Machine Learning Prediction of Seizure Outcome with Presurgical Resting-State fMRI Data

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Rationale:

Developing a quantitative algorithm for predicting seizure outcome following anterior temporal lobectomy (ATL) in temporal lobe epilepsy (TLE) patients would constitute a significant advance for presurgical decision making. In this project, we tested the ability of topographic properties extracted from presurgical resting-state fMRI (rsfMRI) data to predict surgical outcome, using two separate machine learning classification methods (support vector machine, SVM, and random forest, RF).

Methods:

Subjects: **Fifty-six unilateral TLE patients** (L/R=26/30) underwent five minutes of rsfMRI.

Table 1: Sample demographic and clinical characteristics

Sample Group (N)	Good Outcome TLE (35)	Poor Outcome TLE (21)
Epileptogenic Temporal Lobe (L/R)	18/17	8/13
Age (M±SD)	41.25±12.60	38.58±13.25
Gender (M/F)	21/14	9/12
Handedness (R/L)	30/5	14/7
Age at Epilepsy Onset (M±SD)	23.73±12.60	21.55±10.87
Duration of Epilepsy (M±SD)	17.52±14.53	17.03±11.21
Seizure Focality (With/Without GS or 2nd GS)	15/20	10/11
Interictal Spike (Ipsilateral/Bilateral)	29/6	15/6
Temporal Pathology (NB/MTS/Other)	14/15/6	13/5/3

Abbreviations & Definitions: TLE, temporal lobe epilepsy; NB, normal brain; MTS, mesial temporal sclerosis; Other, other temporal pathologies (heterotopia, dysplasia, tumor, etc.)

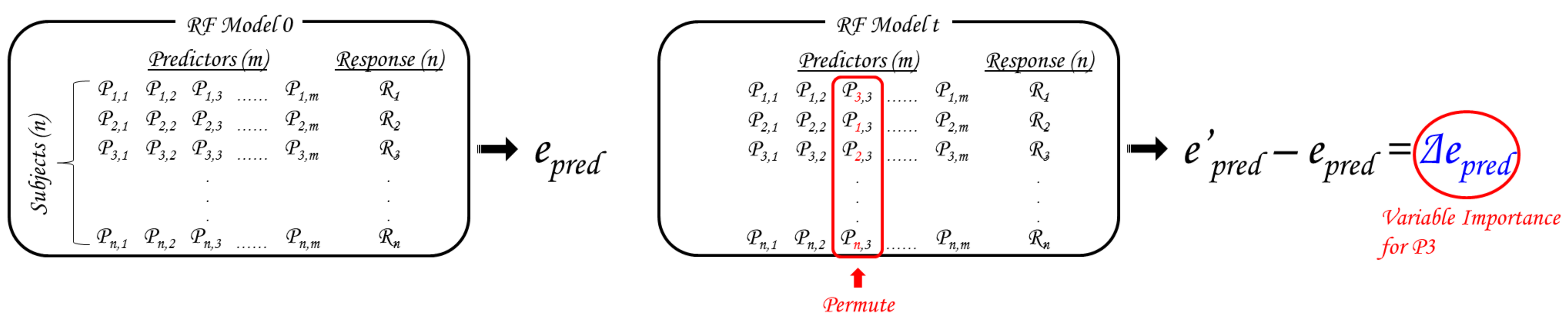
Data Preprocessing: Data was preprocessed using a standard pipeline in SPM12. Regional parcellation was carried out using AAL template (45 cortical regions per hemisphere). The maximal overlap discrete wavelet transform was used to extract information in the frequency interval approximately 0.05-0.1 Hz (scale 2). Then we used a minimal spine tree method to build individual binary undirected graphs in the range 5-50%.

Predictors: The following topological parameters were estimated: global efficiency (Eglob), global clustering coefficient (CCglob), degree centrality (DC), betweenness centrality (BC), and eigenvector centrality (EC). All the topological parameters were averaged over all the densities. This produced 272 variables [(2 (Eglobal, CCglob) + 3 (DC, BC, EC))×90 nodes]. In addition, 9 demographic and clinical variables (Table 1) were also utilized, yielding a total of 281 variables.

