EEG-Based Deep Neural Network Model for Brain Age Prediction and Its Association with Patient Health Conditions

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Introduction

Electroencephalogram (EEG) provides clinically relevant information for patient health evaluation and comprehensive assessment of sleep [1]. EEG-based indices have been associated with various health conditions and diseases, and hold promise as biomarkers for brain health [2]. Increase in age has been associated with a range of characteristics that exist within EEG signals recorded during sleep, such as: fragmented sleep with higher N1 sleep, reduced slow-wave sleep, reduced REM sleep, and decreased amount of sleep spindles and vertex waves [3]. Thus, EEG signals show potential for encoding the physiological information that, with the correct analysis, allows for the accurate assessment of age. Previous research have shown that the age of patients can be predicted from magnetic resonance images (MRI) with a mean absolute error (MAE) of 5 years [4] and from EEG with a MAE of 7.8 years [2]. The more the age assessment methodology is accurate, the more any deviation of the assessed age (brain age; BA) from the real age (chronological age; CA) can then be confidently utilized to provide deeper insights to supplement the current clinical evaluation paradigm and ultimately in better understanding and realizing individualized therapeutic pathways.

The Dataset

- The dataset contained adult patients of ages 18-85 years old.
- Train set: 126,241 polysomnography (PSG) studies.
- Validation set: 6,638 PSG studies
- Test set: 1,172 PSG studies
- The test set contained the following patient information and Patient-Reported Outcomes (PROs) :
  - Age
  - Sex
  - BMI
  - Apnea-hypopnea index (AHI)
  - Arousal Index (ArI)
  - Oxygen desaturation index (ODI)
  - Epworth sleepiness score (ESS)
  - Sleep efficiency (SE)
  - History of depression (yes/no)
  - Diabetes (yes/no)
  - Hypertension (yes/no)
  - Issues with memory and concentration (1-yes, 0-no)
  - History of epilepsy/seizures (yes/no)
  - History of strokes (yes/no)

Methodology

The AI Model

In order to predict the age of a patient from the EEG signals, a deep convolutional neural network (DCNN) was trained. The input to the model was the full night raw 8-channel EEG and electrooculogram (EOG) montage (6 EEG leads and 2 EOG leads), and the target output was the CA of the patients.

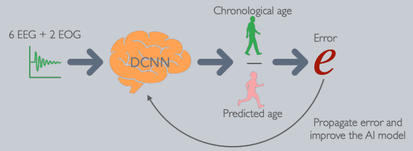

Figure 1. The Training Process. The DCNN model was trained to predict the CA of a patient. During each iteration, the model generates a prediction for the age based on the raw signals and optimizes an error function such that the predicted age will match the CA as much as possible.

The Brain Age Index

- The trained model can take a full night recording of 8 raw channels and output a prediction for the age of the patient.
- The predicted age (BA) together with the CA were used to derive representative indices that could be analyzed and correlated with different patient conditions.
- We've calculated the brain age index (BAI) using the following equation: $BAI = BA - CA$
- The BAI allows for the evaluation of the directionality of the deviation between the BA and CA.
- We've calculated the absolute brain age index (ABAI) using the following equation: $ABAI = |BA - CA|$
- The ABAI allows for the evaluation of patient populations that due to specific characteristics in their recorded signals, the model was not able to accurately predict their CA.

Results

Overall Performance of the Brain Age Model

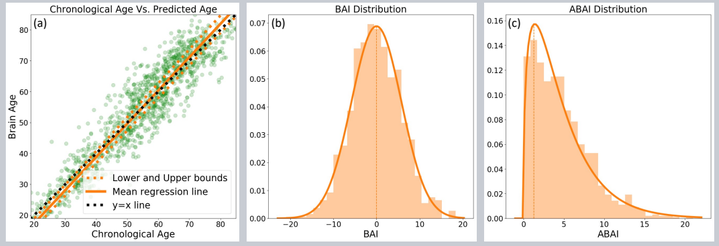

Figure 2. Overall regression performance and BAI/ABAI populations. (a) The brain age model produced a MAE value of 4.61 with a 95% bootstrap confidence interval (BCI) of [4.406, 4.811]. Furthermore, a Deming regression for the BA and CA comparison produced a mean slope value of 1.076 with a BCI of [1.056, 1.098] and a mean intercept value of -4.242 with a BCI of [-5.435, -3.1]. (b) The general population has a normally distributed BAI with a mean of -0.04 and a standard deviation of 5.8. (c) The general population has a gamma distributed ABAI with peak density at 1.29.

A Sample of Three Variable's BAI Population Comparisons

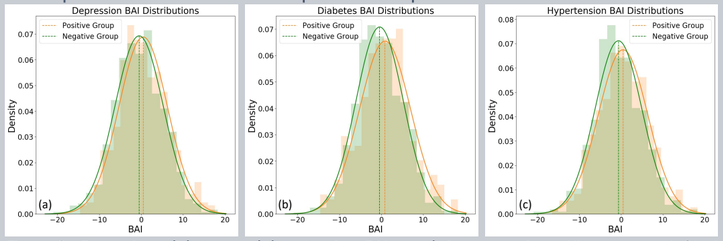

Figure 3. Depression, diabetes, and hypertension BAI population comparison. Histograms and fitted distributions of the BAI for each population group (see table 1 for a summary of the p-values and means of each distribution). A statistically significant shift between the populations was observed. (a) The orange distribution represents the depression group while the green distribution represents the no depression group. (b) The orange distribution represents the diabetes group while the green distribution represents the no diabetes group. (c) The orange distribution represents the hypertension group while the the green distribution represents the no hypertension group.

