Surrogate Modelling to Study E/I Imbalances in Children with Developmental Dyslexia

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***Abstract*— Effective language processing relies on the brain's capacity to decode rhythmic cues in speech, a function primarily supported by activity in the theta frequency band. According to the Temporal Sampling Framework, impairments in this process may contribute to the phonological deficits observed in individuals with Developmental Dyslexia (DD). These challenges cascade into higher-frequency bands, affecting the integration of phonemes, words, and phrases, ultimately compromising reading and writing fluency. Early diagnosis and treatment are crucial for ensuring proper personal and academic development in children. In this study, we propose a non-invasive methodology that combines ElectroEncephaloGraphy (EEG) data with a surrogate modelling framework to detect early imbalances in Excitation/Inhibition (E/I) mechanisms. We applied this methodology to a cohort of children, divided into controls and DD groups, and compared the inferred E/I mechanisms with patterns predicted by the neural noise hypothesis. We found that the results obtained using this framework align with both the Temporal Sampling Framework and the Neural Noise Hypothesis.**

***Keywords-Developmental Dyslexia*; *EEG*; *E/I ratio*; *Neural Noise Hypothesis*; *Temporal Sampling Framework*; *Machine Learning*; *Mechanistic modelling*; *Surrogate model*; *Feature extraction*.**

I. INTRODUCTION

Developmental Dyslexia (DD) is a learning disorder that affects an individual's ability to read and write fluently. Contrary to popular belief, this condition is not associated with a motor, visual or cognitive disability, nor is it indicative of lower intellectual abilities. People with dyslexia encounter challenges in correlating words with their corresponding auditory representations, thereby impeding their capacity to effortlessly decode words with precision, a difficulty associated with the phonological processing area [1]. The Temporal Sampling Framework (TSF) [2] suggests that DD arises from a deficit in the ability to process rhythmic cues in speech, specifically within the theta frequency band (4-7 Hz), which is critical for syllable segmentation. This deficit disrupts the accurate temporal alignment necessary for decoding linguistic information, thereby impeding the formation of robust phonological representations. Consequently, these impairments extend to higher-frequency bands associated with the processing of phonemes and the integration of words and phrases, further complicating language comprehension and fluency.

Early identification of this disorder is crucial for ensuring optimal development and preventing the onset of self-esteem issues in early childhood. The diagnosis of DD is based on tests that evaluate accuracy and fluency in reading and writing [3]. However, this approach is subject to external influences, and in the case of children, their results may be inadequate to rule out the disorder. Therefore, it would be worth exploring the development of an objective, neurophysiology-based diagnostic method that can be applied universally to all patients, complementing the existing neuropsychological tests. ElectroEncephaloGraphy (EEG) techniques emerge as a promising candidate for addressing this need due to their non-invasive nature, wide applicability in conjunction with various diagnostic tests, and cost-effectiveness. There are some studies that have documented differences in EEG patterns between individuals with and without developmental dyslexia, particularly in the theta, alpha and beta bands [4]. This underscores the importance of exploring potential biomarkers associated with specific EEG signal patterns to enhance diagnosis and monitoring of DD.

In recent years, considerable attention has been directed toward investigating the relationship between neural noise

and DD [5]. Evidence suggests that a flatter aperiodic component in neural power (i.e., higher neural noise) can serve as an indicator of DD [6]. This flattening is believed to be associated with an increase in hyperexcitability in cortical circuits, offering deeper insight into the neural mechanisms underlying DD.

In this study, we employ a mechanistic brain model combined with machine learning techniques to investigate the relationship between excitation-inhibition imbalances and DD. Specifically, we developed a surrogate model utilizing the *catch22* feature subset [7] and employed it as an inference tool to estimate cortical circuit parameters from EEG data. We applied this methodology to a cohort of 50 children, divided into control and DD groups, who were exposed to auditory stimuli at frequencies associated with different stages of language processing. The objective of this study is to assess whether our inference framework can reliably identify potential biomarkers of dysregulated brain activity linked to DD, ultimately contributing to improved diagnostic and predictive tools.

The rest of the paper is structured as follows. In Section II, we explain the methodology followed in the study, explaining how the proposed framework works, and the database used to obtain the results. In Section III, we present the results computed following the previous section. In Section IV, we discuss the results, comparing them with the Temporal Sampling Framework and neural noise hypothesis in Dyslexia. Finally, we provide a conclusion and future work directives in Section V.

