Towards the Development of a Diagnostic EEG Protocol for ADHD

UNIVERSITY OF MARYLAND

FIRE: THE FIRST-YEAR INNOVATION & RESEARCH EXPERIENCE
DEEP BRAIN NEUROTECH

A. JAMES CLARK SCHOOL OF ENGINEERING

COMPUTER SCIENCE

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Abstract

Attention Deficit Hyperactivity Disorder (ADHD) is a heterogeneous neuro-behavioral disorder characterized by ongoing patterns of inattention and hyperactivity that interfere with functionality. Many papers point to the hypothesis that electroencephalography (EEG) signals from ADHD patients are described as having elevated power of low-frequency waves and/or reduced ability of high-frequency waves. Other emerging proposals seem to link lack of empathy with ADHD. Currently, the diagnostic procedures are based on subjective evaluation of behavior, and a reliable objective method of diagnosis does not exist. This project was conducted to create a more objective and dependable diagnosis procedure for ADHD. Data was collected from 6 young adult subjects with ADHD and six controls using both a three-electrode configuration. Spectrograms were generated from the signals and classified. Transfer learning was used with the Inception V3 model to classify the ADHD spectrograms versus the healthy spectrograms. Additionally, The raw signal was separated into empathy and focus epochs and SVM was applied to the data received from a power spectral density graph of the raw EEG signal data to classify frequency features for an ADHD diagnosis. There was also a logistic regression model run on features extracted from a wavelet transform of the raw data which had similar results. The signals during the empathy epoch gave better results than the focus epoch for all models. This lays the foundation for an objective method for diagnosing ADHD which would progressively lead to a more accurate diagnosis of the disorder.

Introduction

Attention Deficit/Hyperactivity Disorder (ADHD) is a common neurodevelopmental condition involving symptoms such as inattention, distractibility, hyperactivity, indecisiveness, and altered reinforcement learning (Ziegler, S. et al, 2016). Though the cause of ADHD is unknown, it is hypothesized that individuals with ADHD have a deficiency in certain neurotransmitters such as dopamine and noradrenaline, especially in the frontal and prefrontal lobes which are involved in attention. Some studies indicate ADHD is associated with abnormality in the basal ganglia, especially the caudate, putamen and globus pallidus nuclei (Soreff, S. 2017).

Research studies have identified potential 'markers' to support diagnostic, functional assessment and treatment decisions of ADHD. However, there is little consensus about these markers. Some studies point to deficits in regulation of emotion and feeling in ADHD such as empathy (William et.,al 2010). There is evidence that the neural activity involved in emotions related to empathy is due to the activation of mirror neurons in the anterior cingulate and the insular cortices (Schulte-Rüther, 2007). The Theory of Mind (ToM), which is the ability to understand and predict other people's behavior, seems to be compromised in ADHD subjects.

Electroencephalogram (EEG) is a non-invasive technique used to measure weak electromagnetic signals induced by neural generators. The collection of EEG data allows for the analysis of different types of brain waves through a multi-channeled electrode system. The most robust EEG feature associated with ADHD is an underactive nervous system, or hypoarousal (Mayer, 2016).

The Toronto Empathy Quotient (TEQ), which was developed to encompass empathy at the broadest level and derive a measure based on existing empathy scales, was adapted for our current protocol. The algorithms that were applied to the EEG data collected were: SVM, which was implemented using a "leave one out" approach; Inception V3 which was retrained for the spectrograms of the EEG collected; and the last approach was using logistic regression on the orthogonal functions of the time signal.

This poster represents a work in progress for designing the most efficient protocol that can capture diagnostic markers of ADHD patients.

Resources

- MNE-Python, an M/EEG data processing software package in Python.
- Python and scikit learn module
- Neurosteer EEG 1 Channel System and EEG Analyses
- MATLab EEG data processing software
- EMOTIV Epoc+, a mobile EEG based on the 10-20 channel system
- Google Inception V3

Methods

Protocol:

- 6 test subjects with ADHD of unspecified DSM subtypes and 6 controls were chosen for the study.
- Patients did not take their medications for at least a day before the study was conducted.
- 2 sensors were placed on the forehead of each subject.
- The subjects were asked to play 5 minutes of the mobile phone game *Piano Tiles 2!*.
- Subjects were asked to take an empathy test adapted from the TEQ before an empathy video.
- Subjects were shown an empathy-inducing set of images, including both "happy" and "sad" pictures. Emotional music was played in the background during the course of the test.
- Subjects were asked to retake the empathy test adapted from the TEQ for situational empathy.

Data Preprocessing:

Image Processing Approach

- Neurosteer generates a spectrogram in real time of the signals received. The x-axis represents time, y-axis represents frequency, and the third dimension, intensity, represents amplitude of a certain frequency at a certain time (by the color intensity).
- The spectrograms generated are modified to remove artifacts or noise.
- The images are imported to Photoshop to convert their resolution from 72 dpi to 128 dpi.
- The images were cropped for a focus epoch and an empathy epoch.
- To create the dataset, 3 folders (Empathy, Focus, and Entire spectrogram) with two subfolders were specified for the test subjects: ADHD and Non-ADHD.
- Data was sorted into the corresponding subfolder for each category.

