**Literature review:**

**Predictive value of functional MRI and EEG in epilepsy diagnosis after a first seizure:**

[**https://www.sciencedirect.com/science/article/pii/S1525505020308313**](https://www.sciencedirect.com/science/article/pii/S1525505020308313)

In this study, the predictive value of physiological signals measured using Electroencephalography (EEG) and functional MRI (fMRI) is assessed. A logistic regression classifier was trained on epilepsy and first-seizure subjects. This EEG/fMRI model showed significant improvements compared to the clinical diagnosis. A diagnosis of epilepsy requires at least one unprovoked seizure and/or a risk of recurrent seizures. Electroencephalography (EEG) can aid the diagnosis of new onset epilepsy.

CT or MRI allows detection of abnormalities specific for epilepsy and aid in a more accurate diagnosis. Electroencephalography (EEG) measures spontaneous electrical brain activity directly via electrodes on the scalp. Functional MRI (fMRI) measures changes in the blood-oxygen level as an indirect consequence of neural activity. While EEG has superior temporal resolution allowing analysis of high frequency temporal activity, fMRI has a high spatial resolution providing insights into specific brain structures. The EEG recordings with a 250-Hz sample frequency were first resampled to a sample frequency of 256 Hz using the EEGLAB toolbox in Matlab.

To ensure stability of the calculated EEG metrics, the two 3-min periods (hyperventilation and rest) were each divided into six consecutive epochs. FMRI-Preprocessing of the fMRI data and T1w structural images was performed using the Statistical Parametric Mapping software package, SPM12 (https://www.fil.ion.ac.uk/spm/) in Matlab R2016b. The functional images were smoothed through convolution with a 6-mm full-width half maximum (FWHM) Gaussian kernel. Fractal amplitude of low-frequency fluctuation (fALFF) analysis was performed. The fALFF is the ratio of the power spectrum in a specific subband to that of the full frequency range (0–250 mHz).

The amplitudes of fluctuations were calculated for well-known predefined frequency subbands. Graph metrics of fMRI time series were found to be different in patients with epilepsy compared to healthy controls. Functional network was quantitatively described by two of the most robust and widely applied global graph metrics. Graph metrics were calculated using the Brain Connectivity Toolbox (http://www.brain-connectivity-toolbox.net). The total feature set consists of 93 features; 51 fMRI and 42 EEG features.

Since there is only a limited number of independent observations, high correlations in the feature set are removed. This result seems to imply that EEG and fMRI measurements complement each other in terms of predictive value after a first seizure. SL (synchronization and coherence) measures are highly dependent on seizure type and activity. Previous research has shown that SL is higher in patients with epilepsy compared to those with new-onset epilepsy. Differences could be explained due to the heterogeneous nature of the first-fit clinic samples.

In the study, the fALFF measures in the thalamus are found to be most valuable predictors. The global normalized clustering coefficient was also selected as a valuable predictor. Using information from the fMRI and EEG can result in a more accurate risk assessment of seizure recurrence after a single seizure. Neurological signals measured using EEG and/or function MRI in a first-seizure clinical sample are evaluated. Predictive value is assessed using logistic regression models, which are tested on subjects that developed epilepsy (e.g. a second unprovoked seizure). These subjects were initially evaluated as having a low risk of seizure recurrence.

**A Sparse EEG-Informed fMRI Model for Hybrid EEG-fMRI Neurofeedback** <https://www.frontiersin.org/articles/10.3389/fnins.2019.01451/full>

NF-EEG and NF-fMRI provide real-time feedback to a subject about his or her brain activity. EEG measures the electrical activity of the brain through electrodes located on the scalp. Using fMRI and EEG simultaneously for bi-modal neurofeedback is very promising for the design of brain rehabilitation protocols. However, fMRI is cumbersome and more exhausting for patients. They propose a sparse regression model able to exploit EEG only to predict NF-eigthorpe MRI scores in motor imagery tasks.

They showed that predicting NF-fMRI scores from EEG signals adds information to NF-EEG scores and significantly improves the correlation with bi-modal NF sessions compared to classical NF-EEG scores. EEG measures changes in electrical potential occurring in the brain in real time, while fMRI indirectly estimates brain activity by measuring changes in the BOLD signal. Both modalities are sensitive to different aspects of brain activity with different speeds. Several studies have investigated correlations between EEG signal and BOLD activity in specific and simple tasks. The methodology to extract information from fMRI with EEG has been intensively investigated.

