# Validity of Neural Network in Sleep Apnea

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**Summary.** Clinical assessment of obstructive sleep apnea (OSA) is poor. Overnight polysomnography (OPG) is the standard reference test, but it is expensive and time-consuming. We developed an artificial neural network (ANN) using anthropomorphic measurements and clinical information to predict the apnea-hypopnea index (AHI). All patients completed a questionnaire about sleep symptoms, sleep behavior, and demographic information prior to undergoing OPG. Neck circumference, height, and weight were obtained on presentation to the sleep center. Twelve variables were used as inputs. The output was an estimate of the AHI. The network was trained with a back-propagation algorithm on 189 patients and validated prospectively on 80 additional patients. Data from the derivation group was used to calculate the 95% confidence interval of the estimated AHI. Predictive accuracy at different AHI thresholds was assessed by the c-index, which is equivalent to the area under the receiver operator characteristic curve. The c-index for predicting OSA in the validation set was 0.96 ± 0.0191 SE, 0.951 ± 0.0203 SE, and 0.935 ± 0.0274 SE, using thresholds of >10, >15, and >20/hour respectively. The actual AHI of the 80 patients in the validation data set fell within the 95% confidence limits of the values predicted by the ANN. This study suggests that ANN may be useful as a predictive tool for OSA.
**Key words:** Artificial neural network; classification and regression tree; sleep apnea; apnea/hypopnea index; c-index

OBSTRUCTIVE SLEEP APNEA (OSA) has been recognized increasingly as an important public health problem with potentially serious cardiovascular and psychomotor morbidity and possibly excessive mortality.[1,2] The increased awareness of the risks associated with OSA in recent years has led to a rise in the number of referrals to specialists and sleep laboratories. In the absence of an accurate and validated screening test, the gold standard for the diagnosis of OSA remains the overnight polysomnograph. Overnight polysomnography is an expensive, labor-intensive, and time-consuming procedure. As a result, there has been considerable interest in developing a practical and less work-intensive screening test to allow physicians to estimate, with a certain probability, whether patients have sleep apnea.[3-7]

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Questionnaire-based prediction models[4-8] have identified a number of physical features and clinical traits indicative of high risk for OSA. Several studies[9-11] have developed regression models using these variables to produce sleep apnea prediction rules that can be applied to individuals with features suspicious for OSA. These rules, however, lack specificity, and offer only a dichotomous output based on a predetermined cutoff value of apnea/hypopnea index (AHI). The cutoff values chosen are arbitrary, and vary from one study to another. Moreover, the statistical methods utilized in the derivation of these models may not take full advantage of the complex relation of behavioral processes with nonlinear attributes. In areas of complex interactions, the artificial neural network (ANN) has been found to be a more appropriate alternative to linear, parametric statistical methods due to its inherent property of seeking information embedded in relations among variables thought to be independent.

Implementation of neural networks to medical specialties has been found to be extremely helpful in assisting physicians in clinical diagnosis.[12,13] In particular instances,

the networks have outperformed physicians in predicting clinical outcome.[14] In this study, we have attempted to develop and validate a neural network using anthropomorphic measurements and clinical information obtained from patient's questionnaire to predict AHI.

## METHODS

### Study Population

All patients referred to the Sleep Center at Buffalo General Hospital between November 1995 and August 1996 were identified retrospectively from the registration records and represented the derivation cohort. The majority of patients were referred by internists (54%), internal medicine subspecialists (36%), or ear, nose, and throat surgeons (7%) for suspicion of sleep apnea. Two hundred ninety three sleep studies were performed during this period. Patients were excluded from the study if they had been previously treated for sleep apnea, if they were referred for a specific sleep disorder other than sleep apnea, or if they failed to complete the sleep study. A questionnaire related to sleep symptoms and motor functions was filled out by all patients prior to undergoing overnight polysomnography. Demographic information (age, gender) and anthropomorphic measurements (neck circumference, height, and weight) were obtained on presentation to the Sleep Center.

### Questionnaire

A questionnaire was administered to each patient addressing a range of clinical variables thought to contribute or to raise suspicion of sleep apnea. Nineteen questions were subjected to detailed analysis. The questions had a six-item Likert response with the following options: never (or strongly disagree), rarely (or disagree), sometimes (or somewhat agree), frequently (somewhat agree), always (strongly agree), and not sure (or not applicable). The presence of hypertension and the amount of alcohol ingestion were determined by patient's self-report.

