Localising the Seizure Onset Zone from SPES Responses Using Deep Learning

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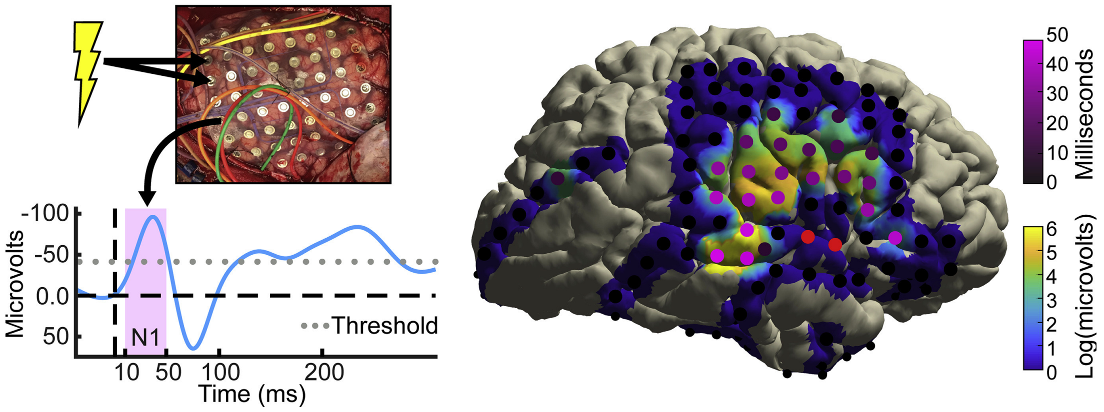
Outline

- Single-pulse electrical stimulation (SPES)
- Existing deep learning approach for SOZ localisation
- Implementation on open-source dataset
- Modifications to existing method
- Analysis of final model

Single pulse electrical stimulation (SPES)

- Investigational tool in epilepsy surgery *(Valentin et al., 2005)*
- Electrical stimulus applied through adjacent electrode pairs
- Frequency: typically, between 0.2 – 1 Hz
- Primarily used to 1) probe seizure networks and 2) probe epileptogenicity

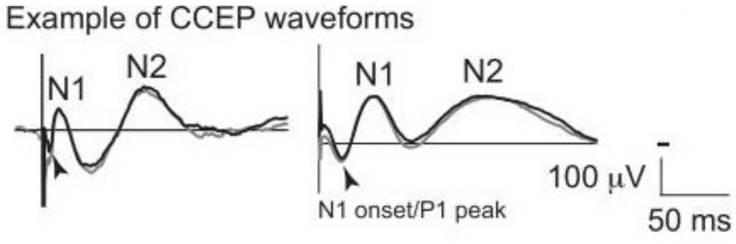


Dynamic tractography: Integrating cortico-cortical evoked potentials and diffusion imaging. Silverstein et al. (2020)

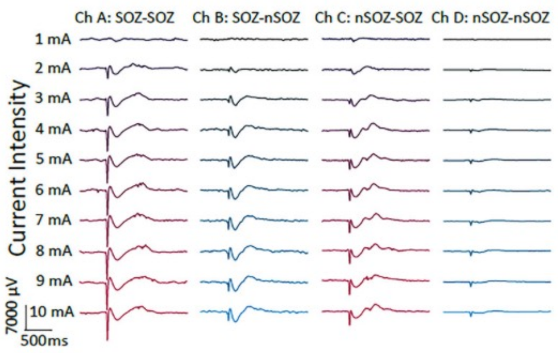
Early Responses to SPES: Cortico-Cortical Evoked Potentials (CCEPs)

CCEPs for probing seizure networks

- Emerge within 100ms post-stimulation
- Reflective of effective connectivity
- Consistent across trials: averaged to increase SNR



Single pulse electrical stimulation to probe functional and pathological connectivity in epilepsy. Matsumoto et al. (2018)

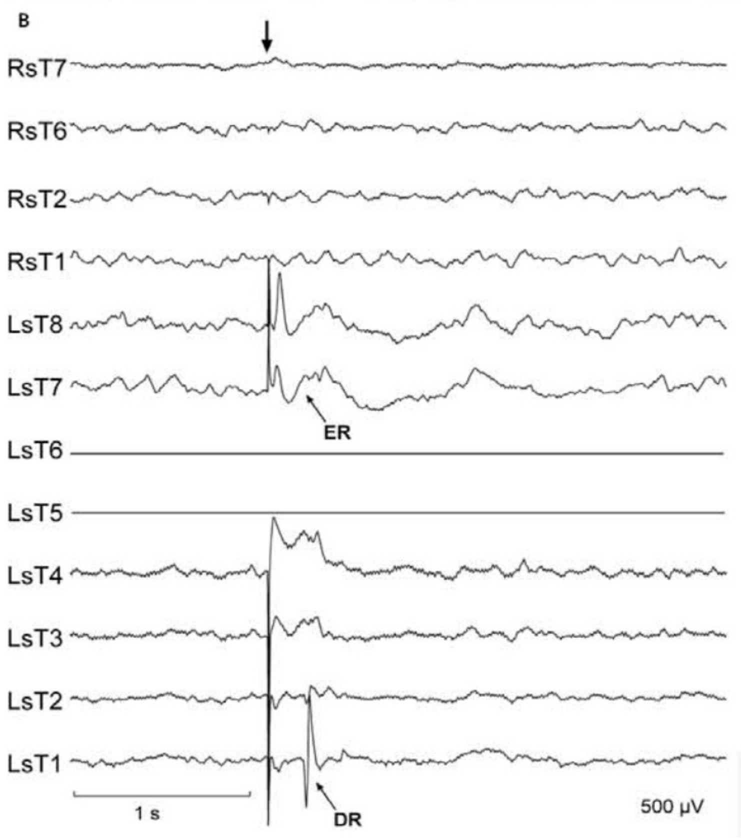


Stimulation to probe, excite, and inhibit the epileptic brain. Frauscher et al. (2023)

CCEPs and epileptogenicity

- Presence not indicative of epileptogenicity
- Some differences in epileptogenic sites: e.g., N1 amplitude is generally larger