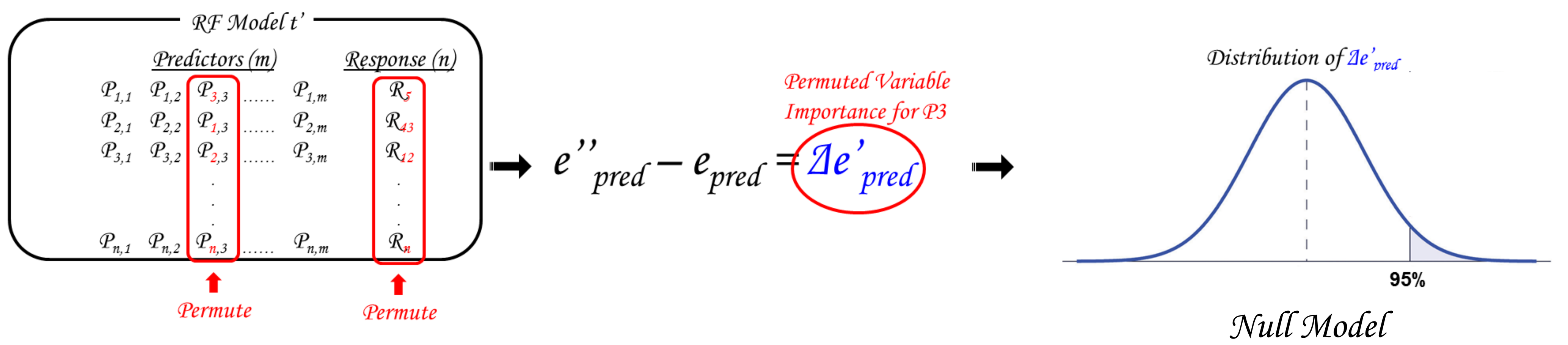
Responses: Patients were classified as good outcome (**GO**: 35, Class I) and poor outcome (**PO**: 21, Class II~IV) (Engel et al., 1993) at 1 year post-surgery.

Predictor Selection: In order to identify the best predictors, we utilize a permutation method using the variable importance feature of the RF.

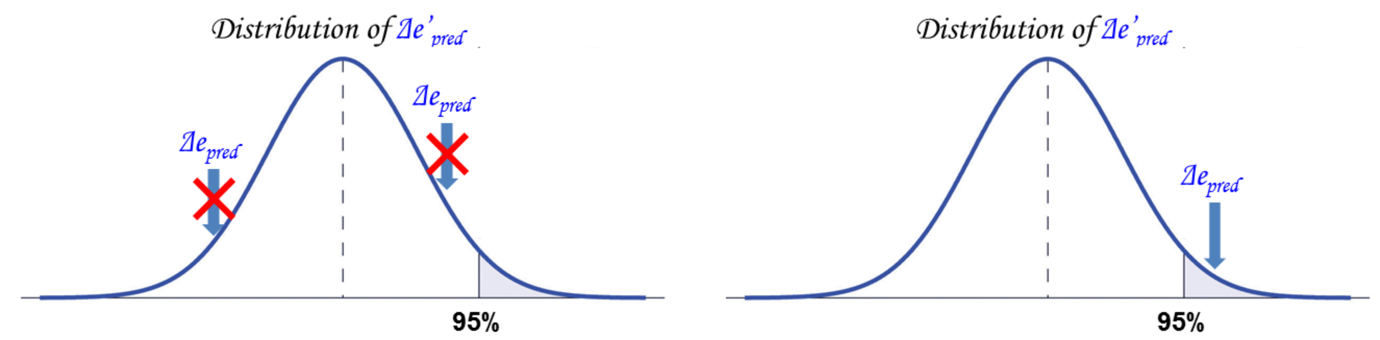
Step 1 Estimate Variable Importance for each predictor, using RF.



Step 2 Estimate Permuted Variable Importance using RF, by 1000 times, to build Null Model of Variable Importance, for each predictor.



Step 3 Predictors with Variable Importance higher than 95% of corresponding Permuted Variable Importance were considered significant.