### Sleep Studies

Overnight polysomnography was conducted on all patients enrolled in the study at the Sleep Center of the Buffalo General Hospital. Continuous electroencephalogram, electrooculogram, electrocardiogram, and submental electromyogram were recorded on a 16-channel polygraph, and digitized on a computerized system (Aequitron Medical, Minneapolis, Minn). Airflow was measured by the sum of oral and nasal thermistor signals (Graphic Control, Buffalo, NY). Arterial oxyhemoglobin saturation was measured with a pulse oximeter with the probe placed on the patient's finger (Biox IIA or 3700, Ohmeda, Louisville, Colo). Abdominal wall and ribcage motions were recorded with an inductive plethysmograph (Respitrace Corporation, Ardsley, NY). A 3-minute period of quiet breathing was observed at the beginning of the study to establish a reference for airflow amplitude.

Sleep stages were scored in 30-second epochs using the Rechtschaffen and Kales sleep scoring criteria.[15] Each epoch was analyzed for the number of apneas, hypopneas, arousals, oxyhemoglobin desaturation, and disturbances in cardiac rate and rhythm. Apnea was defined as a reduction in airflow of >80% at the nose and the mouth for at least 10 seconds. Hypopnea was defined as a 50% reduction in oronasal airflow associated with either a 4% or greater decrease in oxygen saturation, or an arousal. Arousal was defined according to the recent ASDA position paper.[16] The record was scored manually by a polysomography technician and reviewed by a physician certified in sleep medicine. The number of apneas and hypopneas per hour of total sleep time was derived, and reported as the apnea-hypopnea index (AHI). A positive sleep study for sleep apnea was defined as a AHI >10/hour, and other thresholds were also considered (>15 or >20/hour) to determine the effect of altering the definition on the diagnostic accuracy of the predictive models.

### Analytical Methods

Descriptive statistics for continuous variables were expressed as mean ± 1 SD. Difference in mean values was assessed using Student's *t* test. All tests were two-tailed, and statistical significance was set at a p value of less than 0.05. Commercially available software were used for the multiple linear regression and regression tree (S-Plus, Statsci, Seattle, Wash), artificial neural networks (Neuroshell 2, Ward Systems, Frederick, Md), and for confidence interval analyses (CIA, British Medical Journal, London, UK). A logarithmic transformation of AHI was used for both the ANN and the multiple linear regression in order to achieve a normal distribution of residuals.

**Artificial Neural Networks.**—The variables used as inputs for the ANN were selected from the list of items obtained from the patient's questionnaire and anthropomorphic measurements. We used the classification and regression tree to choose those variables more likely to influence the predictive properties of the ANN. Because logistic regression models sometimes perform better than a decision tree,[17] a logistic regression was also performed to identify predictor variables. The continuous variables were transformed on a linear scale to a value over a range between -1 and 1. The responses to the Likert scale were processed as ordinal data, and were spaced equally at intervals of 0.5 over this range. The response to the hypertension question was entered as a dichotomous value, -1 for absent, and 1 for present. Missing values and responses marked as "not applicable" were substituted with the class

mean.

The ANN described in this study was based on three layers: an input layer with 12 nodes, an output layer with a linear function, and a hidden layer. The hidden layer consisted of a direct connection between the input and the output layers, and two groups of 21 nodes with differing activation functions.[18] The activation function describes the nature of the linkage between the input layer and the hidden layer. A Gaussian function was used for one group and a hyperbolic function (tanh) for the other. Connections and outputs from the two groups in the hidden layer were linked to the output layer by linear functions. Each link was assigned a coefficient or weights that was updated during the learning process. The weights are assigned initially at random between -0.6 and +0.6.

The ANN is exposed to a training set during which the net is presented with a set of input and output patterns. During the training phase, the inputs are fed into the network and the corresponding outcome is computed. The difference between the actual and desired outcome is propagated backward. Adjustments to the connection weights are made to minimize the error between the output predicted by the ANN and the measured AHI. During training, the ANN is tested at regular intervals to determine the prediction error on a subset of data (evaluation data set) that is not included in the training process. As training proceeds, the prediction error on the evaluation data set decreases initially but then increases when overtraining occurs. The ANN that produced the smallest error is retained for further analysis.