Delayed responses to SPES



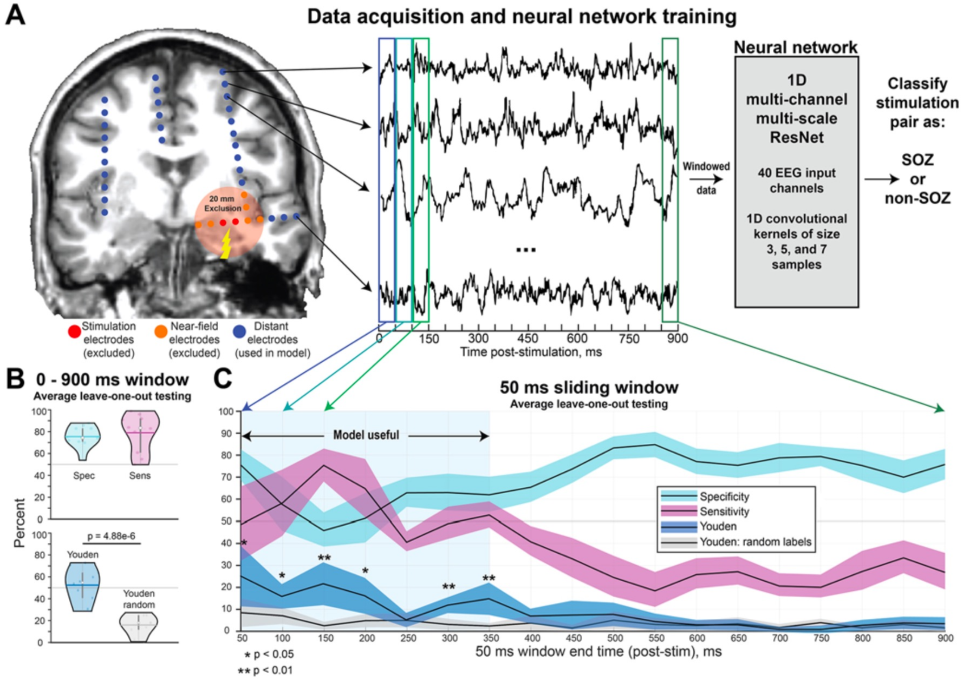
Single pulse electrical stimulation for identification of structural abnormalities and prediction of seizure outcome after epilepsy surgery: a prospective study. Valentin et al. (2005)

- Typically occur 100ms – 1s post-stimulation
- Occur in a subset of trials (not time-locked)
- Resemble interictal epileptiform discharges (IEDs)
- Suggestive of increased excitability and potential epileptogenicity ⇒ usually within SOZ
- Complementary to other methods in surgical planning

Existing deep learning approach

Localizing seizure onset zones in surgical epilepsy with neurostimulation deep learning

Graham W. Johnson, BS,[1,7,8] Leon Y. Cai, BS,[1,8] Derek J. Doss, BE,[1,7,8] Jasmine W. Jiang, BE,[7–9] Aarushi S. Negi,[9] Saramati Narasimhan, PhD,[1,7–9] Danika L. Paulo, MD,[9] Hernán F. J. González, MD, PhD,[1,7,8] Shawniqua Williams Roberson, MEng, MD,[1,10] Sarah K. Bick, MD,[9] Catie E. Chang, PhD,[2] Victoria L. Morgan, PhD,[1,7–10] Mark T. Wallace, PhD,[3–6] and Dario J. Englot, MD, PhD[1,2,7–11]



Patient demographics:

- Total Patients: 10 (Ages 23–51)
- Temporal lobe epilepsy

Methodology:

- Electrode Type: SEEG
- Algorithm: Convolutional neural net (CNN)
- Validation: K-fold cross-validation
- Sensitivity: 78.1%
- Specificity: 74.6%

Applying CNN to an open-source dataset

Dataset (1)

Brief Communication

https://doi.org/10.1038/s41593-023-01272-0

Developmental trajectory of transmission speed in the human brain

Received: 17 March 2022

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Dorien van Blooijs[1,2,3,5], Max A. van den Boom[1,4,5], Jaap F. van der Aar[2], Geertjan M. Huiskamp[2], Giulio Castegnaro[2], Matteo Demuru[2], Willemiek J. E. M. Zweiphenning[2], Pieter van Eijsden[2], Kai J. Miller[4], Frans S. S. Leijten[2] & Dora Hermes[1]

- Total Patients: 74
- Patients with SOZ Labels: 35
- Temporal and extratemporal lobe epilepsies
- Electrode Type: ECoG

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iEEG CCEP ECoG dataset across age 4-51

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Dataset description

This dataset consists of 74 patients age 4-51 years old where Cortico-Cortical Evoked Potentials (CCEPs) were measured with Electro-CorticoGraphy (ECoG) during single pulse electrical stimulation. For a detailed description see:

- Developmental trajectory of transmission speed in the human brain. D. van Blooijs[1], M.A. van den Boom[1], J.F. van der Aar, G.J.M. Huiskamp, G. Castegnaro, M. Demuru, W.J.E.M. Zweiphenning, P. van Eijsden, K. J. Miller, F.S.S. Leijten, D. Hermes, Nature Neuroscience, 2023, https://doi.org/10.1038/s41593-023-01272-0
  [1] these authors contributed equally.

This dataset is part of the RESPect (Registry for Epilepsy Surgery Patients) database, a dataset recorded at the University Medical Center of Utrecht, the Netherlands. The study was approved by the Medical Ethical Committee from the UMC Utrecht.

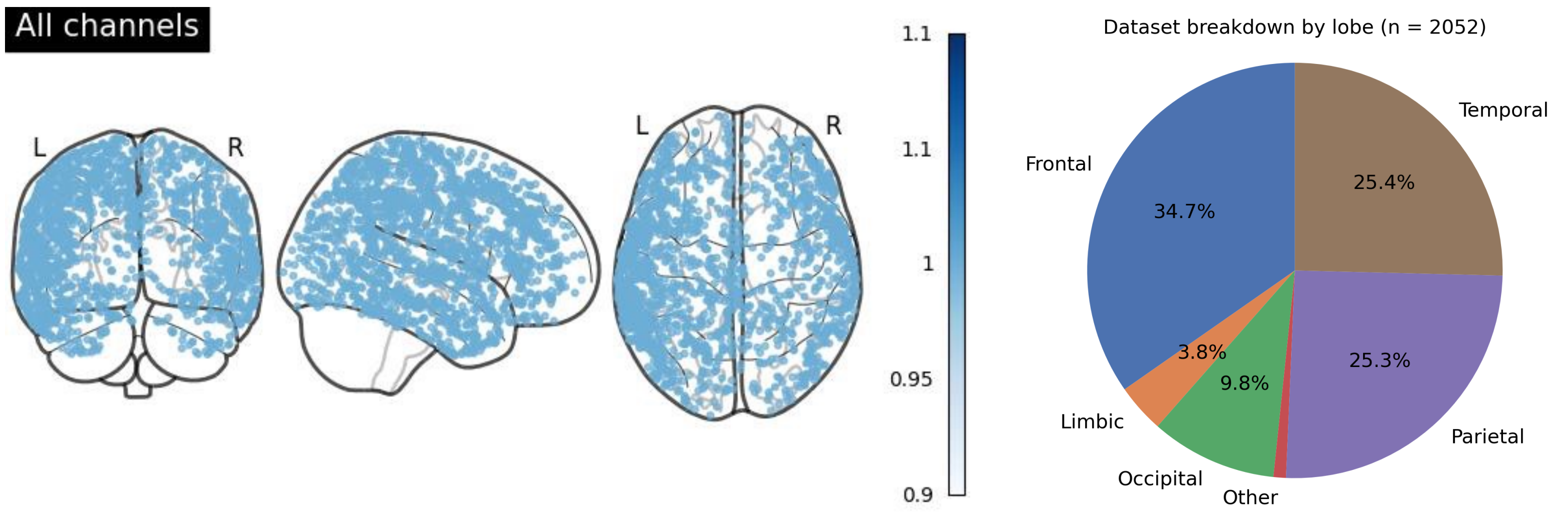
Dataset (2)