The term EEG-informed fMRI refers to methods extracting features from EEG signals in order to derive a predictor of the associated BOLD signal in the region of interest under study. Different strategies have been investigated, depending on the type of activity under study (epilepsy, resting state, open/closed eyes, relaxation). Schwab et al. (2015), the authors used a spatial, spectral, and temporal decomposition of the EEG signals to map EEG onto BOLD bOLD signal changes in the thalamus. Using a more symmetrical approach, Noorzadeh & Co. (2017) proposed a method for the estimation of brain source activation. The recent methodology synchronizing both signals for real-time neurofeedback allows the construction of a new kind of data named NF-EEG-fMRI data.

Most of the methods intend to predict the fMRI information outside the scanner, but some use EEG or BOLD fMRI only. It has been shown that the quality of a neurofeedback session is improved when using both modalities simultaneously. However, in the context of neurofeedback, using simultaneous recording of EEG-fMRI to estimate neurofeedback scores computed in real time from features of both modalities (NF-EEG-fMRI) is a recent application that was first introduced and its feasibility demonstrated by Zotev et al. (2014), Mano et al. (2017), and Perronnet et al. (2017).

**Robust and interpretable graph neural networks for the analysis of MRI and EEG to classify epilepsy subtypes and predict patient outcomes**

<https://www.findaphd.com/phds/project/robust-and-interpretable-graph-neural-networks-for-the-analysis-of-mri-and-eeg-to-classify-epilepsy-subtypes-and-predict-patient-outcomes/?p131366>

Epilepsy is one of the most common serious neurological disorders. Magnetic resonance imaging (MRI) and electroencephalography (EEG) are routinely used for the clinical assessment of patients with epilepsy. They propose to apply Artificial Intelligence (AI) methods to MRI and EEG data to improve diagnostic classification of epilepsy subtypes and predict treatment outcomes. This work will offer a unique collaboration between the departments of computer science and pharmacology and therapeutics at the University of Liverpool. The Liverpool BRAIN lab has considerable expertise in the reconstruction and analysis of brain networks from MRI/EEG data.

Graph neural networks (GNNs), which are deep learning models that capture the dependence of graphs via message passing between nodes of graphs, will be considered as the primary technique. For diagnostic purposes, a key technical question needs to be addressed -- interpretability. We will develop interpretability techniques to support each diagnosis result with an explanation (or evidence).

**Design of MRI structured spiking neural networks and learning algorithms for personalized modelling, analysis, and prediction of EEG signals**

<https://www.nature.com/articles/s41598-021-90029-5>

The study of biological signals, which contain information about the activity and structure of the brain, has received much attention. Few studies combine data such as EEG and MRI to enhance reliability, accuracy and interpretability of the models. This approach can be applied for personalized modeling, analysis, and prediction of EEG signals. Spiking neural networks (SNN) emerge as suitable techniques for modelling spatio-temporal brain data (STBD) such as EEG3, fMRI9,21, or fMRI and DTI. A brain-inspired SNN architecture, called NeuCube, to model STBD has already been introduced.

The proposed here 3D MRI-SNNr architecture uses the Izhikevich neuronal model16 allowing for continuous EEG signals. The proposed MRI-SNNr architecture consists of a SNNr and Output module (Fig. 1). The boundary element method (BEM)26 using FieldTrip tool27 and MATLAB software are used to localize brain activity. Spiking neurons are positioned proportional to the locations of the EEG channels providing input information. The regulator/classifier module has the task of normalizing and filtering (0 ~ 60 or 70 Hz)28,29 the output data from the observed neurons to produce continuous value output signals.

In this framework, it is presumed that there is a bi-directional link between neurons in a neighborhood, and each neuron output is connected to the same neuron as a feedback. This paper proposes a new formula for the calculation of the input current Ii to the ith observed neuron of the Izhikevich type. Eq. (5) can mitigate the calculation cost of the error backpropagation process ahead. The method for the modification of the observed-neuron-synaptic weights is presented here.