A tenfold cross-validation approach was used for evaluation.[19] The entire data set of 189 patients was divided with a random number generator into ten subsets. Nine out of the ten subsets was pooled and used for training. The data from the tenth subset was used as an evaluation set during training. The entire process was repeated nine additional times by rotating the subset used as the evaluation set during training. The mean square error was computed for each of the 10 neural networks on the entire derivation data set. The mean square errors were averaged and the ANN that had a mean square error closest to the average was selected.

A multiple linear regression was employed to develop a model of AHI score based on the same independent variables used in the ANN. Interaction terms were not included to determine the extent to which nonlinearities and interaction terms contributed to the predictive accuracy of the ANN.

**Performance evaluation.**—The predictive model derived from the ANN was tested on an entirely different set of patients (validation cohort) that were not included in the derivation set. The validation cohort comprised all patients who underwent a sleep study between September 1996 and December 1996.

**Predictive properties of the artificial neural network.**—A receiver operator characteristic (ROC) curve[20] was generated for the ANN. The ROC curve represents a graphic display of the true positives (sensitivity) plotted against the false positives (1-specificity) for various thresholds that are used to define sleep apnea. The c-index was used to estimate diagnostic accuracy by a method described in detail elsewhere.[21] The c-index is equivalent to the area under the ROC curve. In brief, it is calculated by determining the probability of diagnosing sleep apnea correctly in every possible pair of patients: one who has sleep apnea, the other who does not. A bootstrap method was used to calculate directly this measure of accuracy by generating 1000 data sets from our database by random sampling with replacement. Comparisons between the c-index for both models were assessed based on the confidence intervals. Statistical significance was accepted at the 5% level.

To determine the predictive performance of the ANN, the relation between the actual and predictive values of the AHI were compared by linear regression. The pointwise 95% confidence limits of that linear regression were used to establish the confidence interval of the predicted AHI. Comparison between the predictive accuracy of the ANN and multiple linear regression was made with correlation coefficients. The correlation coefficient was calculated from the actual values of AHI in the derivation data set and the values predicted by the ANN and compared with the correlation coefficient from the corresponding values obtained by multiple linear regression.

## RESULTS

Between November 1995 and December 1996, 289 sleep studies were performed at the Sleep Center. Twenty were excluded from further analysis: 12 patients were already diagnosed with sleep apnea, 6 patients were referred for a evaluation of sleep disorder other than sleep apnea, and 2 patients did not complete the sleep study. The derivation cohort was comprised of 189 patients, 66% males and 34% females. There were no significant differences in age, gender ratio, body mass index, or neck circumference of patients of the derivation data set compared with the validation data set (Table 1).

Even accounting for the greater number of men than women in the cohort, there was a predominance of sleep apnea among males (chi-square Yates corrected p=0.022). The age ranged from 14 to 95 years, with a mean of 48.1±12.1 for those with sleep apnea and 47.0±14.8 for those without sleep apnea (p=0.2) (Table 2). Fifty-eight (31%) were found to be nonapneic (AHI 0-10), 23 (12%) to have mild obstructive sleep apnea (AHI 11-20), 28(15%) to have moderate sleep apnea (AHI 21-40), and 80 (42%) to have severe sleep apnea (AHI>40). Patients with sleep

Table 1.—Demographics of the derivation and validation cohort.

| | Derivation cohort (n=189) | Validation cohort (n=80) |
|---|---|---|
| AGE ± SD (years) | 47.9 ± 13.0 | 47.9 ± 11.2 |
| GENDER (M:F) | 1.95:1 | 2.07:1 |
| BMI ± SD (kg/m²) | 35.4 ± 9.2 | 34.4 ± 9.0 |
| NC ± SD (cm) | 41.6 ± 5.8 | 41.9 ± 5.2 |

No significant differences detected

apnea were significantly more obese ($p<0.01$) and had a larger neck circumference ($p<0.01$) than their nonapneic counterparts (Table 2). The validation cohort consisted of 80 patients—54 males (68%) and 26 (32%) females. Eighty one percent of respondents had no missing data. The number of respondents missing one, two, three, or four apnea symptoms items were 32 (13%), 12 (6%), 2 (0.7%), and 1 (0.3%), respectively.

## Artificial Neural Network

Nine of 19 independent variables were selected in the final construction of the classification and regression tree. Six of the 19 independent variables of the logistic regression had coefficients that were statistically significant. Three of the six were not present in the classification and regression tree. Therefore, 12 variables were used as inputs to the ANN: nine from the classification and regression tree, and three additional variables from the logistic regression analysis. The questions to which responses were deemed to have significant predictive power for sleep apnea by the classification and regression tree and by logistic regression analysis are listed in Table 3. Only body mass index, neck circumference, and episodes of apneic events during sleep were parameters common to both analyses.