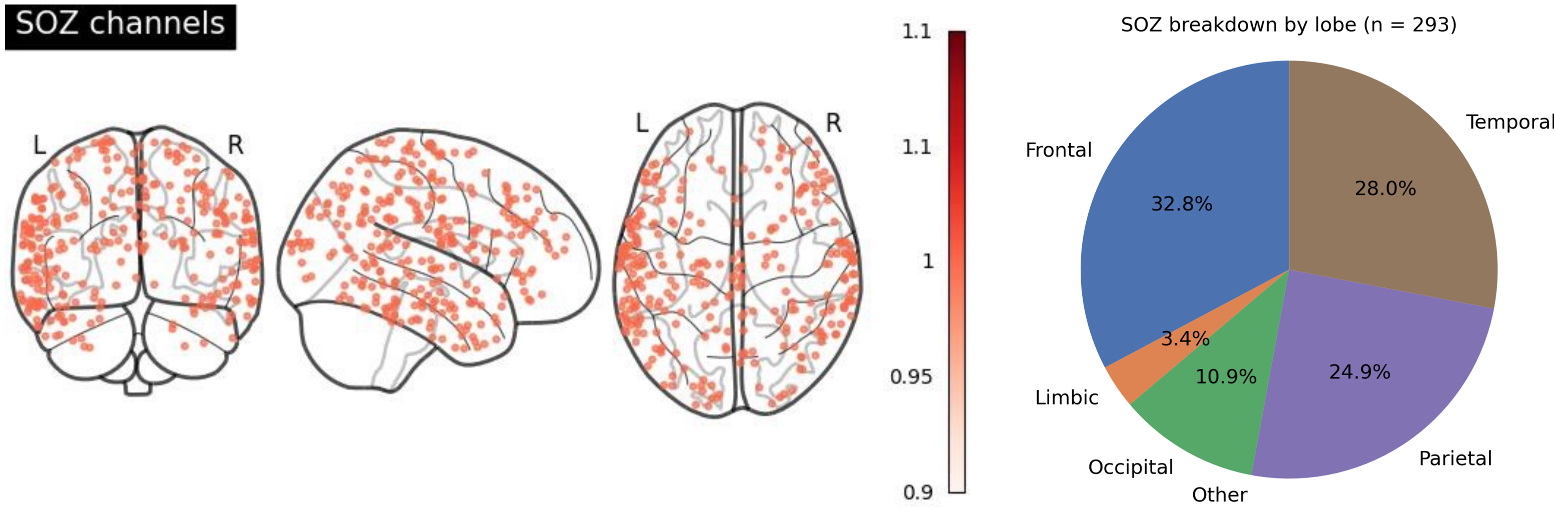
Patient demographics:

- Mean age: 22.1 years
- 53% Male, 47% Female

SPES parameters:

- Intensity: 4 – 8 mA
- Frequency: 0.2 Hz
- Ten monophasic stimuli
- Pulse Width: 1 ms





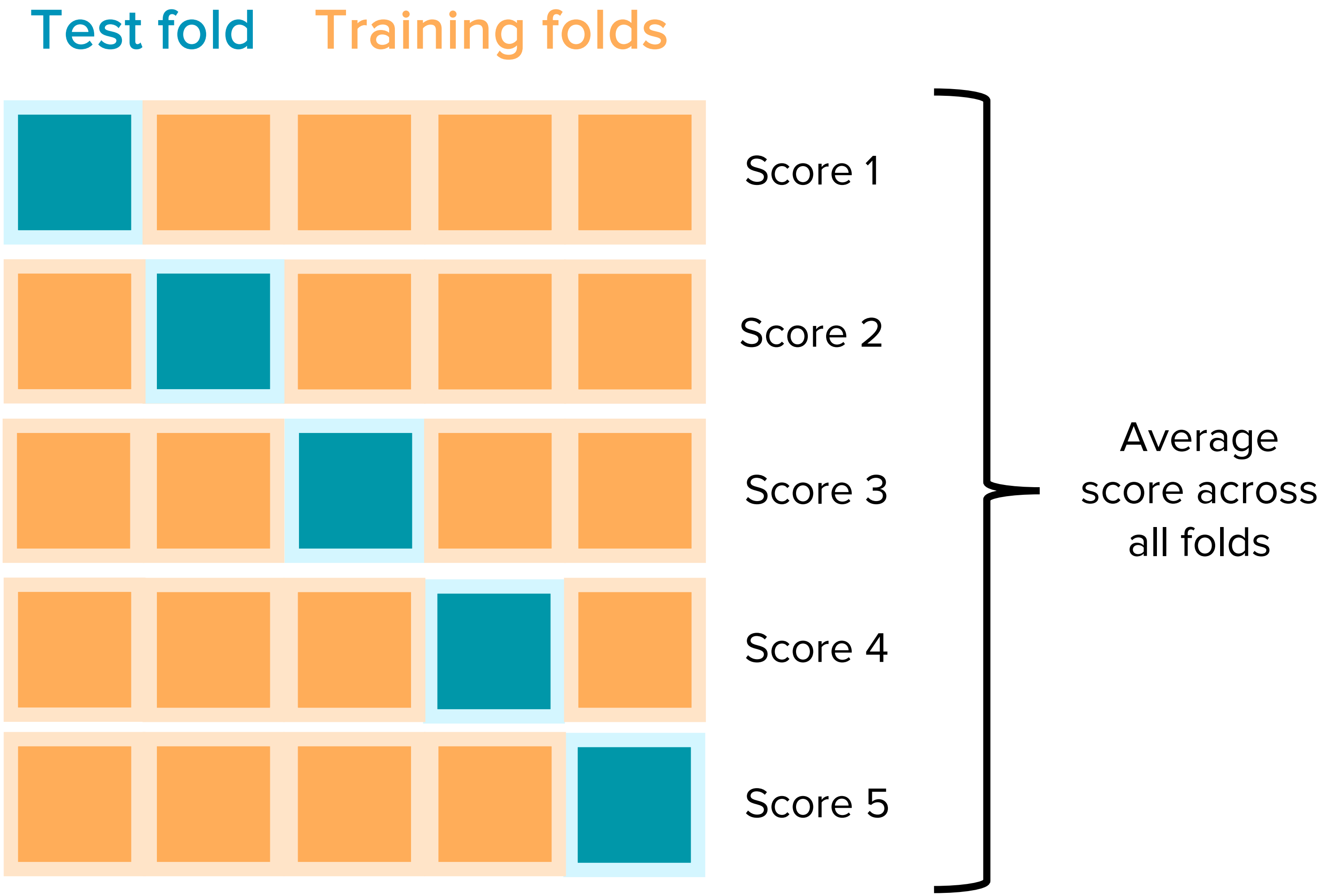
Model training strategy

Training strategy:

