilitating more accurate comparisons of outcomes across groups, and evaluating trends in surgical practices over time.

A neural network approach is also preferable in that ANNs are model independent and very flexible .ANNs have the added advantage that they can learn to predict arbitrarily complex nonlinear relationships between independent and dependent variables by including more processing elements in the hidden layer or more hidden layers in the network. These advantages make the ANN a more robust paradigm for application to a real world setting.

In a previous study by Jim Grigsby et al [12], it is found that the ANN accuracy in predicting epilepsy surgery outcome is significantly high compared to discriminant function analysis.

In the present study the Engel outcome model developed by BLR and ANN (MLP). The sensitivity, specificity and accuracy for predicting the outcome of anterior temporal lobectomy for both the BLR and ANN module are similar.

The area under the ROC curve (AUC) is a measure of a model's discriminatory power. According to the observation by Swets et al [15] , an AUC of ≧ 0.7 is diagnostically useful. The AUC of ROC BLR model is 0.703 and for ANN model the AUC is 0.732 respectively. Thus the area under cover of ROC higher in ANN model compared to BLR model.

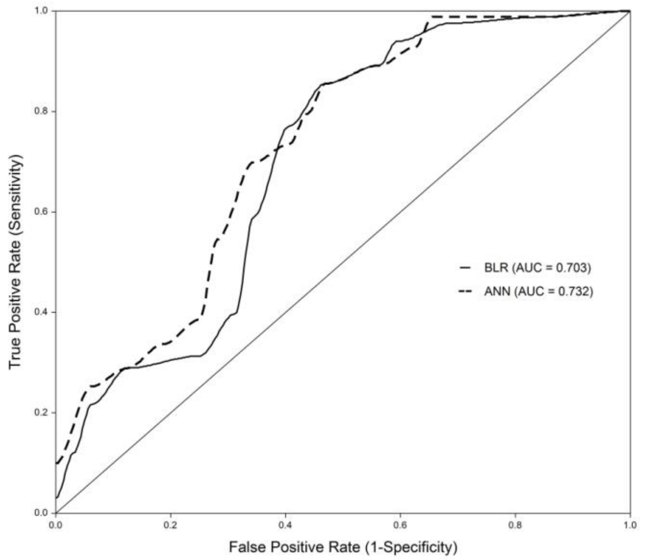

Figure 2: ROC curves for both BLR and ANN models

The present study was performed in the dataset recorded retrospectively and the ANN model has important role to play in medical field for prediction analysis.

5. Conclusion

Both the BLR and ANN models are good for predicting the outcome of epilepsy surgery. However in the area under the curve of ROC of ANN model is slightly more compared to BLR model and has definite role in predicting outcome in medical field.

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