Is Brain Age Malleable to Sleep Apnea Therapy? An Exploratory Positive Airway Pressure Titration and Machine Learning-based Brain Age Study

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Introduction

Machine learning (ML) techniques are increasingly redefining the landscape of sleep medicine by enabling the extraction of novel biomarkers from complex physiologic data. Among these is the ML-derived Brain Age Index (BAI), which quantifies the deviation between a person's predicted brain age (BA), inferred from sleep EEG signals, and their chronological age (CA).

Prior research has established associations between elevated BAI and a range of disease states, suggesting that accelerated brain aging during sleep may serve as a signal of systemic and neurological dysfunction. However, it remains unknown whether BAI is modifiable in response to clinical interventions.

PAP therapy is known to improve sleep EEG metrics and cognitive performance in OSA patients, but its impact on BAI has not been studied. Addressing this gap could position BAI as a treatment-response biomarker.

Methodology

We performed a comprehensive analysis of the impact of Positive Airway Pressure (PAP) therapy on BAI and sleep architecture. A deep neural network model was trained on a dataset of 54,000 polysomnography (PSG) studies to predict patients' BA.

Additionally, a real-world dataset of 4,686 split-night PSG studies was collected, where patients underwent the first half of the study without PAP therapy and transitioned to PAP therapy midway through the night.

For each patient, split-night polysomnography was used to quantify sleep architecture (Wake, N1, N2, N3, REM) and derive BAI before and during PAP therapy.

The analysis included histograms and density estimates of age and BAI distributions, as well as regression analysis to compare the predicted brain age to the chronological age. Sleep architecture was summarized using bar plots with means and 95% confidence intervals to compare sleep stage percentages between pre-PAP and PAP periods, and Ordinary Least Squares (OLS) regression was used to model BAI as a function of PAP treatment and sleep stage percentages.

Results

Demographics

The cohort ranges from approximately 20 to 90 years, with a peak between ages 50 and 70, ensuring broad demographic representation for sleep analysis, (see Figure 1). Males comprise ~60% of the population, while females represent ~40%, reflecting the typical sex ratio in sleep study cohorts.

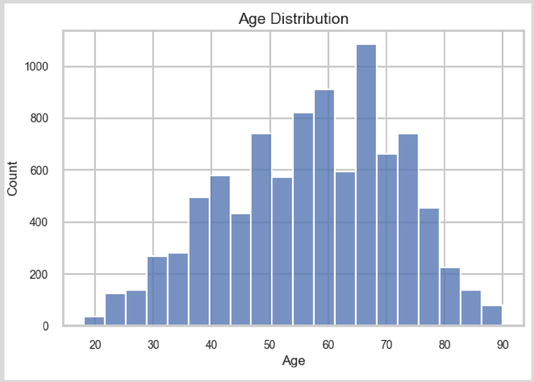

Figure 1. Age Distribution. Histogram displaying the age distribution of the study population.

BAI Distributions

The BAI distributions for pre-PAP and PAP periods largely overlapped but showed a slight leftward shift during PAP, suggesting potential BAI improvement, (see Figure 2).

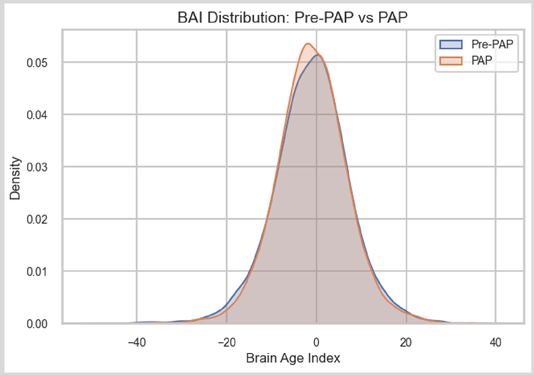

Figure 2. Brain Age Index (BAI) Distribution: Pre-PAP vs PAP. Density plot comparing BAI before and during PAP therapy.

Deming Regression

The Deming regression analysis compares between BA and CA for both the pre-PAP and PAP periods.

It can be noticed that for the PAP period, the slop is a bit closer to 1 and the intercept is lower, suggesting that a better alignment between BA and CA could be achieved with PAP therapy.

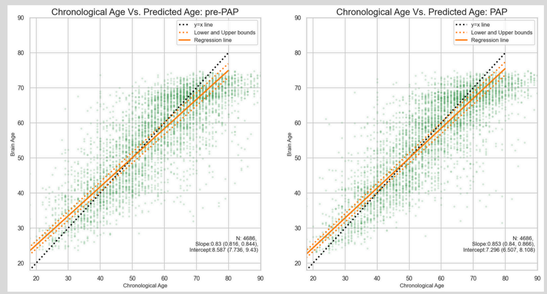

Figure 3. Chronological Age vs. Predicted Age. Scatterplots with Deming regression lines comparing predicted brain age to chronological age for pre-PAP (left) and PAP (right) periods. The regression lines, confidence bounds, and y=x reference line help visualize model calibration and any global differences between the pre-PAP and PAP portions of the studies.

Sleep Architecture

Significant differences were observed in sleep stage distributions: wake percentage decreased, and REM percentage increased with PAP therapy, indicating improved sleep continuity and architecture (see Figure 4).

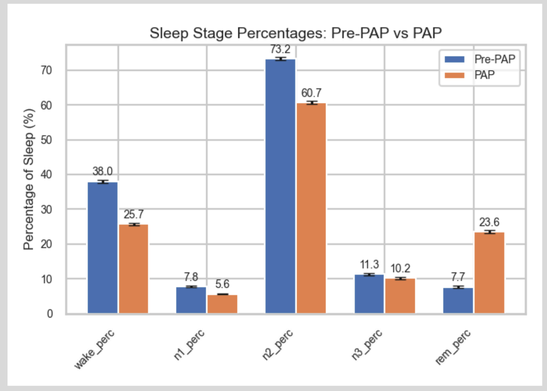

Figure 4. Brain Age Index (BAI) Distribution: Pre-PAP vs PAP. Bar plot comparing BAI before and during PAP therapy.

OLS Analysis

The OLS model demonstrated that PAP therapy was associated with a statistically significant reduction in BAI (coefficient = -0.61, p = 0.004), with several sleep architecture variables also showing significant associations (see Table 1).

PAP therapy was coded as 0 (Pre-PAP) and 1 (PAP).

The negative PAP coefficient indicates that, controlling for sleep stage percentages, mean BAI decreased by 0.61 units with PAP therapy.

This suggests that PAP therapy may help reverse or slow EEG-detected brain aging.

While this change is modest (roughly 7 months younger brain age), it is valuable given that prior studies suggest that even small BAI increases have been linked to reduced cognitive function and lifespan.

Predictor	Coefficient	p-value
PAP	-0.6131	0.004
% Wake	-2.8348	<0.001
% N1	4.7070	<0.001
% N2	-1.9445	<0.001
% N3	-2.1185	0.001
% REM	0.8334	0.234

Table 1. OLS Analysis Results. The analysis models BAI as a function of PAP treatment and sleep stage percentages.

Conclusions

The OLS analysis, controlling for sleep-related metrics, as well as the BAI distribution plot and Deming regression analysis, demonstrated improvements in BAI with initiation of PAP therapy.

This suggests BAI is "malleable" and responsive to therapies that improve sleep and thus highlights its value as a potential biomarker of brain health.

Overall, the study encourages further research into biomarkers for studying the neurocognitive benefits associated with Obstructive Sleep Apnea treatment.