- k-fold cross validation (k = 5)
- 28 patient training sets
- 7 patient test sets

Reported metrics:

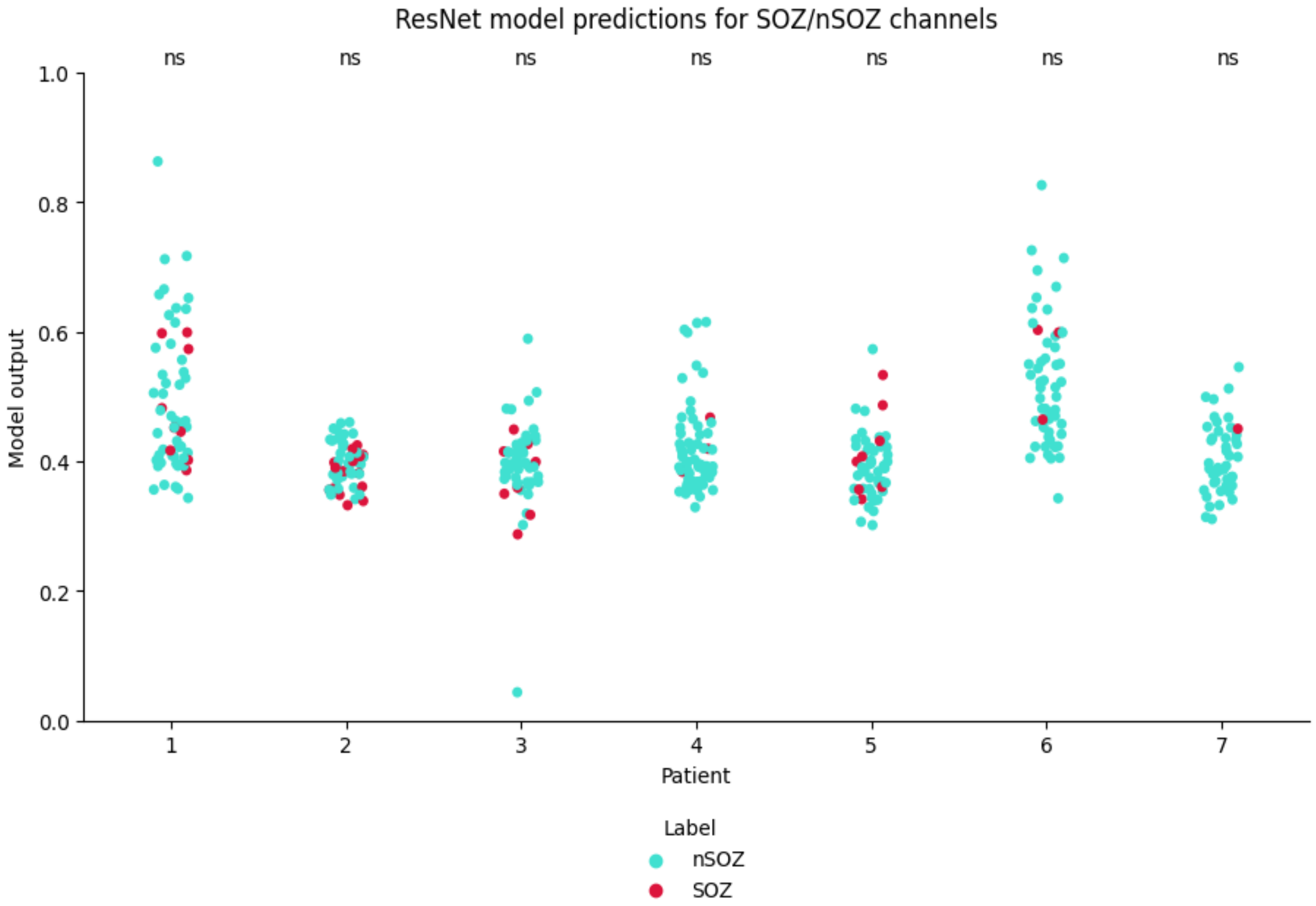
- Area under the precision-recall curve (AUPRC)
- Area under the receiver operating characteristic (AUROC)



Baseline model performance

Model	AUPRC	AUROC
Random	0.14	0.50
CNN	0.17	0.48

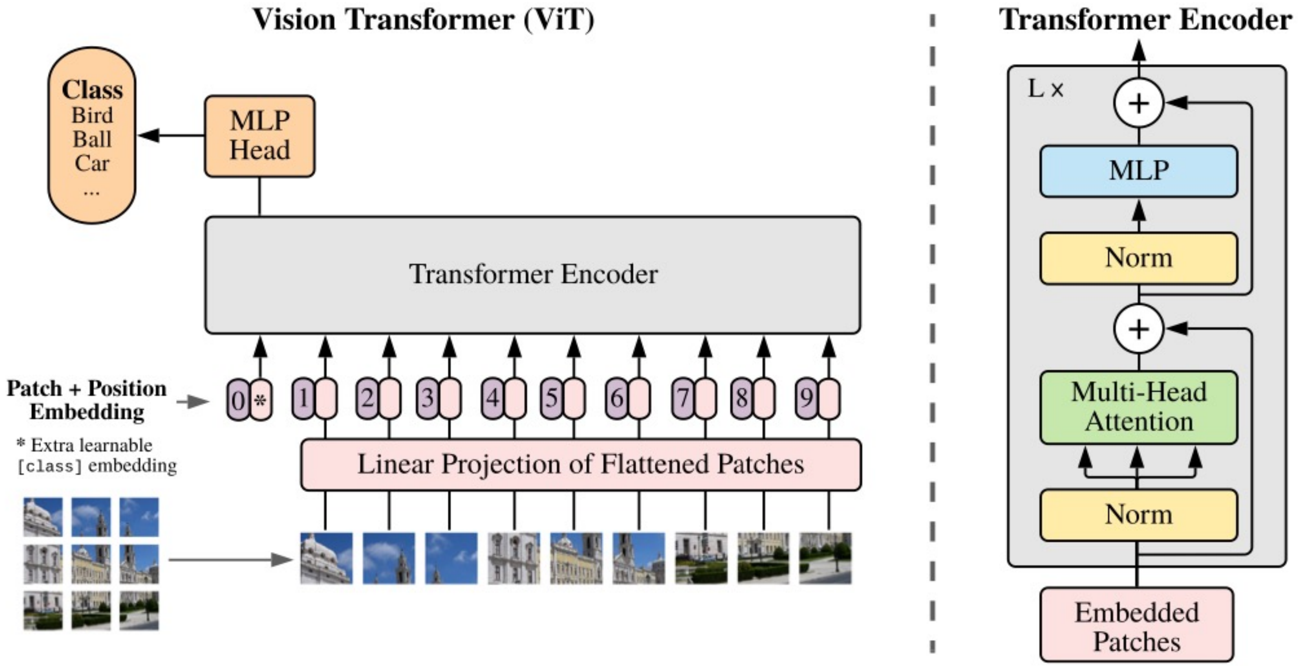
- Poor performance: doesn’t beat random classifier