The average of the mean square error of the ten ANNs performed was 0.089 (range 0.174-0.023). The ANN selected for this study had a mean square error of 0.092. The correlation coefficient from the ANN's predicted values of AHI and the actual values in the derivation set was 0.856. The corresponding correlation coefficient for the multiple linear regression with the same predictor variables was 0.509. This was significantly less than the correlation coefficient obtained with the ANN ($p<0.01$).

The performance of the ANN using a dichotomous definition of the OSA is shown in Fig. 1 for the derivation data set as ROC curves. The c-index, which is equivalent to the area under the curve, was 0.946±00151SE,

Table 2.—Comparison between patients with and without sleep apnea

| | DERIVATION COHORT (N=189) | | VALIDATION COHORT (N=80) | |
|---|---|---|---|---|
| | Sleep Apnea (n=131) | No Sleep Apnea (n=58) | Sleep Apnea (n=51) | No Sleep Apnea (n=29) |
| AGE ± SD (years) | 48.6 ± 12.2 | 47.1 ± 14.9 | 47.6 ± 11.1 | 48.3 ± 11.4 |
| BMI ± SD (kg/m²) | 36.7 ± 9.0 | 32.3 ± 8.2* | 37.5 ± 8.9 | 28.7 ± 5.9* |
| NC ± SD (cm) | 43.1 ± 5.6 | 38.4 ± 4.5* | 43.8 ± 4.6 | 38.3 ± 4.0* |
| AHI ± SD | 61.3 ± 40.6 | 4.1 ± 3.0 | 52.5 ± 33.4 | 4.0 ± 3.3 |

(* indicates $p<0.01$ when those subjects with sleep apnea are compared to those with no sleep apnea)

Table3.—Variables selected by CART and stepwise logistic regression

CART variables
1. Response to "I am told I stop breathing in my sleep."
2. Response to "I feel tired upon awakening and want to go back to sleep."
3. Response to "My desire or interest in sex is less than it used to be."
4. Response to "At night, my sleep disturbs my bed partner's sleep."
5. Response to "I am very sleepy during the daytime and struggle to stay awake."
6. Response to "I have or have been told that I have restless legs."
7. Body mass index.
8. Neck circumference.
9. Age.

Logistic regression variables
1. Response to "I am told I stop breathing in my sleep."
2. Response to "I suddenly awake gasping for breath during the night."
3. Response to "I am told I snore in my sleep."
4. Response to "Do you have or are you being treated for high blood pressure?"
5. Body mass index
6. Neck circumference

Variables not selected
1. Response to "Falling asleep while engaged in an activity"
2. Response to "Falling asleep while in a quiet, passive, or relaxing situation"
3. Response to "I have had accidents or near accidents while operating a motor vehicle"
4. Response to "I have difficulty falling asleep"
5. Response to "When I awaken during the night, I have difficulty falling back to sleep"
6. Gender
7. Amount of alcohol ingestion.

Table 4.—The sensitivities, specificities, positive predictive values, and negative predictive values for the neural network prediction in the derivation set using AHI of 10, 15, and 20 as cutoff value for definition of sleep apnea

| AHI | Sensitivity (95% CI) | Specificity (95% CI) | PPV (95% CI) | NPV (95% CI) |
|---|---|---|---|---|
| 10 | 94.9% (89.9%-97.9%) | 64.7% (50.1%-77.6%) | 87.9% (82.7%-93.2% | 85.2% (67.2%-92.7%) |
| 15 | 95.3% (90.2% -98.3%) | 60.0% (46.5%-72.4%) | 83.7% (77.7%-89.6%) | 85.7% (71.5%-94.6%) |
| 20 | 95.5% (89.7%-98.5%) | 73.4% (62.3%-82.7%) | 83.3% (76.8%-89.8%) | 92.1% (82.4%-97.4%) |