SVM Approach

- Neurosteer returns signal data in a .txt file which can be used to graph the signal.
- The signal data was segregated into focus and empathy signal data.
- A Fast Fourier Transform algorithm was applied on the data to create a power spectral density graph.
- Ranges of frequencies for each type of brain wave were created and the average power was found for each brain wave band.
- A matrix was created to feed the data into an SVM model.

Logistic Regression Approach:

- Neurosteer has its own wavelet transform of the raw EEG which finds 121 orthogonal functions to the signal called Brain Activity Features (BAFs), which show activity of functional areas of the brain (not geographic location).
- These BAFs all have their own activity levels based on how active that functional area of the brain is.
- The activity levels of these BAFs were run through a basic t-test to find those which were active statistically differently active between ADHD and control subjects.
- These BAFs were then used as features in the logistic regression to predict ADHD.

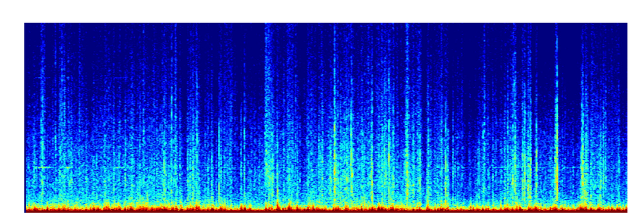

Figure 1: An example of a spectrogram of raw data produced using Neurosteer.

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Varied Approaches for EEG Data Analysis

Transfer Learning

- Transfer Learning is a process where pre-trained models are used as a starting point on a different task than what the model was already trained on. The Google Inception V3 model was used which consists of a feature extraction part with a convolutional neural network, and a classification part with fully-connected and softmax layers.
- The feature extraction function of the Google Inception V3 was reused and the classification part was retrained with the dataset.
- Inception V3 was trained with the following configurations---input image resolution of 128px and the relative size of the model as a fraction of the largest mobilenet of 0.5.
- During the retraining process, the first phase analyzes all the images and calculates the bottleneck values.
- It runs training steps where each step chooses images at random from the training set, finds their bottlenecks, and feeds them into the final layer to get predictions. Those predictions are compared to the actual labels, and are used to update the final layer weights through a backpropagation process.

	Focus epoch	Empathy epoch	Entire spectrogram
Training accuracy (avg)	65%	80%	70%
Testing accuracy (avg)	50%	50%	50%
Cross Entropy	2.32	0.64	1.67

Table 2. Results of Transfer Learning with Inception V3, showing cross entropy training accuracy of each method of transfer learning as well as the accuracy of each model in predicting an ADHD or non-ADHD subject.

SVM Analysis:

- The Scikit learn package was used for the SVM algorithm.
- A "leave one out" approach was used where one ADHD subject and one non-ADHD subject were left out to validate the model.
- The inputs for the SVM were an array of 7 elements, correlating to the average power of the different types of brain waves in order of frequency

	Focus epoch	Empathy epoch
Accuracy	65%	70%

Table 3. The percent accuracy of the SVM model on the focus and empathy epochs separately.

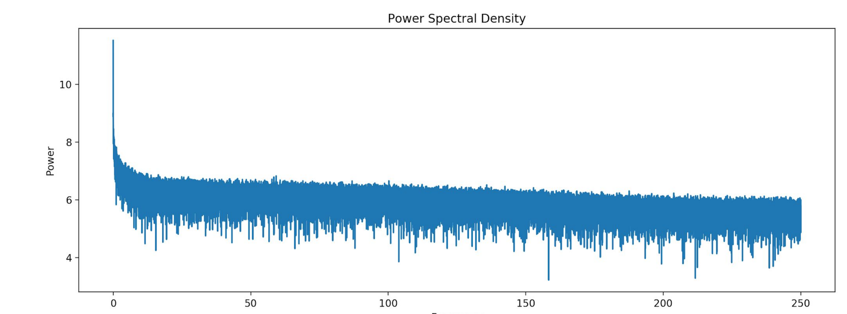

Figure 2: Graph of spectral power density across the many frequencies of EEG signals coming from the brain for an individual subject, where the SVM extracted features from this to make its predictions about whether an individual had ADHD or not.

Clustering Analysis:

- Both unsupervised and supervised learning were conducted on the same data used for the SVM.
- Hierarchical agglomerative clustering was used as a method of unsupervised learning, while the "leave one out" approach was used for supervised learning, using the average of the training data matrix.