The proposed MRI-SNNr architecture and learning algorithms are utilized here in two realizations: (a) continuous value EEG signals are used as inputs for the MRI-sSNr and (b) spike sequences are used to train the SNNr. In both realisations, neurons are located using the same personalized MRI data and parameters of the neurons and STDP learning are set according to Table 1. To compare the performance of two MRI-SNNr models with other methods for EEG signal modelling and prediction, two cases of study data have been used. The first case-study data is raw EEG but the second one has been pre-processed by 0.5–70 Hz filter with additional 50 Hz notch filter. The experimented MRI-SNNr has 300 Izhikevich neurons consisting of 15 observed (EEG channels) and 285 hidden neurons.

Modeling properties of the network are set such that 20% of neurons are inhibitory and the rest are excitatory. Both the input EEG signals and the network outputs are filtered simultaneously using a MATLAB–designed-Minimum-Ordered-Equripple-FIR filter. To evaluate the performance of the proposed MRI—SNNr models, simulation is performed with the same EEG data. 70% of the data is used for training and 30% for testing. During training, hidden neurons update their synaptic weights by using STDP law.

During testing, there is no update of the connection weights of observed neurons. An MRI-SNNr model can predict signals at other locations of the SNNr corresponding to unmonitored/ not measured areas of the brain. A Kaiser filter with 0–70 Hz frequency band and 80 dB attenuation at higher frequencies, has been imposed as post-processor of raw EEG signals. In this section the performance of the two MRI-SNNr models to predict signals at SNNr locations that correspond to non-recoded EEG channel is evaluated. 15 channels of EEG signals are considered as inputs and 25 EEG channel locations as outputs.

MSE of the EEG signal prediction across all 10 new sites as well as 15 inputs' prediction is shown in Table 2. Neuronal activity analysis could be used to better understand functions of the brain. In their model, the activation degree of each neuron is defined as suggest in9 by:Dj=∑j(wij+wji)NumberofneuronsinNij∈Ni(22)where wij and wji are the weights of bidirectional connections between neurons i and j. EEG signals were reported from a patient undergoing hyperventilation (HV) The degree of activation of the brain's central and parietal lobes under HV rises compared to other regions. A similar power spectrum of the signal is produced by the model to the one of the input EEG signal which is also an indication for an accurate modelling result.

A new method is introduced for the creation of personalized SNN models, MRI-SNNr, for the analysis, prediction and understanding of EEG signals. The 3D SNNr model consists of observed (input/output) neurons and hidden neurons. A new machine-learning algorithm is proposed to learn the EEG data using gradient descent learning rules. Preliminary experimental results on case study personal EEG data manifest a better performance of the proposed method applied on continuous value EEG signals rather than spike encoded signals. MRI pre-structured personalised SNN model can be used to predict the activity of other areas of the brain corresponding to EEG channels that are not used for training the model.

Dynamic changes in EEG spatial–temporal patterns in different brain areas were discovered, which could be explained by transitions between epileptiform, preictal, and ictal events. The accuracy of modeling depends on many parameters, related but not limited to how MRI-SNNr is structured to map a personal MRI. Representing spatio-temporal patterns of activities during learning is also a challenging task. More research is planned to examine and optimize these parameters for a better personalized predictive modelling of EEG data.

**Multimodal Prediction of Alzheimer's Disease Severity Level Based on Resting-State EEG and Structural MRI**

<https://www.frontiersin.org/articles/10.3389/fnhum.2021.700627/full>

While several biomarkers have been developed for the detection of Alzheimer's disease, not many are available for the prediction of disease severity. In this paper, they explore the multimodal prediction of Mini-Mental State Examination (MMSE) scores using resting-state electroencephalography and MRI scans. Diagnosis of AD is currently only achievable with postmortem neuropathological examination. In vivo diagnosis is often based on clinical criteria, which rely on clinical interview with support from cognitive assessments. Research has focused on developing biomarkers of the disease that may help to increase confidence in the diagnosis.

With the availability of such biomarker features, healthcare professionals and clinical trial teams would have additional tools to monitor the disease. Relying upon cognitive assessment only may be problematic, as performance on tasks such as the MMSE may be subject to confounding variables. Several biomarkers from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database have been suggested. As Alzheimer's disease (AD) progresses, it is expected that a single biomarker may not provide sufficient information to determine disease severity accurately. Instead, a multimodal biomarker system would be needed for accurate diagnosis and monitoring of AD.