PPV = Positive Predictive Value
NPV = Negative Predictive Value

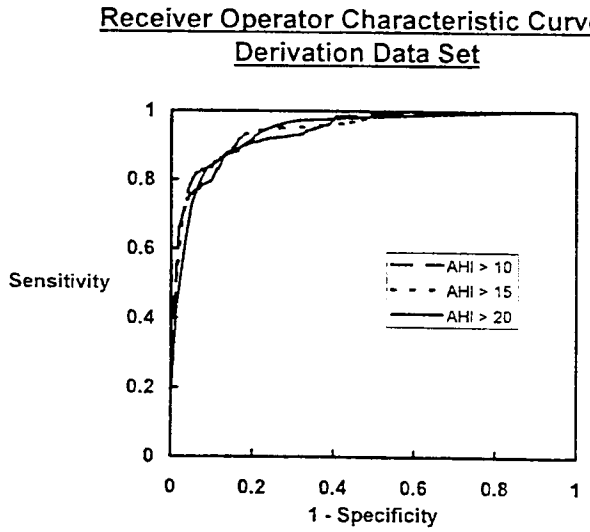


Figure 1.—Comparison of ROC curves of the artificial neural network for the derivation data set.

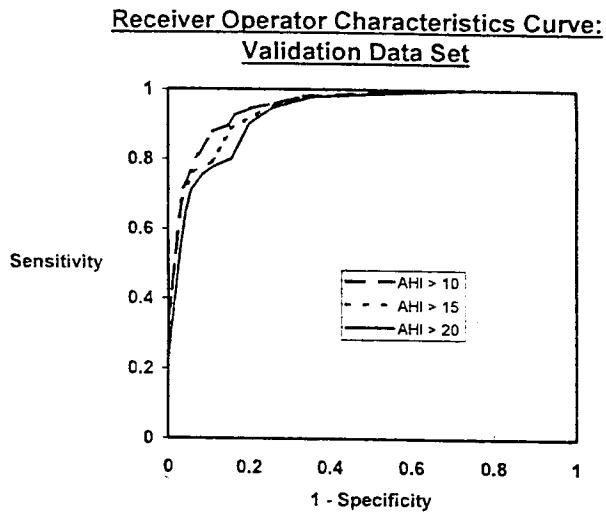


Figure 2. —Comparison of ROC curves of the artificial neural network for the validation data set.

0.948±0.0149SE, and 0.944±0.0159SE when OSA is defined as an AHI >10, 15, and 20/hour, respectively. There were no statistically significant differences between these c-indices. Table 4 provides the sensitivity, specificity, positive predictive value, and negative predictive value for each of the AHI value selected. Similarly, the performance of the ANN using a dichotomous definition of OSA is shown in Fig. 2 for the validation data set as ROC curves. The c-index was 0.96±0.0191 SE, 0.951±0.0203 SE, and 0.935±0.0274 SE when OSA is defined as an AHI of >10, >15 and >20/hour, respectively. There were no statistically significant differences between these c-indices or with the corresponding c-indices obtained with the derivation data set.

Figure 3 shows the relation between the predicted and actual values of AHI for the patients in the validation data set together with the pointwise 95% confidence limits. Only one of the 80 values (1.25% 95% CI:0-6.7%) fell outside of the 95% confidence limits.

## DISCUSSION

With the advances in computer technology, neural networks have emerged as a powerful tool in analyzing correlation among variables with nonlinear attributes. We have seen recently an increasing trend of the use of artificial neural networks in medicine and surgery in predicting outcomes.[14,22-24] To our knowledge, previous neural networks to predict sleep apnea have been described only in abstract form. Chafin et al[25] developed two neural networks with age, gender, body mass index, the complaint of excessive daytime somnolence, and snoring as inputs. One of the networks had oxygen saturation added to the inputs. The areas under the ROC for the networks with and without oximetry data were 0.892, and 0.868, respectively. Validation of the predictive ability of the networks was not presented. In addition, their ANN predicted the presence or absence of OSA rather than the AHI.

The present study is the first to present a validated ANN to predict sleep apnea that uses a combination of

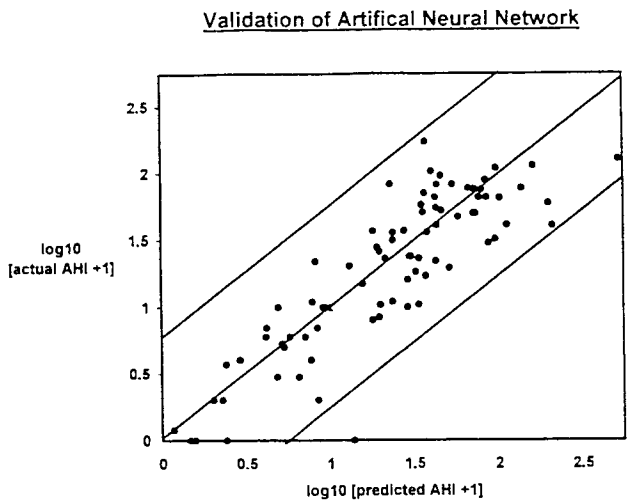


**Figure 3.**—Relation between the actual and ANNs predicted values of AHI for the validation data set (closed circles). The lines represent the mean and 95% confidence intervals for pointwise estimation of the actual values.