II. METHODS

In this section, we present the framework used to infer E/I imbalances in DD, detailing the computation of artificial EEG signals, the extracted features, and the creation of the surrogate model. We also describe the statistical analysis after inference and, finally, introduce the empirical dataset where our framework is applied.

A. Simulation of EEG signals

The EEG signal generation methodology employed in this study is based on the approach outlined in [8]. First, to generate cortical activity, we used a neural network of recurrent Excitatory (E) and Inhibitory (I) populations, composed of Leaky Integrate-and-Fire (LIF) neuronal models, with external stimuli generated by a fixed-rate Poisson process. We employed the best-fit parameters of the model given in [9], except for J_{EE}, J_{EI}, J_{IE}, J_{II}, τ_{exc}, τ_{inh} and J_{ext}. These parameters represent, respectively, the weights of the synaptic currents between different neuron populations (J_{YX}, where X is the presynaptic populations and Y is the postsynaptic populations), the time constants of the excitatory and inhibitory synaptic currents, and the weight for the external synaptic current. By varying these parameters, we generated a set of nearly two million simulations.

To generate the current dipole moment that will determine the EEG signal, we convolved the simulated spike rates with spatiotemporal kernels that account for the biophysics of neurons and synapses, as well as their spatiotemporal distributions and the connectivity of an equivalent conductance-based multicompartmental neural model. We selected a ball-and-stick model for the multicompartmental neurons for the sake of simplicity.

B. Feature extraction

For the feature extraction process, we used *catch22* [7], a set of features from the highly comparative time-series analysis toolbox [10] (*hctsa*). This set consists of the 22 best features from *hctsa* tested in different datasets that capture a broad and interpretable range of time-series characteristics, making it particularly well suited for analyzing the intricate temporal dynamics inherent in EEG signals.

C. Machine learning for the inference of simulation parameters

A multi-layer perceptron from *scikit-learn* Python library was trained considering the totality of the *catch22* set as the inputs, and the parameters of the cortical circuit model as outputs. The model was trained using 20 repeats of 10-fold Cross Validation to ensure that it captures the general patterns of our problem, avoiding overfitting the simulation data.

D. Statistical analysis

To test if the parameters inferred from the database are statistically different between groups, we applied Linear Mixed-Effects (LME) models that consider variability between individuals and sensor location. Package *lme4* from R was used to apply LME. We implemented group membership and sensor location as fixed effects in the model. We implemented individual variability by using patient ID as a random effect, adjusting correlation between patients.

After the model fitting, we computed the marginal means of the parameters for each group and electrode using the package *emmeans.* Following this, we conducted pairwise comparison between groups for each sensor, adjusting the p-value using Holm-Bonferroni correction.

E. Empirical dataset

The data used in this research were provided by the LEEDUCA research group at the University of Malaga (Spain) [11]. This data comes from a study involving more than 1400 children aged 4 to 8 years. The empirical data used consists of a dataset of 50 subjects where 31 were control subjects and 19 subjects had developmental dyslexia. Each subject was in a resting state while receiving Auditory Steady-State Response-like (ASSR) auditory stimuli of three different frequencies: 4.8 Hz, 18 Hz and 40 Hz. The experiment started with a progressive increase of the frequency from 4.8 Hz up to 40 Hz and then returned to 4.8 Hz. During the process, cortical activity was recorded using an EEG cap of 31 electrodes following the 10-20 system, with a sampling rate of 500 Hz. The captured signal on each electrode was split into 8 seconds epochs and then normalized using the z-score metric.

III. RESULTS

The study started by generating a dataset of 2 million simulations of cortical activity using a model consisting of a recurrent network of excitatory and inhibitory neurons. Following this, we created synthetic EEG data by convolving biophysical spatiotemporal kernels with simulated spike rates and we then extracted the 22 features provided by *catch22* from the artificial EEG signals. We trained a neural network using simulated data, generating a surrogate model that allows us to infer the parameters of the model that can describe real EEG data. Once trained, we used the surrogate model to infer cortical parameters on a dataset that included 50 subjects divided into two groups: DD and control. We computed the metric E/I by using the inferred weights of the synaptic currents. We split the results for the three different auditory stimuli frequencies: 4.8 Hz, 16 Hz and 40 Hz, and applied LME analysis to compute significant differences between the two groups for each model parameter separately.