A Sample of Three Variable's ABAI Population Comparison

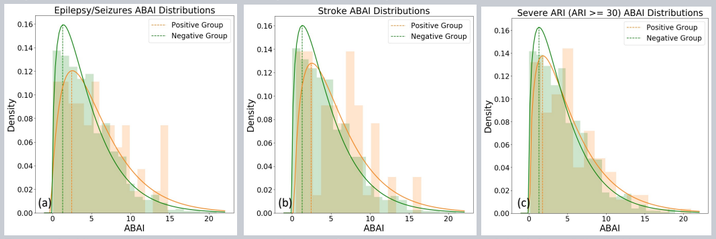

Figure 4. History of epilepsy/seizures, history of strokes, and severe ArI (ArI ≥ 30) ABAI population comparison. Histograms and fitted distributions of the ABAI for each population group (see table 1 for a summary of the p-values and means of each distribution). A statistically significant shift between the populations was observed. (a) The orange distribution represents the epilepsy/seizures group while the green distribution represents the no epilepsy/seizures group. (b) The orange distribution represents the strokes group while the green distribution represents the no strokes group. (c) The orange distribution represents the severe ArI group while the green distribution represents the no severe ArI group.

Summary of statistically significant binary variables for BAI/ABAI population comparison

Table 1. Distributions Summary. The positive mean BAI/ABAI and negative mean ABAI/BAI along with the p-value comparing the means of the negative and positive distributions for all binary variables that produced statistically significant results.

BAI				ABAI			
	Positive Mean BAI	Negative Mean BAI	P-VALUE		Positive Mean BAI	Negative Mean BAI	P-VALUE
Diabetes	0.881	-0.404	0.001	Low SE (SE <= 0.7)	5.028	4.194	0.000
Hypertension	0.461	-0.633	0.001	Severe ArI (ArI >= 30)	5.398	4.469	0.001
Depression	0.469	-0.496	0.004	Stroke	5.935	4.539	0.002
Low SE (SE <= 0.7)	0.368	-0.453	0.015	Epilepsy/Seizures	5.815	4.552	0.009
ESS (Epworth Score >= 16)	0.866	-0.209	0.021	Severe ODI (ODI >= 30)	5.063	4.507	0.034
Memory and Concentration	0.415	-0.285	0.049				

BAI/ABAI ordinary least squares (OLS) analysis

Table 2. OLS summary. We ran all variables through an OLS model where each time one variable was varied while all other variables were controlled for. The table summarizes the effect (in terms of percent standard deviation where the sign signifies the directionality of the relationship between each variable and the BAI/ABAI) and the p-value for all variables that produced statistically significant results.

BAI			ABAI		
	Effect [%STD]	P-VALUE		Effect [%STD]	P-VALUE
Depression	19.6%	0.0022	ArI	0.83%	0.0000
Diabetes	16.7%	0.0134	Low SE (SE <= 0.7)	21.5%	0.0005
Hypertension	14.7%	0.0225	Severe ArI (ArI >= 30)	23.7%	0.0041
ESS (Epworth Score >= 16)	17.5%	0.0301	Stroke	36.4%	0.0062
SE	-39.7%	0.0372	Epilepsy/Seizures	36.8%	0.0077
Low SE (SE <= 0.7)	12.3%	0.0431	ODI	0.36%	0.0078
BMI	0.64%	0.0504	AHI	0.36%	0.0084

Conclusion

- We show the power of AI's potential to exceed human capabilities and perform tasks that humans cannot. While clinicians can only grossly estimate or quantify the age of a patient based on their EEG, this study shows an AI model can predict a patient's age with high precision.
- The model's precision enables shifts in the predicted age from the chronological age to express correlations with major disease families and comorbidities.
- Since the AI model was trained to predict age, an objective value that is not subject to label noise, any divergence of the prediction from the target output is associated with either signal artifact in the input data or other underlying physiological conditions. This presents the potential for identifying novel clinical phenotypes that exist within physiological signals utilizing AI model deviations.

Future Work

- Analyze additional patient health disorders and examine their association with the BAI and ABAI.
- Attempt to achieve a larger separation between healthy and diseased population such that a range of normal and abnormal values of BAI and ABAI could be defined and leveraged in order to affect the patients' individualized diagnostic and therapeutic pathways.
- Overall, the results in this study provide initial evidence for the potential of utilizing AI to assess the brain age of a patient. Our hope is that with continued investigation, research, and clinical studies, a brain age index will one day become a diagnostic biomarker of brain health, much like high blood pressure is for risks of stroke and other cardiovascular disorders.

References

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