EEG tests could further improve the accuracy of a disease severity monitoring system relying on neuroimaging information. Analyses on data from 89 patients show the usefulness of multimodal AD severity level models for patients at early stages of the disease. Access to an automated tool could be useful for clinicians to help with better diagnostics and monitoring. The data used herein was collected from a multi-site clinical trial exploring the use of electrophysiological markers to study Alzheimer's disease.

It is comprised of a signal acquisition step, followed by pre-processing, feature extraction, feature selection, and finally a regression mapping. The main goal is to predict the patient's MMSE score based on EEG, MRI and combined features. Images captured from the MRI scanner were pre-processed using the default command "recon-all". The T1-weighted MRI scans, in turn, were processed using FreeSurfer1, a universally used open-access software package. Aiming for automaticity, reliability and reproducibility, the pipeline was applied without manual intervention.

Spectral power features are defined by the power measurements within each of the following EEG frequency subbands: delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz) and low-gamma (30–45 Hz). Coherence features were used to measure the co-variance between two power spectra. Recently, Cassani and Falk (2020) showed that improved AD diagnostics could be achieved if non-conventional bands were used. These so-called "patches" were shown to be important in discriminating mild cognitive impairment from AD, as well as moderate AD from severe AD. Overall, a total of 286 features were extracted from each of the 8-s epochs.

Average thickness and surface area of the cortical parcellation were calculated. Measurements of cortical structure were determined for the left and right hemisphere ROIs. White matter volumes were calculated based on proximity to the cortical label, and a constraint in the form of an extension of 5 mm into the white matter. A total of 1,716 features were calculated from the EEG signals and a total of 285 features from MRI scans. Feature selection or ranking aims to rank available features based on their potential impact on the downstream classification task.

Three different techniques of filtering the features were tested:. Pearson correlation, Spearman correlation, and Minimum Redundancy Maximum Relevance (MRMR). Correlation-based feature selection relies on measures between the tested features and the outcome variables. Different types of correlations are available to measure different associations between the two variables. Minimum redundancy maximum relevance (MRMR) feature selection algorithm has been proposed.

MRMR algorithm selects a subset of features having the most relation with a class (relevance) and the least relation between themselves (redundancy). They are interested in AD severity monitoring, a regression task is needed to estimate the MMSE score of an AD patient. Motivated by insights from Cassani et al. (2018), three supervised regression models are explored. Data partitioning was done five times in order to ensure that selected features are not overly sensitive to data partitioning. The support vector machine regression (SVMR) model searches for a regression function in which all the obtained target errors will be under a specific value.

The k-nearest neighbor classifier assumes that an unseen sample likely belongs to the same class as the k most analogous-distant neighbors. In this section, they explore the benefits of AD severity prediction using unimodal and multimodal systems. They evaluate each model's performance using root mean squared error (RMSE), Pearson, and Spearman correlation between predicted and observed MMSE score as metrics. For the sake of brevity, they focus on MRMR for feature selection and random forest as a regression model. Figure 6 presents the distributions of the overall average RMSE scores based on the different groups of features.

MRMR is less sensitive to data partitioning than the other feature selection techniques, since it was able to select similar features across the five runs consistently. This is an important aspect that needs to also be taken into account when evaluating overall system performance. The features kurtosis − R2oR3, P3, and P4 were shown to be those most often selected from the EEG modality. The recently-proposed modulation spectral patch features represented half of the top-20 EEG features selected by MRMR. These features are important for unimodal EEG-based monitoring systems.

Damage to white matter has been linked to Alzheimer's disease (AD). Damage to the white matter of the frontal, temporal, parietal, and occipital lobes has also been reported. Of the 29 unique features consistently-selected from group 3, only six were from MRI. For both unimodal and multimodal systems, the amplitude modulation features were shown to be extremely important. The R2/R3 modulation patch regions, in turn, were extremely important for the unimodeal systems. From the MRI features, features derived from the cortical parcellation and white matter volume ROIs were more often selected than subcortical volumetric features.