Machine Learning EEG Biomarkers in SYNGAP1 Rodent Models

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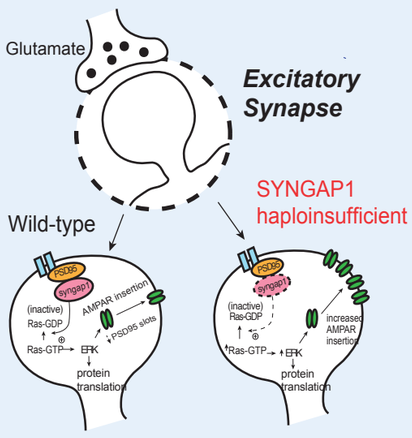
SIDB Simons Initiative for the Developing Brain

Linkedin

SYNGAP1

SYNGAP1 regulates excitatory synapse structure and function

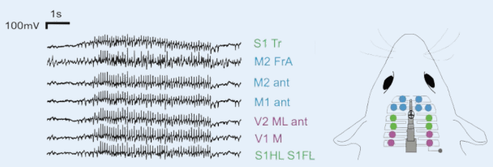


Syngap1-related disorder (SRD) is a rare disease where a mutation in the Syngap1 gene results in severe disruption of neurodevelopment, causing intellectual disability, autism and epilepsy. Most SRD patients are non-verbal and requiring lifelong care.
There are currently no interventions to treat these symptoms effectively.

EEG

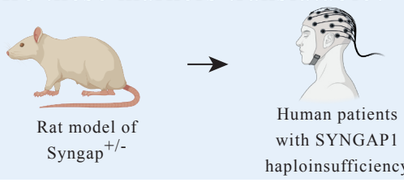
Multiple gene modification strategies are in development, but clinical trials require quantitative biomarkers to objectively measure effectiveness of intervention. Currently, no validated biomarkers exist for SRD. EEGs have great potential as biomarkers. ML technique offers a principled way to simultaneously analyse large numbers of EEG features.

1. Is it possible to identify synapse dysfunction caused by SYNGAP1 haploinsufficiency in EEG signals?



EEG recordings from a Rat model of Syngap$^{+/-}$

2. Are these markers translatable?

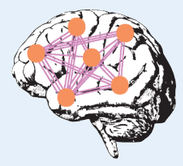


FEATURE EXTRACTION

Extracted features from 5-second non-seizure epochs

Connectivity Abnormalities

- Cross Correlation
- Phase Locking Value

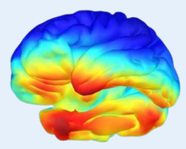


Complexity Abnormalities

- Dispersion Entropy
- Higuchi's Fractal Dimension

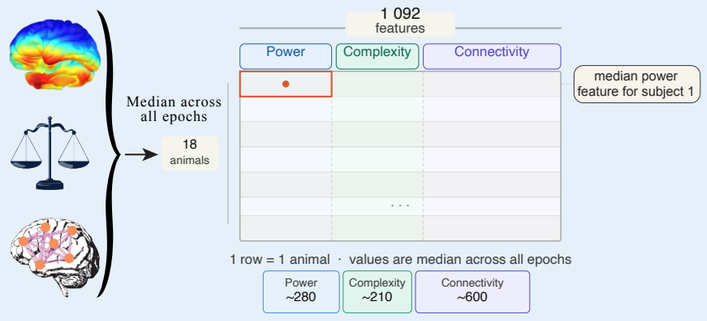
Power Spectra

- Average Band Power
- Spectral Slope and Intercept
- Band Power Ratios



MACHINE LEARNING

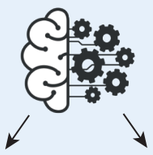
Input features into classifier



Feature Selection with **BorutaSHAP**

Baysian Hyperparameter Tunning

Model training
LOOCV (N=18)



Syngap$^{+/-}$ Wild-type

Predictin and Evaluation (Permutation Test)

AIMS

1. Can a machine learning classifier distinguish SYNGAP1 haploinsufficient rats from wild-type controls using interictal EEG features?

