Redefining Positive Airway Pressure Adherence Phenotypes Utilizing Deep Neural Networks and Unsupervised Clustering

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Introduction

Improving positive airway pressure (PAP) adherence is crucial to obstructive sleep apnea (OSA) treatment success. Behavioral and technical interventions such as patient outreach, coaching, troubleshooting, and resupply may be deployed to positively impact adherence. In order to fully leverage these methods of interventions, it is critical to detect early signs and risks of non-compliance to trigger early outreach. We have previously shown the potential of utilizing Deep Convolutional Neural Network (DCNN) models to accurately forecast future PAP usage, based on predefined compliance phenotypes, to enable early patient outreach and interventions. These phenotypes were limited, based solely on usage patterns. We propose an unsupervised learning methodology for redefining these adherence phenotypes in order to assist with the creation of more precise and personalized patient categorization.

The Dataset

- The dataset contained 10,273 patients.
- 455 days of PAP usage were recorded for each patient.
- Furthermore, the dataset contained the age, sex, and apnea-hypopnea index (AHI) for each patient.

The Rating System

- Split 30 days of usage data into 10-day groupings.
- The mode of each group was labeled with one of the following ratings:
  - A: >4 hours of usage.
  - B: <4 hours of usage.
  - C: 0 hours of usage.
- Overall, 30 days of usage can now be represented by a three-letter group.
- This rating system produces overall 10 different group combinations.

The Phenotypes

We've previously defined four different phenotypes based on the 10 different rating combinations as followed:

Table 1. The four phenotypes. Definitions of the four phenotypes based on the rating combinations.

Phenotype	Score	Rating Combination
Good User	3	AAA, AAB
Variable User	2	AAC, ABB, ABC, BBB
Occasional User	1	ACC, BBC, BCC
Non-User	0	CCC

In this study we strived to challenge these four group definitions and attempt to redefine them based on an unsupervised clustering algorithm.

Methodology

The AI Model

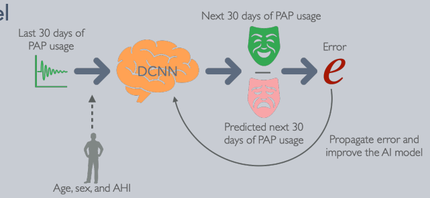

Figure 1. The Training Process. The DCNN model was trained to predict the next 30 days of PAP usage based on the previous 30 days of PAP usage. During each iteration, the model generates a prediction for the next 30 days based on the previous and optimizes an error function such that the predicted next 30 days of PAP usage will match the actual recorded next 30 days of PAP usage as much as possible. The prediction can then be converted to one of the defined phenotypes. In addition, the age, sex, and AHI of each patient can be used as well in order to improve overall performance and allow for a more personalized outreach triggering.

Principal Component Analysis (PCA)

PCA is a dimensionality reduction method that is usually used in exploratory data analysis. The PCA algorithm transforms the features of data samples into their orthonormal, linearly uncorrelated components thus, allowing the data to be projected onto their first n principal components. This enables high dimensionality data to be visualized in a more intuitive feature space (such as 2D or 3D space).

Hierarchical Density-Based Spatial Clustering of Applications with Noise (HDBSCAN)

HDBSCAN is an unsupervised clustering algorithm which can take a large amount of data samples with m number of features and find meaningful structures in the data thus, clustering them into j unique clusters. These clusters can then be associated with known characteristics of the analyzed data and allows for the samples to be gathered into meaningful groups based on their unique features.

Results

The Ratings and Phenotypes in 2D

We sampled 10,000 samples each containing 30 days of usage data. We then ran all samples through a PCA algorithm which allowed us to visualize them in a 2D plane.

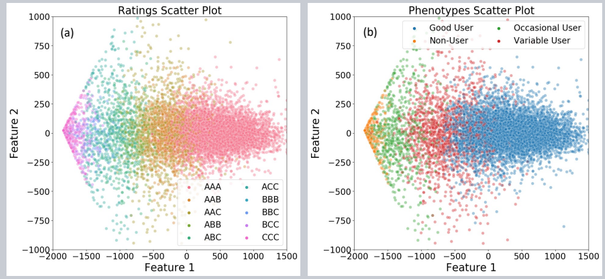

Figure 2. Visualization of the ratings and phenotypes. (a) A scatter plot of all samples color coded with the rating of each sample. (b) A scatter plot of all samples color coded with the phenotype of each sample.

We then ran all 10,000 samples through an HDBSCAN algorithm. One of the main advantages of HDBSCAN is that it can determine the number of clusters in the data without needing to predefine the number of clusters beforehand (as appose to other clustering algorithms like K-Means which requires the user to specify the number of clusters as a parameter of the algorithm). This allowed us to redefine the phenotypes such that they match the output of the HDBSCAN algorithm.

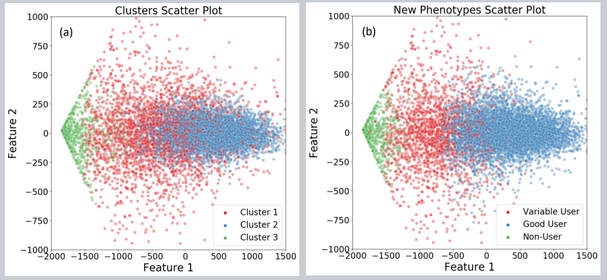

Figure 3. Visualization of the clusters and new phenotypes. (a) A scatter plot of all samples color coded with the 3 different cluster labels. (b) A scatter plot of all samples color coded with the new phenotype of each sample.

Redefining the Phenotypes

The clustering algorithm revealed that only three main phenotypes exist (good users, variable users, and non-users) which are defined in table 2.

Table 2. The new three phenotypes. Definitions of the new phenotypes based on the clustering algorithm.

Phenotype	Score	Rating Combination
Good User	2	AAA, AAB
Variable User	1	AAC, ABB, ABC, BBB, ACC
Non-User	0	BBC, BCC, CCC

The Effect of Patient Metadata on Phenotype Forecasting

We trained our model utilizing the usage data together with the age, sex, and AHI of each patient to forecast the phenotype for the next 30 days of PAP usage. We've observed an increase in performance compared to our previously published results.

Table 3. Phenotype forecasting. Confusion matrix for the forecasting of the four phenotypes utilizing both the PAP usage data and the additional patient information.

	Non-User	Occasional User	Variable User	Good User
Non-User	117,361	5,228	733	0
Occasional User	3,809	39,553	9,669	503
Variable User	125	7,370	87,831	15,668
Good User	0	1	15,996	503,158
Sensitivity: 93%, Specificity: 96%, Accuracy: 96%				

The Effect of the New Phenotypes on Phenotype Forecasting

We then analyzed the same model once more using the new phenotype definitions and received a further increase in the sensitivity of the model.

Table 4. New phenotype forecasting. Confusion matrix for the forecasting of the three new phenotypes utilizing both the PAP usage data and the additional patient information.

	Non-User	Variable User	Good User
Non-User	134,420	8,655	0
Variable User	2,464	126,120	16,171
Good User	0	15,997	503,158
Sensitivity: 95%, Specificity: 96% , Accuracy: 96%			

Conclusion

- In this research, we have shown that by utilizing historical PAP usage patterns along with additional patient information we can identify PAP specific adherence phenotypes and improve overall patient phenotype forecasting.
- This allows focus of PAP adherence program resources to be targeted early on patients susceptible to treatment non-adherence.
- The transition between the phenotypes (variable users) can also indicate when personalized intervention is necessary to maximize treatment success and outcomes.
- Lastly, providers can transition patients in the highly non-compliant group more quickly to alternative therapies.