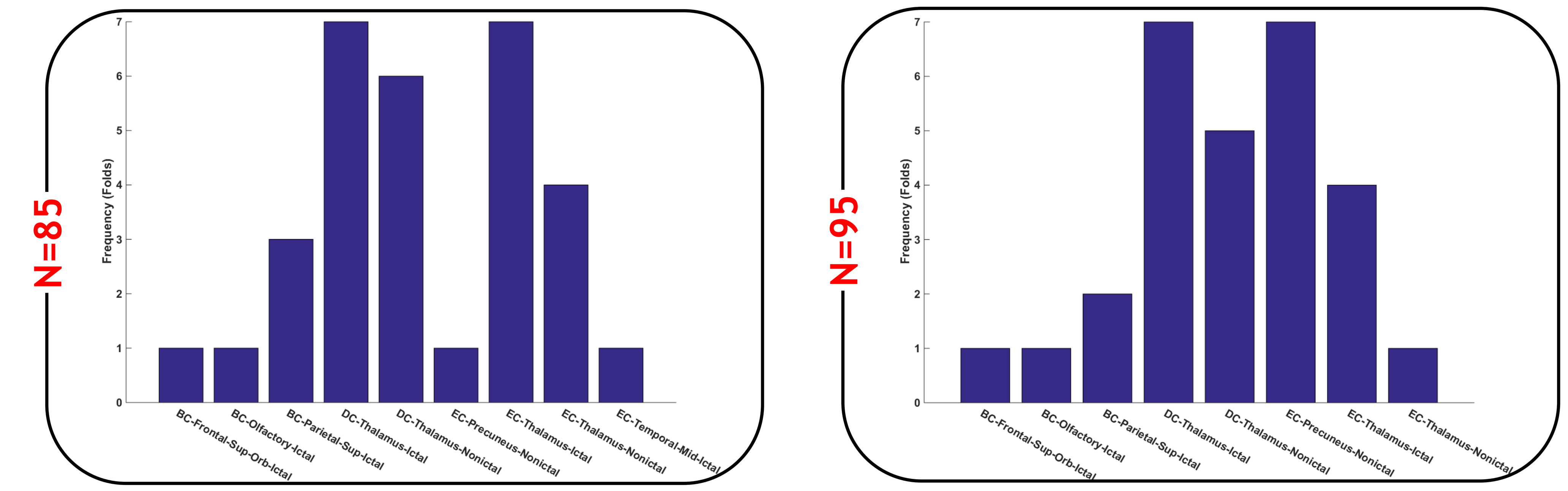
Step 4 **Repeat step 1-3 100 times.** The best predictors were defined as those found significant during step 3 for **over N** times. **We tested N=85 (loose condition, more predictors survived, highly probability of over-fitting) and N=95 (Strict condition, less predictors survived, lower probability of over-fitting).**

Model Building: Linear SVM model and RF model were trained separately with the predictors selected from above procedure.

Validation Scheme: **7-fold.** The Predictor Selection and Model Building procedures were carried out only with training samples (n=48). Prediction accuracies reported were estimated only with independent testing samples (n=8).

Results:

(1) Variables mostly selected as the best predictors:



(2) Prediction Comparison Table:

Models	Accuracy	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Optimal SVM (N=85)	**75%**	**88.57%**	52.38%	75.61%	**73.33%**
Optimal SVM (N=95)	**75%**	**88.57%**	52.38%	75.61%	**73.33%**
Optimal RF (N=85)	69.64%	80%	52.38%	73.68%	61.11%
Optimal RF (N=95)	73.21%	82.86%	**57.14%**	**76.32%**	66.67%
Clinical SVM	51.79%	65.71%	28.57%	60.53%	33.33%
Clinical RF	64.29%	82.86%	33.33%	67.44%	53.85%
Null	62.5%	100%	0%	62.5%	N.A.

Conclusion:

(1) RsfMRI data can be used to predict seizure outcome, outperforming the clinical characteristics commonly used in epilepsy surgical centers.
(2) Variables mostly selected as the best predictors are DC and EC of bilateral thalamus.
(3) In cases there are much more attributes than instances, as in our study and many other neuroimaging studies, RF can serve as a powerful tool in identification of the best predictors for prediction algorithms.
(4) Using selected predictors, linear SVM achieved a more stable performance profile for outcome prediction compared to RF.
(5) Best combination: Predict with SVM, using predictors selected by RF.
(6) Future analyses can focus on fine-tuning the RF parameters such as pruning trees to increase the robustness of RF.

References:

Engel J., et al. (1993) Outcome with respect to epileptic seizures. Raven, New York. P. 609-621.