2. Which feature domains contribute most to the classification?

3. Does the classifier generalise across individual animals, and is the performance above chance as assessed by permutation testing?

MAIN FINDINGS

- Spectral power ratios are the strongest discriminators. SYNGAP1 animals show reduced alpha/delta ratio, and elevated beta/theta ratio compared to wild-type.
- Motor and Somatosensory cortex channel features were ranked most important.
- Genotype classification is statistically robust: permutation testing confirms above-chance performance in XGBoost classifier.

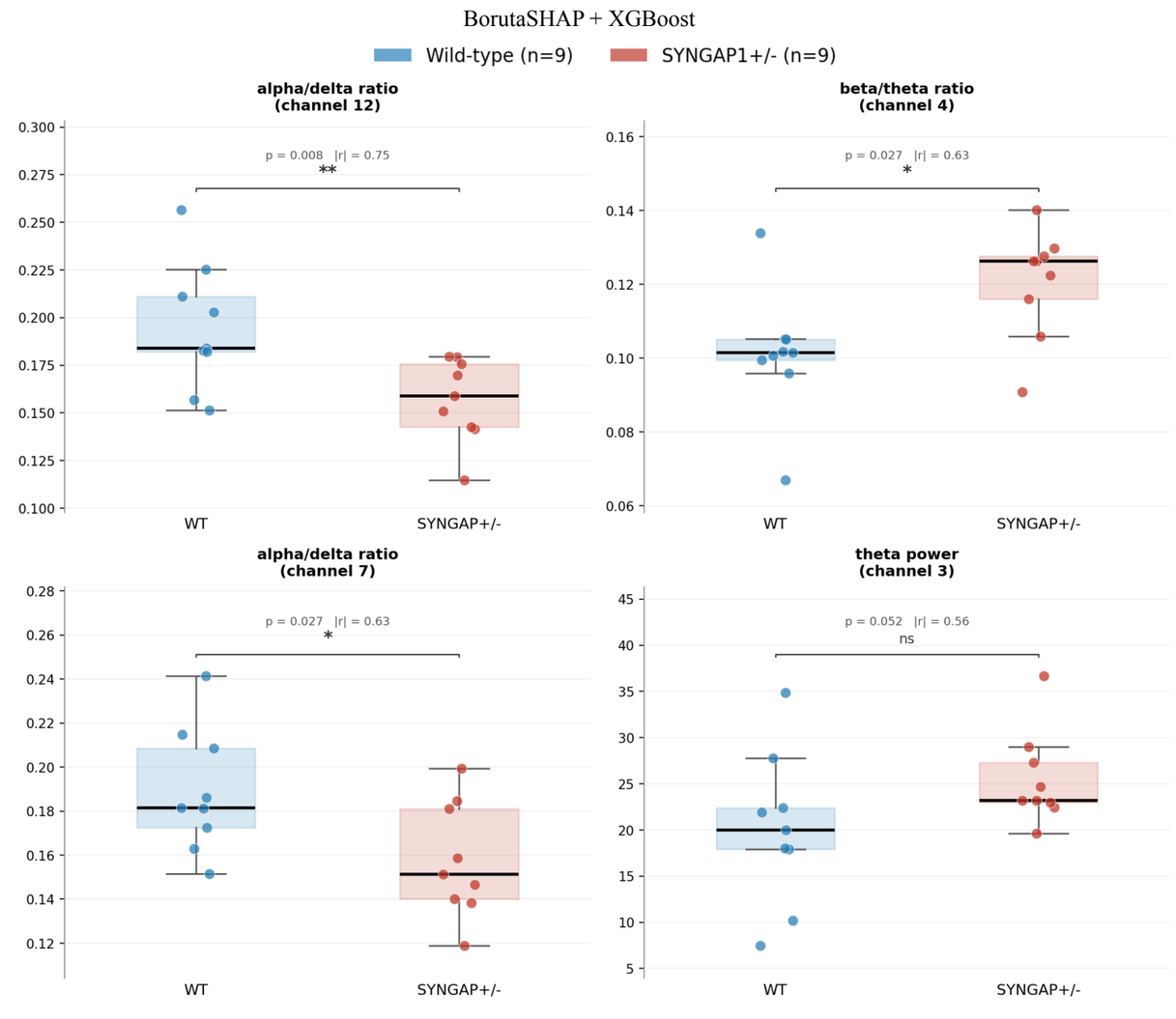
RESULTS:

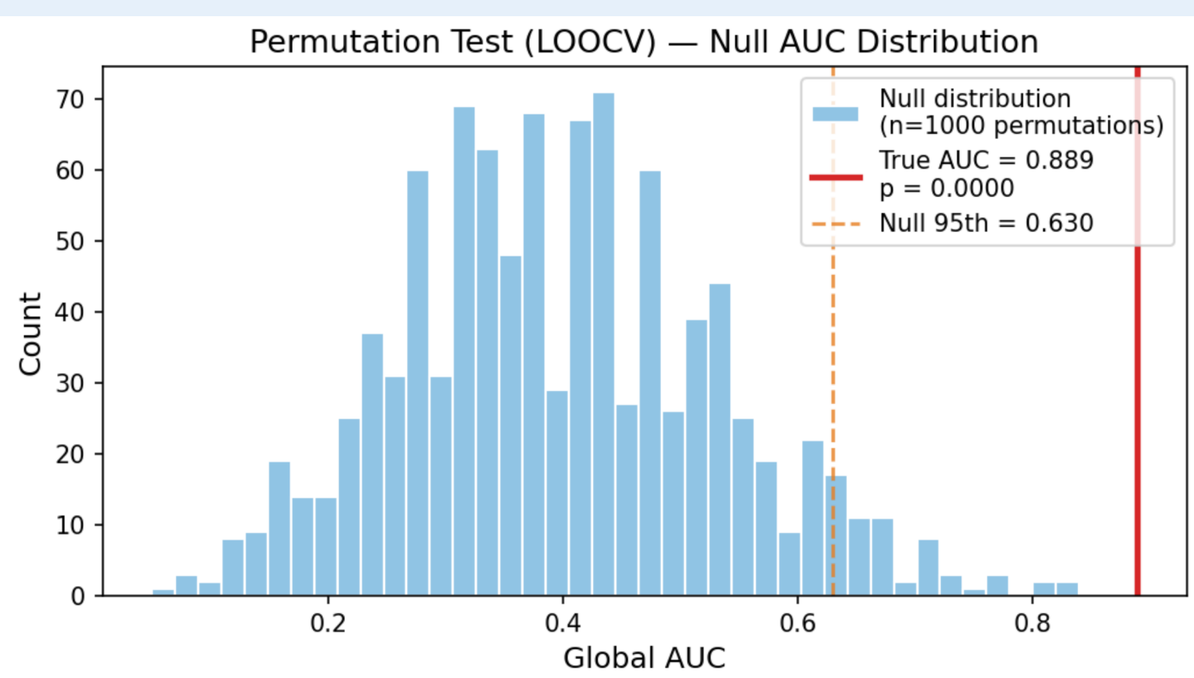
Table 1 — Classification performance (global)

LOOCV results for all model configurations, N = 18 animals (9 SYNGAP1, 9 wild-type) 1000 label permutations per model:

Model	AUC	95% CI	Accuracy	F1	Perm.p
XGBoost BorutaSHAP	0.889	[0.68 - 1.00]	72.2%	0.737	<0.0001
CatBoost BorutaSHAP	0.432	[0.15 - 0.76]	55.6%	0.636	0.425

Mann-Whitney U test: stable features selected in ≥3/18 LOOCV folds





Future Work:

- Translate to human SRD patients: Apply the pipeline to human SYNGAP1 EEG recordings to validate biomarker translatability

- Sleep-stage stratified analysis: Investigate whether classification performance varies across wake, NREM and REM

Acknowledgement and References:

UK Research and Innovation

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D. Katsanevaki et al., "Key roles of C2/GAP domains in SYNGAP1-related pathophysiology," Cell Reports