anthropomorphic data and clinical information obtained from a simplified questionnaire. The majority of the indices presented to the network have been shown in previous studies[3,4,10] to be significant clinical predictors of sleep apnea, but none were discriminating enough by themselves to make accurate predictions.

It is not surprising that this study has demonstrated a higher performance and an improved accuracy of the ANN compared with other methods for prediction of clinical outcome. The relations between variables that have been shown to predict sleep apnea are unclear. The relations describe which factors are relevant to decision-making but not precisely how they might be used in a comprehensive manner. In logistic regression analyses, the predictor variables not contributing significantly to the fit are ignored. Interactions are not readily identified and need to be explicitly stated in the model. The fact that the correlation coefficient of the predicted to actual AHI is much greater for the ANN (0.852) compared with the multiple linear regression model (0.509) indicates that interaction effects between predictor variables and/or nonlinearities are responsible for the greater predictive accuracy of the ANN.

In contrast, the classification and regression tree can be influenced easily by noise in the data with successive partitioning.[12] As a result, the predictive ability of the classification and regression tree becomes impaired. The ability of the network to extract intricate interrelations among variables makes it ideal for application to biological systems. Another potential reason for the improved accuracy of the network is that, in contrast to conventional statistical methods, it is purportedly less susceptible to distortion from missing or incomplete data.[26] Nevertheless, the frequency of missing values in this study was small.

In this study, the artificial neural networks were designed to provide a continuous scale of AHI to relay an estimated frequency of apneic and hypopneic events. The majority of the available predictive models have reduced the responses to binary outcomes. The advantages of having AHI as a continuous variable are multiple. Previous studies[27,28] have suggested an association between OSA and acute cardiovascular events such as myocardial events, sudden death, and cerebrovascular accident. In a retrospective study[2] of 267 adult male subjects diagnosed with OSA, survival in the group of patients with an apnea index (AI) >20/hour was reduced significantly compared to those subjects with an AI ≤20/hour. Maislin et al[29] noted that 42% of patients with AHI >75 events/hour reported falling asleep at the wheel at least once per week. Consequently, *a priori* knowledge of the estimated value of the AHI could provide a stratification of disease severity in patients with possible sleep apnea, and the identification of high-risk groups for early diagnostic and therapeutic intervention. It is noteworthy to mention that the neural network has not been tested or validated in patients with upper airway resistance syndrome.

There are several potential limitations of this study. First, all the data involved in the validation of the network were analyzed retrospectively. We doubt that the outcome would have varied if the data had been collected prospectively, since the validation set was not exposed to the network until the design had been completed. Second, the current network has been developed based on data obtained from patients referred to a sleep center by their primarycare physicians or consulting subspecialists. These patients were in the majority symptomatic, or were evaluated due to concern by their partners for their sleeping patterns. The pretest probability in these cases is likely to be high as the prevalence of the disorder in the group under investigation is significant, which helps to explain the high degree of prediction accuracy provided by the network in the validation set. Thus, the use of our network is currently limited to evaluate a group of patients with a high pretest probability for sleep apnea. Nevertheless, the previous prediction models were also derived from similar patient populations.

Another source of limitation of this study stems from the relatively small data sets. However, the high accuracy performance of the network in the validation group suggests that the network relied on robust features to perform its classification rather than learning the idiosyncrasies in the data.

A further limitation cited frequently in the literature[30] is the fact that little is known about the pathways used by the ANN to reach its conclusion. These pathways are complex and do not convey an understanding of the structure of the

reasoning. The ANN is essentially a black box. Unlike the logistic regression and the classification and regression tree, the relations between variables are not explicit. We acknowledge the above limitation inherent to all ANN, but we are willing to accept it provided the ANN's superior predictive ability has been demonstrated rigorously.

In conclusion, this study describes an ANN that can be used as a tool in the diagnosis of obstructive sleep apnea. A multicenter study designed to compare prospectively the performance of the network on a large number of patients is required to validate this approach further.

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