Modifying methodology to improve performance

Modification 1: Use a Transformer

- CNN limited by fixed channel input; Transformer better suited to patient-specific channel placements (spatial attention).
- Efficiently models cross-channel interactions.
- Global context understanding.
- Common in NLP (e.g., ChatGPT), but we adapt a Vision Transformer

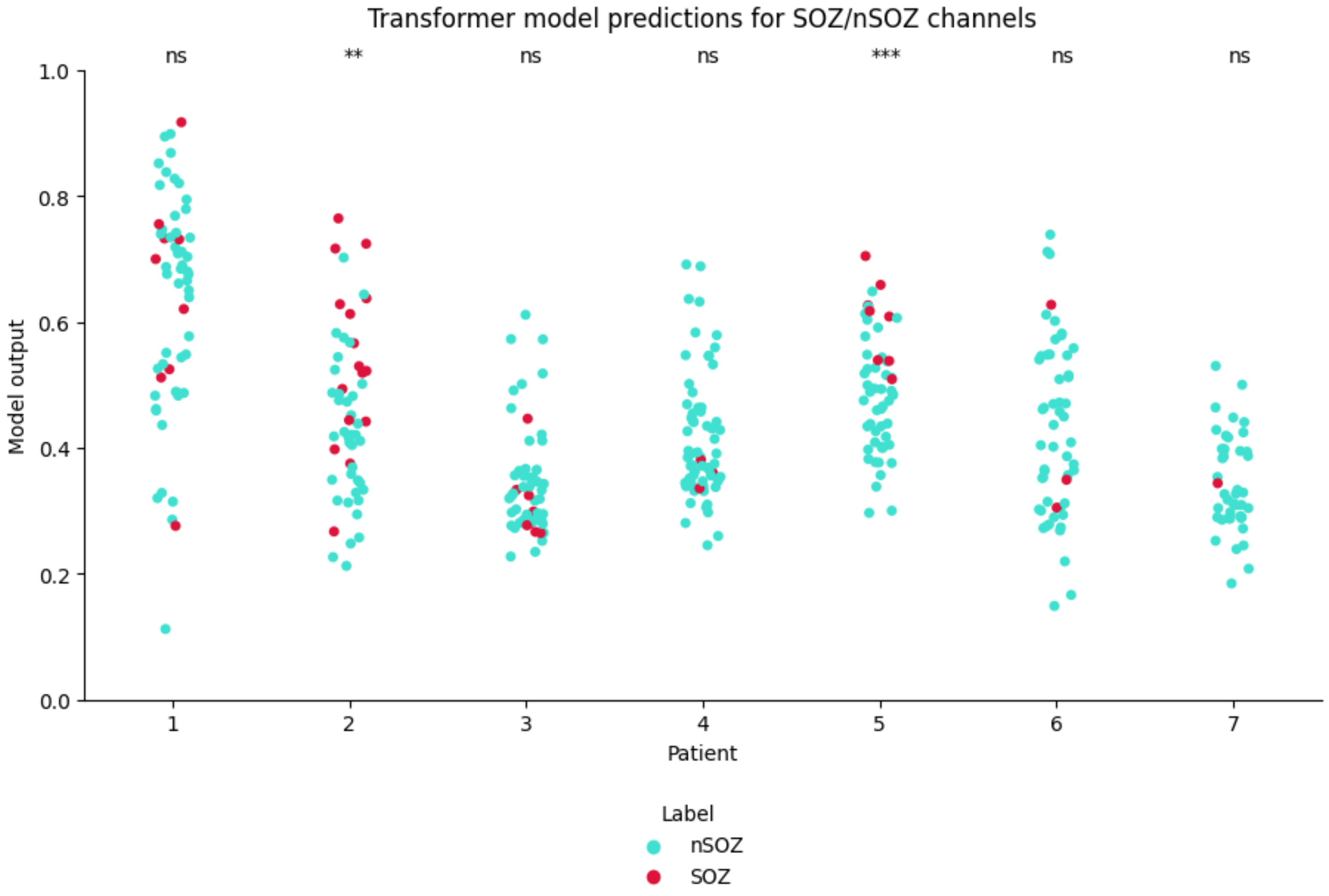


An Image is Worth 16x16 Words: Transformers for Image Recognition at Scale. Dosovitskiy et al. (2020)

Transformer model performance

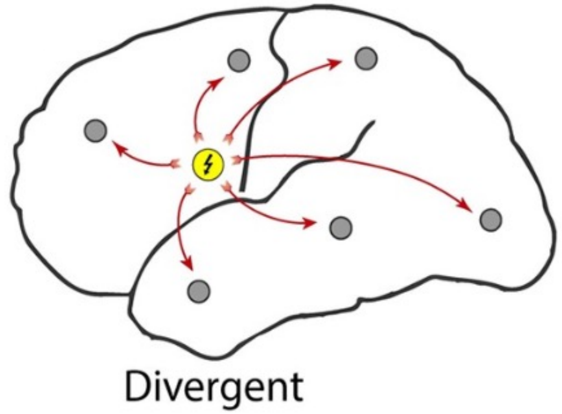
Model	AUPRC	AUROC
Random	0.14	0.50
CNN	0.17	0.48
Transformer	0.22	0.58

- Improvement over CNN, but still poor



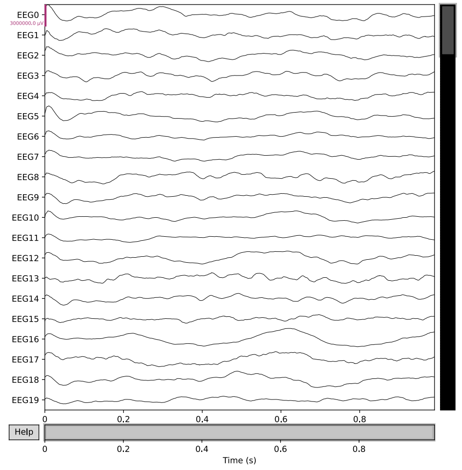
Modification 2: Add convergent paradigm

- Current method uses a divergent paradigm
- Convergent paradigm is better suited to observing the epileptogenicity responses introduced in earlier slides



