Accurate Identification of Subjects with Obstructive Sleep Apnea Using Recurrence Analysis of the Sleep EEG

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Abstract

Analysis of brain recurrence (ABR), a new method for quantifying non-randomness (law-governed complexity) in an EEG signal, when applied to sleep-staged EEGs, accurately identified subjects with OSA.

Introduction

Our objective was to compute and validate markers in the EEG for detecting the presence of OSA. We used ABR (described in earlier publications) to extract four markers from each 30-second epoch of sleep-staged EEGs. Biomarker functions determined using linear discriminant analysis (LDA) were employed to identiy subjects with OSA, using AHI scores as ground truth.

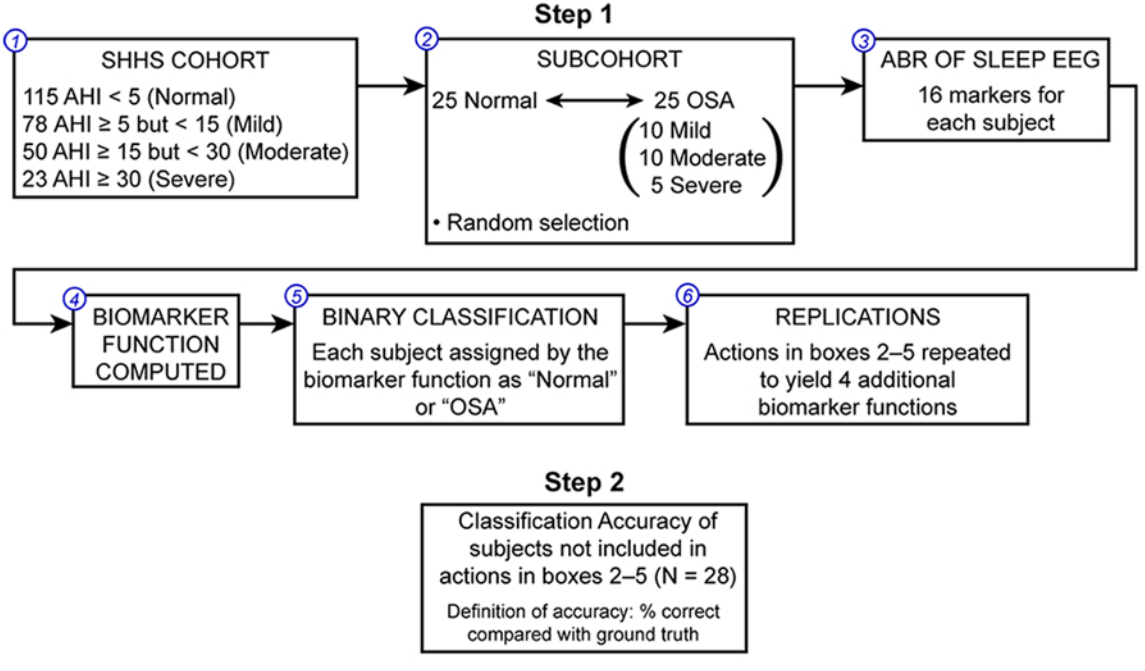
Methods

The study cohort comprised subjects drawn from the SHHS for whom the AHI was known. PSGs for 266 subjects were obtained from the NSRR, and the sleep-staged EEG (C3) was analyzed using ABR.

Summary Demographic Data for Study Cohort

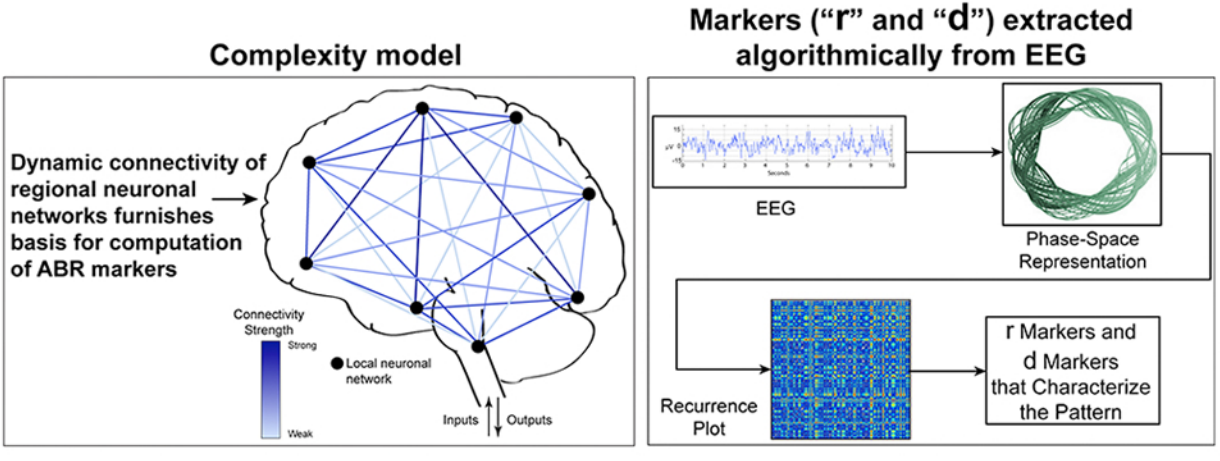
OSA Class	N	Age	Gender	BMI (kg/m^2)	AHI
Normal	115	60.5 ± 9.2	39M/76F	27.0 ± 3.8	1.8 ± 1.4
Mild	78	64.5 ± 8.9	45M/33F	29.5 ± 5.1	8.9 ± 3.1
Moderate	50	65.8 ± 8.3	29M/21F	30.3 ± 4.9	22.3 ± 4.4
Severe	23				