Unsupervised Learning

	Focus	Empathy
Accuracy	50%	58.33%

Table 4. Percentage accuracy of the hierarchical agglomerative clustering algorithm, segmented into focus and empathy epochs

Supervised Learning

	Focus	Empathy
Accuracy	40%	90%

Table 5. Percentage accuracy of the supervised clustering algorithm, segmented into focus and empathy epochs

Logistic Regression Model to Predict ADHD

- Neurosteer's algorithms use wavelet transforms on the raw EEG signal collected using the company's proprietary hardware. The analysis outputs machine learning features from the EEG signal, called Brain Activity Features (BAFs) which are 121 orthogonal functions to the time signal found using the Coifman Wickerhauser Best Basis Method (Coifman, R. R., Wickerhauser, M. V., 1992), which correlate to different brain functionality. These BAFs show functionally connected areas of the brain that are not necessarily geographically connected. (Figure 3) (Intrator, 2018) (Hasson-Meir, et al, 2011)
- The data of every subject was segmented into focus and empathy epochs which would then be tested against each other using a t-test to see which of the 121 BAFs were active differently across the ADHD and control subjects.
- Many of the BAFs have been previously correlated to specific brain states by Neurosteer, and many of these correlated BAFs were active in a statistically different manner between the ADHD and control subjects during the focus and empathy epochs.
  - of these features 35-40 are correlated to the executive function, 20-60 are correlated to cognitive activity, and the combination of 1-12 and 112-121 were correlated to high stress and high emotions.
- The machine learning algorithm used the average of the activity levels of some of the statistically different features.
  - For the focus epoch the BAFs 32-34, 112-113, 118-121 were used.
  - For the empathy epoch the BAFS 6-13, 33-34, 39-40, 80-100, 101-111, and 112-121 were used.
- All 12 data points (6 control subjects and 6 ADHD subjects) were used to train the data.
- The model used a "leave one out" validation and achieved a 75% validation (43% standard deviation).
- With more subjects both models' accuracies should improve, providing more reliable models and a more reliable diagnosis measure.

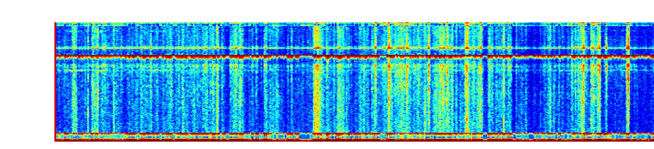

Figure 3: Neurosteer features and their activity levels (shown using color spectrum of red being very active and blue being very inactive). These features are extracted from raw EEG data using wavelet transform on the raw EEG signal and correspond to different functionally connected areas of the brain called Brain Activity Features (BAFs).

Statistical Analysis of the Adapted TEQ

- For the TEQ, scores were taken from the ADHD subjects as well as the control subjects. Their scores were then put into individual distributions, and t-tests were conducted on these distributions to show that there were differences between participants and video effects. Probability values (p-values) for the differences between the different distributions are given in the table below:

Table 6: Statistical test used with their respective p-values calculated and degrees of freedom.

Test-Name	p-value	Degrees of Freedom
Control pre-empathy vs. Control post-empathy	0.502	38
ADHD pre-empathy vs. ADHD post-empathy	0.664	10
Control pre-empathy vs. ADHD pre-empathy	0.439	24
Control post-empathy vs. ADHD post-empathy	0.523	24
Total pre-empathy vs.Total post-empathy	0.519	50

- The statistical test show that there was not a statistically significant difference between the empathetic responses of the ADHD and control subjects, additionally there was no difference between ADHD pre and post video as well as for control subject. This signifies that our empathy response was not as strong as we would have liked.

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Limitations of Study

- Due to a small sample size for both the ADHD test subjects and the control groups, our results cannot be accurately representative of the general public, and overfitting is a likely issue.
- There is randomness in the retraining process of Google Inception V3 which then results in variation in the accuracy and cross entropy.
- No cross validation was used in the logistic regression, so the results for that algorithm especially are preliminary.

Future Directions

- These results reflect preliminary testing and conclusions. The immediate next steps warranted by the current results are to expand the sample size to further validate conclusions and enhance accuracy. The transfer learning model will give more accurate results if the sample size is increased.
- High theta/beta ratios (TBR) have been acknowledged as possible markers for ADHD patients (Loo, Makeig 2012). While it has not been globally established as a diagnostic measure, it has been credited with prognostic diagnosis. We are in the process of refining both the research protocol and corresponding analytics, as well as, verifying whether the TBR can be correlated to other significant markers of ADHD.
- Default Mode Network (DMN) is a functional network that is active when an individual is at rest. During task engagement, the DMN is typically suppressed as the Task Positive Network takes over. The hypothesis that ADHD patients have diminished suppression of DMN during task engagement (Metin et al., 2015) is one that this project will also test in the future.
- Galvanic skin responses, such as heart rate, breathing rate, and blood pressure, can also be recorded to quantify empathy in subjects better.
- The Vagus Nerve Stimulation (VNS) may be tested as possible replacement for pharmaceutical intervention in ADHD.