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Computer-Aided Diagnosis of Epilepsy using Clinical Information

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Our Goal: estimate the probability of Epilepsy (EP) versus Non-Epileptic Seizures (NES) based on the historical factors reported to the neurologist

Important Questions

1. How much does each historical event inform our final diagnosis?
2. How do we combine multiple findings into one diagnosis?
3. Both epilepsy and non-epileptic seizures have numerous heterogeneous causes, how can we harness this heterogeneity to diagnose better?

Definition of Epilepsy (EP) and Non-Epileptic Seizures (NES)

Epilepsy (EP): An enduring predisposition to generate epileptic seizures. Epileptic seizures are "transient signs and/or symptoms due to abnormal excessive or synchronous neural activity." (Fisher *et al.* 2005, *Epilepsia)*

Non-Epileptic Seizures (NES): Temporary behavioral events similar to seizures but are *not* caused by epileptic neural activity.

Challenge of Diagnosing Epilepsy versus Non-Epileptic Seizures

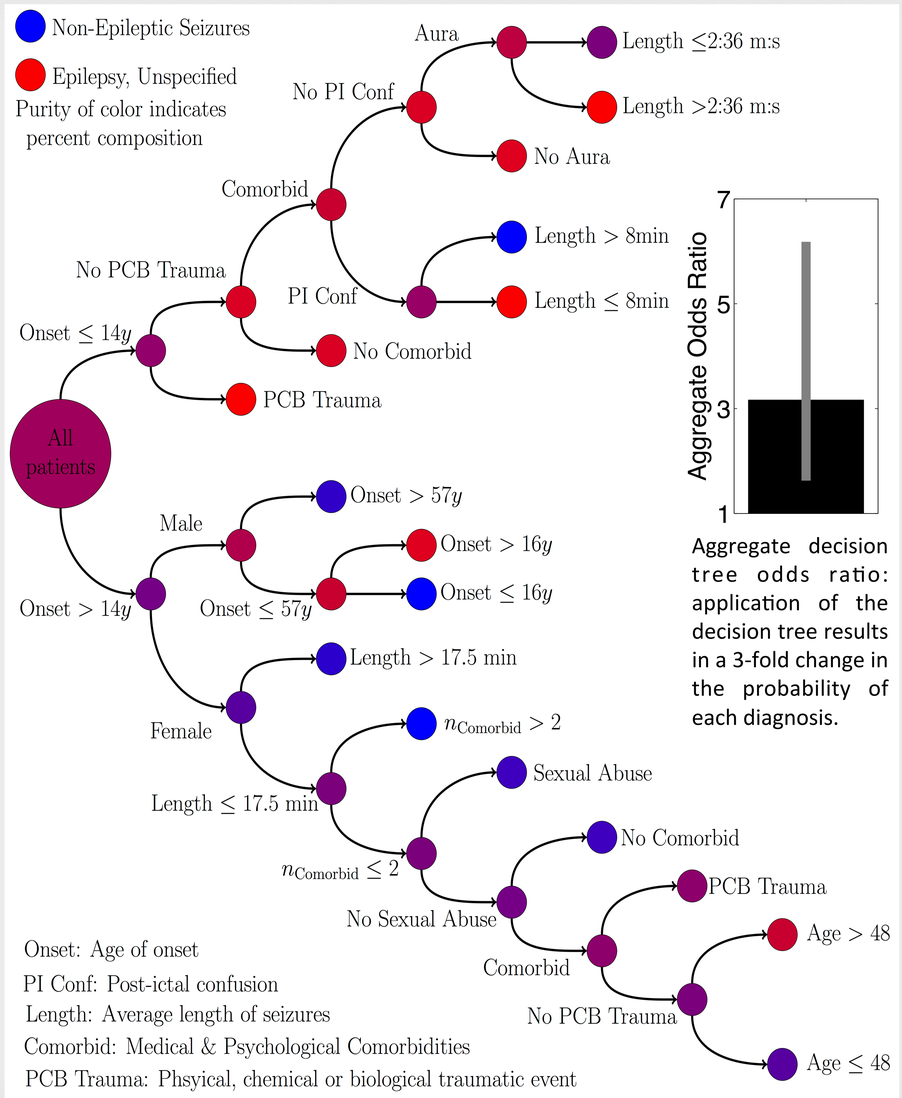
30% of patients with anti-epileptic medication resistant seizures *do not* have epilepsy (Kerr *et al.* 2012, *Epilepsia)*