Analyzing parameter predictions, we observed an increase in E/I concentrated in single-electrode positions of parietal and frontal regions for stimuli of 4.8 Hz and 16 Hz, respectively (Figure 1). We also observed an increase in J_{ext} with 4.8 Hz stimuli in occipital regions while there was a small decrease in parietal zones for the 40 Hz stimuli. For τ_{exc}, there were no significant differences for stimuli of 4.8 Hz and 16 Hz. In contrast, for 40 Hz, there was a significant increase in this parameter on temporo-parietal zone. However, the greatest number of significant differences across electrode positions were observed for τ_{inh}. When subjects were stimulated at 4.8 Hz, this parameter increased in the frontal and parietal-central regions. As the stimulus frequency increases, the significant differences are confined to a smaller subset of electrodes.

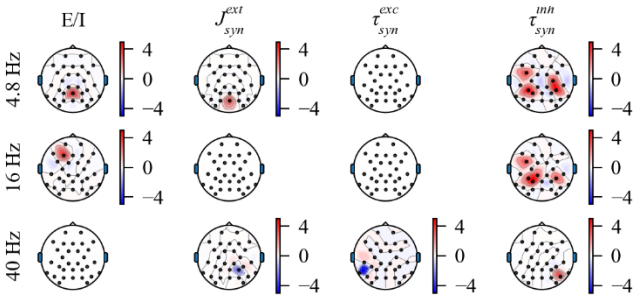

Figure 1. Representation of differences of each model parameter between control and DD groups for the three stimuli frequencies. It is plotted only the z-ratio with p-value ≤ 0.01.

IV. DISCUSSION

In this study, we propose an inference framework combining simulation with machine learning to explore and test predictions of imbalances in excitatory and inhibitory processes observed in individuals with Developmental Dyslexia. Using real EEG data, we extracted time-series features using the *catch22* library, which provides a standardized set of 22 interpretable statistical and nonlinear metrics. These features were used to infer model parameters via a surrogate model and to identify significant group differences within the dataset.

Our results revealed an increase in the Excitatory/Inhibitory (E/I) ratio in the parietal and frontal lobes for some of the stimuli frequencies consistent with the neural noise hypothesis in Dyslexia [5][6]. Additionally, we observed a prominent increment in the inhibitory time constant (τ_{inh}) at a stimulation frequency of 4.8 Hz, which decreases when the stimulus frequencies increased. This increase in the inhibitory time constant may imply a delayed response of inhibitory currents, which may lead to less effective inhibition (i.e., a shift of E/I that favors excitation). This phenomenon aligns with the neural noise hypothesis prediction of hyperexcitability in Dyslexia. The Temporal Sampling Framework hypothesis suggests that DD arises from a deficit in syllables processing. This process is associated with neural oscillations in the Theta band (4-7 Hz), which aligns with the frequency range where our results reveal the most significant group differences. Notably, as the stimulus frequency increases, these significant differences decrease, with almost no significant differences at 40 Hz, which is related to phoneme segmentation.

Our computational model offers a valuable approximation of the neural circuit but is not designed to reproduce all its characteristics. It does not account for large-scale network dynamics, such as long-range corticocortical interactions between different brain regions. To mitigate this limitation, we introduce an external input that simulates the aggregate influence of corticocortical connections from other regions. This strategy helps us approximate the impact of macroscopic dynamics on our local predictions. In future work, incorporating alternative brain models could provide a more comprehensive representation of these large-scale interactions and improve the accuracy of our predictions.

This study was conducted using only the features provided by *catch22*. Consequently, the selection of alternative feature sets, such as those offered by the highly comparative time-series analysis (*hctsa*) toolbox [10], may allow for a more precise characterization of E/I imbalances and the behavior of other model parameters. This, in turn, could contribute to a more comprehensive understanding of the underlying neural dynamics in disorders such as DD.

V. CONCLUSION AND FUTURE WORK

The inference framework proposed in this paper reveals promising results, suggesting that simple techniques such as EEG have potential for the diagnosis and monitoring of individuals with DD. However, this framework has some limitations, with the brain model being the main one. The use of models that account for macroscopic dynamics will be essential to improve the understanding of disorders such as DD. The search for new biomarkers, either by using alternative feature sets or techniques such as autoencoders,

could also enhance the comprehension of different neural dynamics.

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