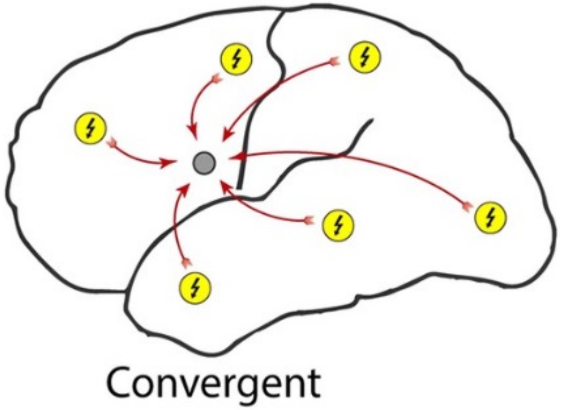
Basis profile curve identification to understand electrical stimulation effects in human brain networks. Miller et al. (2021)

Divergent

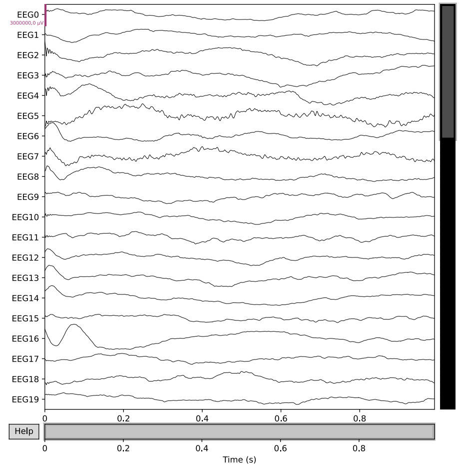


Modification 2:

- For a given site, also consider responses when other sites stimulated



Convergent



Modification 3: Add standard deviation

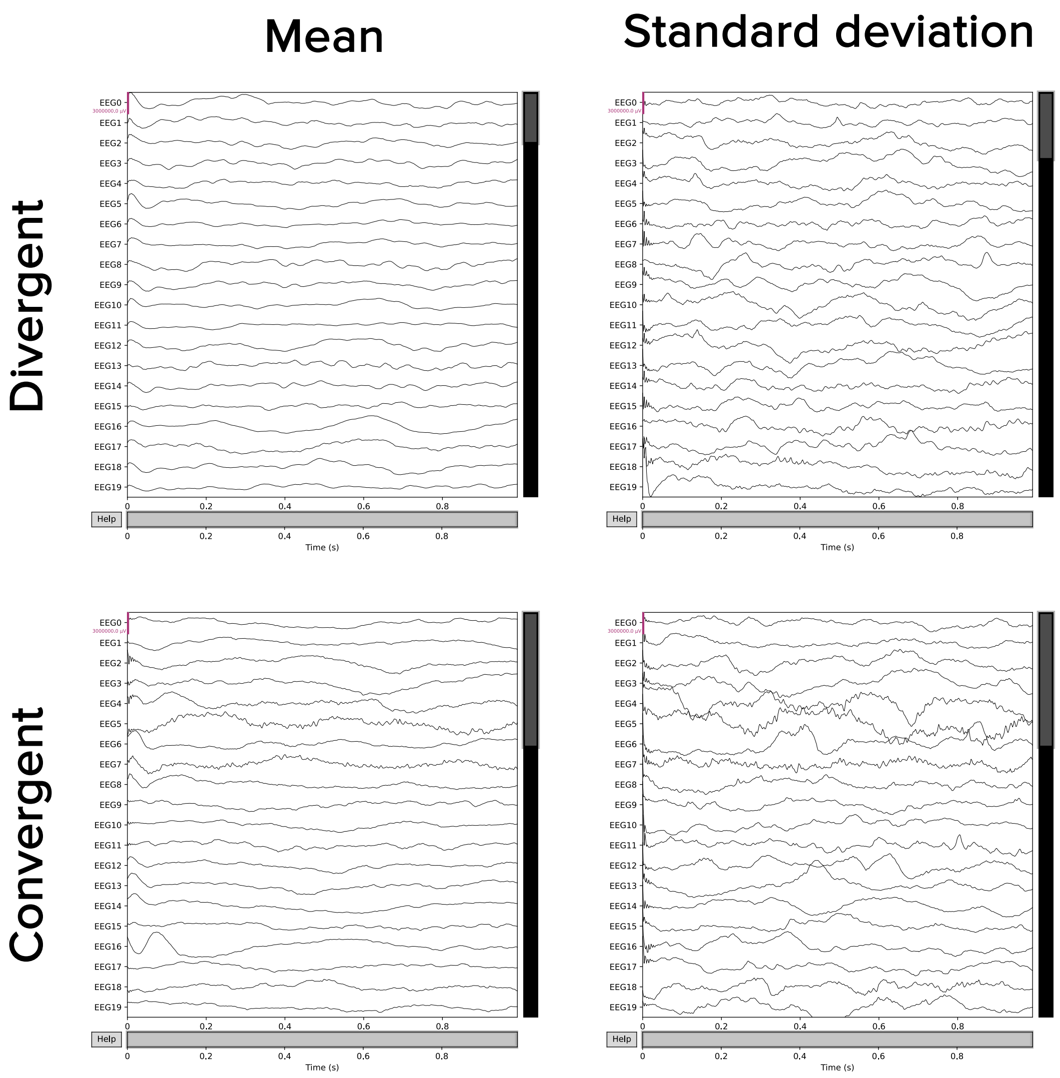
- Averaging responses across trials eliminates delayed responses
- Other information is potentially lost:

Quantifying trial-by-trial variability during cortico-cortical evoked potential mapping of epileptogenic tissue

Eli J. Cornblath[1] | Alfredo Lucas[1,2] | Caren Armstrong[3] | Adam S. Greenblatt[1] | Joel M. Stein[4] | Peter N. Hadar[1] | Ramya Raghupathi[1] | Eric Marsh[1,3,5] | Brian Litt[1] | Kathryn A. Davis[1] | Erin C. Conrad[1]

Modification 3:

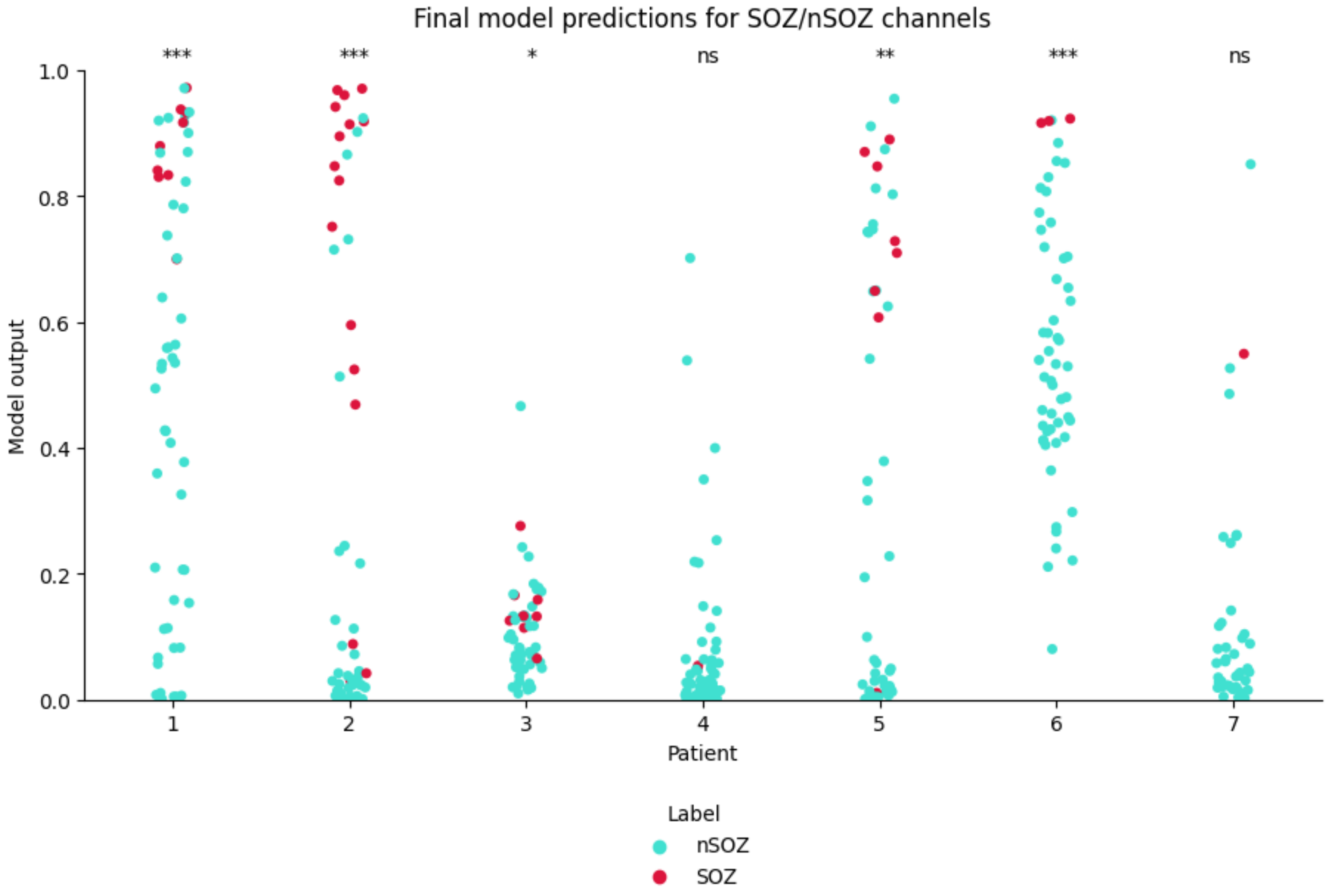
- As well as mean, incorporate standard deviation across trials



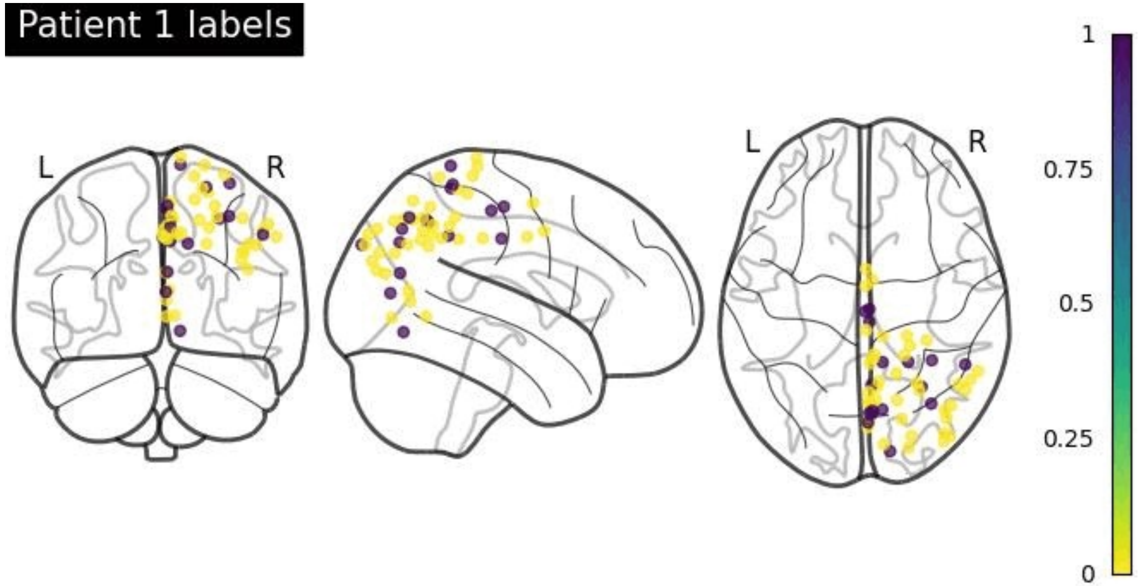
Full model performance

Model	AUPRC	AUROC
Random	0.14	0.50
CNN	0.17	0.48
Transformer	0.22	0.58
Full model	0.37	0.74

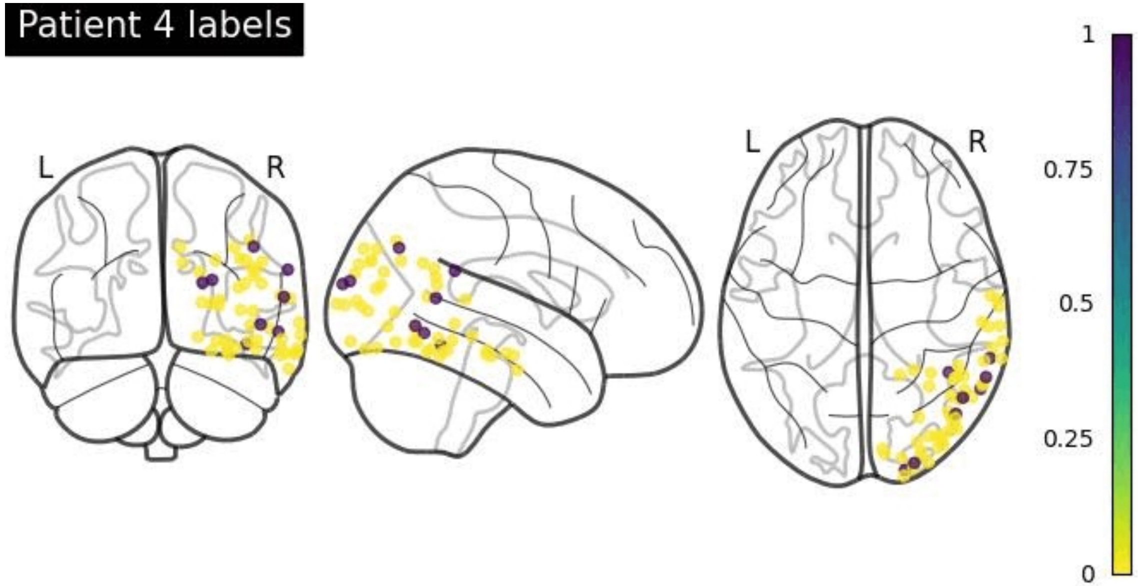
- Considerable improvement over previous methods