Clinicial interview relies on witness and patient report. Witnesses are sometimes no more accurate than random guessing (Syed *et al.* 2011 *Ann Neurol*)

Scalp Electroencephalography (EEG): Requires the observation of rare epileptiform discharges or seizures during a 20+ minute recording. Sensitivity: 50%, False Positive Rate unclear (Gilbert *et al.* 2003*, Neurology)*

Neuroimaging: Only 25% of patients have an interpretable finding at seizure onset, whereas 75% of focal epilepsy patients eventually exhibit structure and/or metabolic changes.

How to we Combine Multiple Findings?



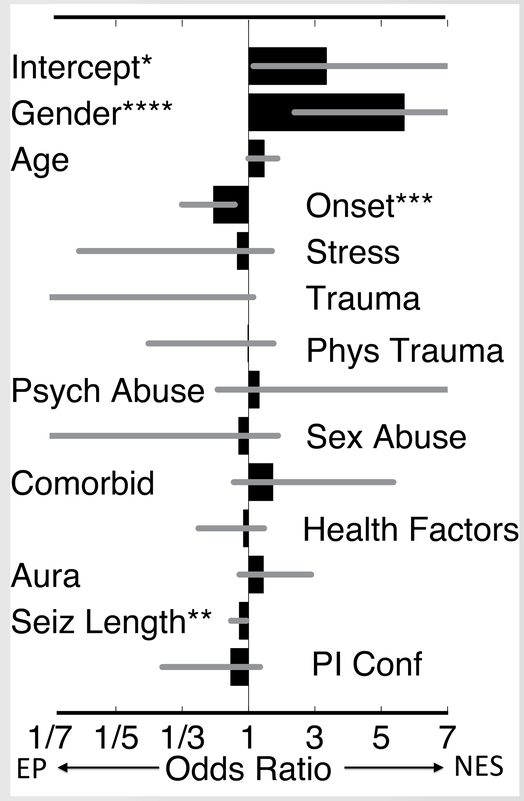
C4.5 tree optimizing the leaf purity after each decision note using all of the data. This reflects a decision algorithm for all patients.

Patient Selection & Quantitative Methods

All 228 patients were admitted to the UCLA video-EEG epilepsy monitoring unit for definitive diagnosis between 2006 and 2013. After this admission, 188 could be definitively diagnosed with either epilepsy (n=121) or non-epileptic seizures (n=67). Historical data (see above and right) was extracted through manual reading of the first outpatient neurology note at UCLA. Not all findings were discussed for all patients. Findings not discussed were considered missing completely at random and were multiply imputed using a multivariate Bayesian logistic regression model on all data (n=228). All priors were unbiased. All intervals are 95% credible intervals.

What is the Effect of Each Factor?

	EP	NES
Means	n=121	n=67
Gender****	53%F	82%F
Age	35YO	40YO
Onset***	16YO	30YO
Stress	18%	22%
Trauma	1%	4%
Phys Trauma	24%	24%
Psych Abuse	2%	3%
Sex Abuse	2%	4%
Comorbid	43%	63%
Health Factors	1.2	1.7
Aura	30%	27%
Seiz Length**	6min	25min
PI Conf	31%	33%



Multivariate Logistic Regression quantifying the odds ratio of each factor, controlling for all others. Larger odds indicate NES. Error bars indicate 95% confidence intervals of odds ratios. Significance: p<0.05*,<0.01**,<0.001***,<0.0001****

Discussion & Future Directions

1. No individual finding is diagnostic for ES or NES. Instead, a complex non-linear combination of findings results in a more full description of the patient.
2. Onset of seizures prior to puberty splits the population into two distinct subgroups.
3. The risk factors for NES differ between men and women, potentially because men and women respond to stressful stimuli differently.
4. Our accuracy (65%), while comparable to physicians, is not clinically useful. This accuracy could be improved by incorporating more factors, imaging and EEG.