Predictions visualised



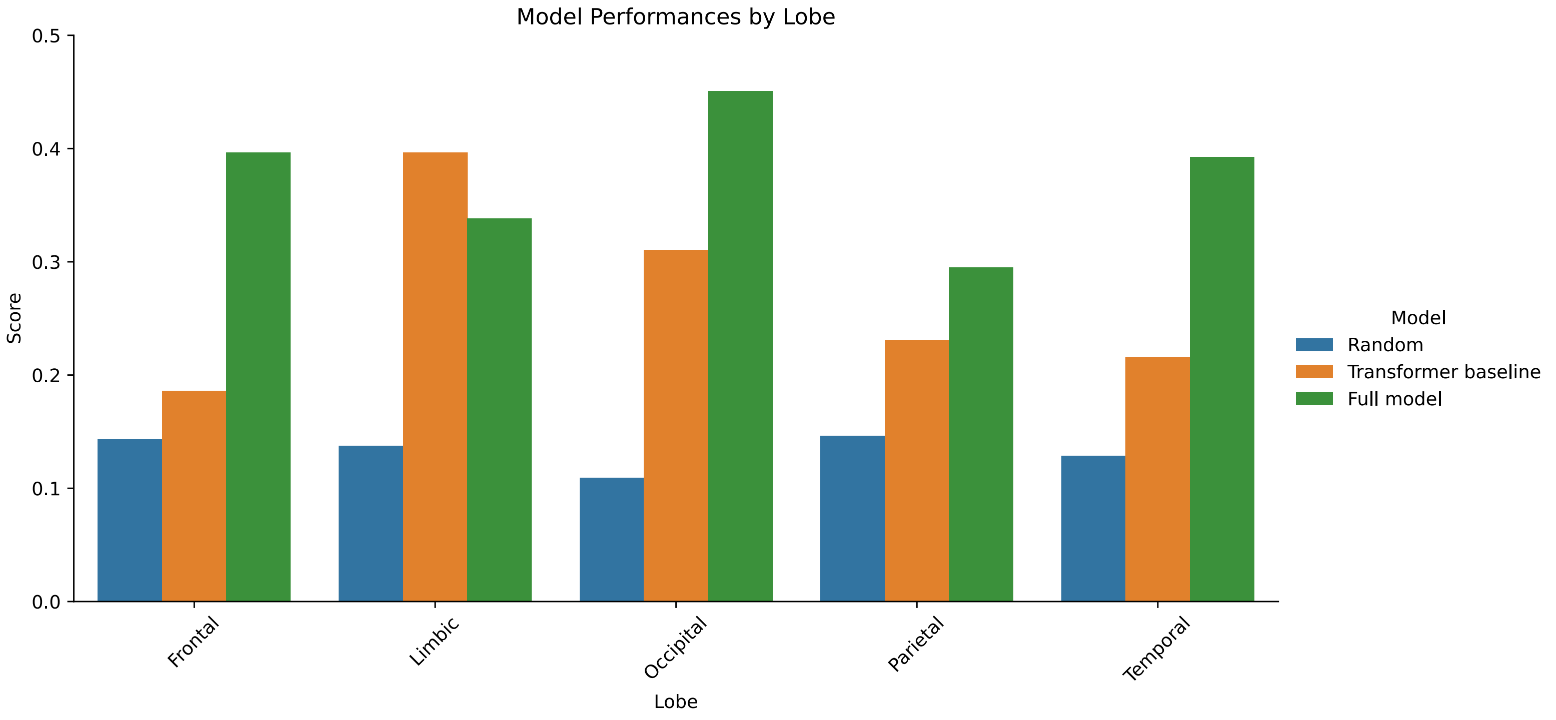
AUROC = 0.88

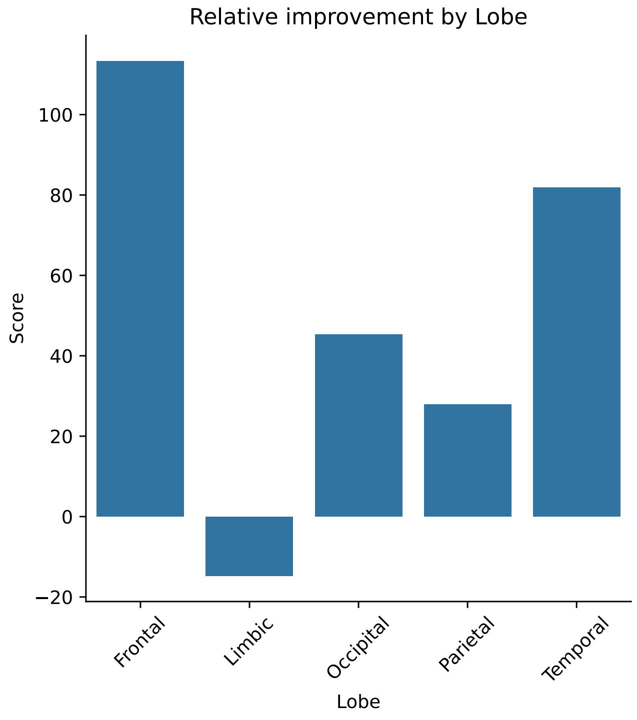


AUROC = 0.77

Performance by lobe

- Delayed responses are typically seen in frontal and temporal lobes
- **Hypothesis:** modifications will have improved performance for these the most





Conclusion

Transformers:

- Better suited to handling diverse channel configurations than CNNs
- Show promise for wide application in intracranial EEG analysis

Performance increase:

- Mostly from data restructuring – exploiting known SPES characteristics

Efficiency (Trained/Tested on MacBook Pro 2021)

- Pre-processing and model training: Under 20 minutes
- Applying model on a new patient: Less than 1 minute

Challenges and Future Directions

- Enhance validity with external validation
- Integrate channel locations for improved accuracy
- Predict outcome given removal of a channel (requires outcome labels)
- Black box: point to salient features?

Clinical Utility:

- Offers a way of efficiently processing large amounts of stimulation data
- Requires a think about how to truly help clinicians

Thanks for listening!