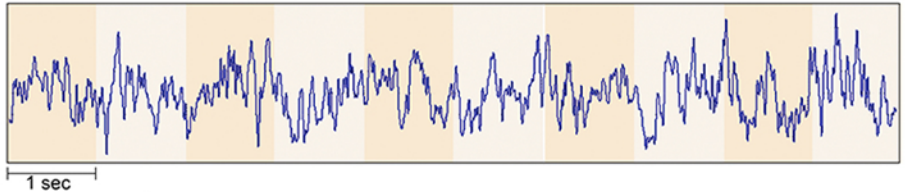
Experimental Design



In Step 1 five independent subcohorts were created, N = 25 normals and N = 25 with OSA in each subcohort, analyzed (ABR, LDA), and the classification accuracy (Normal or OSA) was assessed for each subcohort. In step 2 classification accuracy for the subjects who had not been randomly selected for any subcohort was determined, using the 5 biomarkers created in Step 1.

Analysis of Brain Recurrence (ABR)





Markers r and d ("sleep depth") were computed each second (expressed as %)

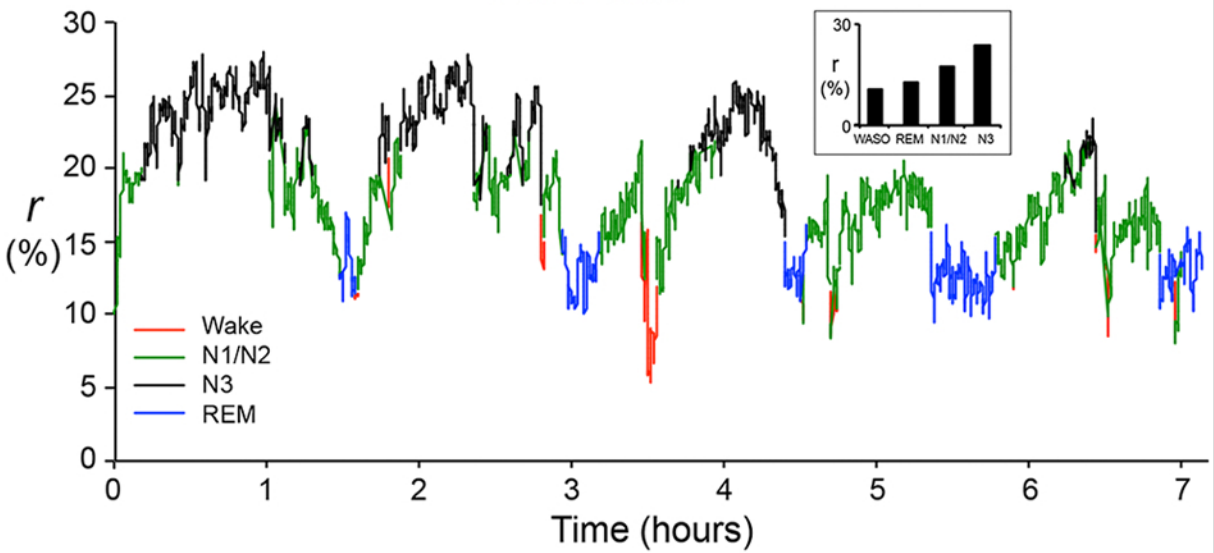
Changes in r and d ("arousals") computed and expressed as an AI (arousals/hr)

r, Δ*r*, *d*, Δ*d* were computed from the sleep EEG for WASO, N1/N2, N3, and REM (total of 16 markers for each subject).

Computation of AI

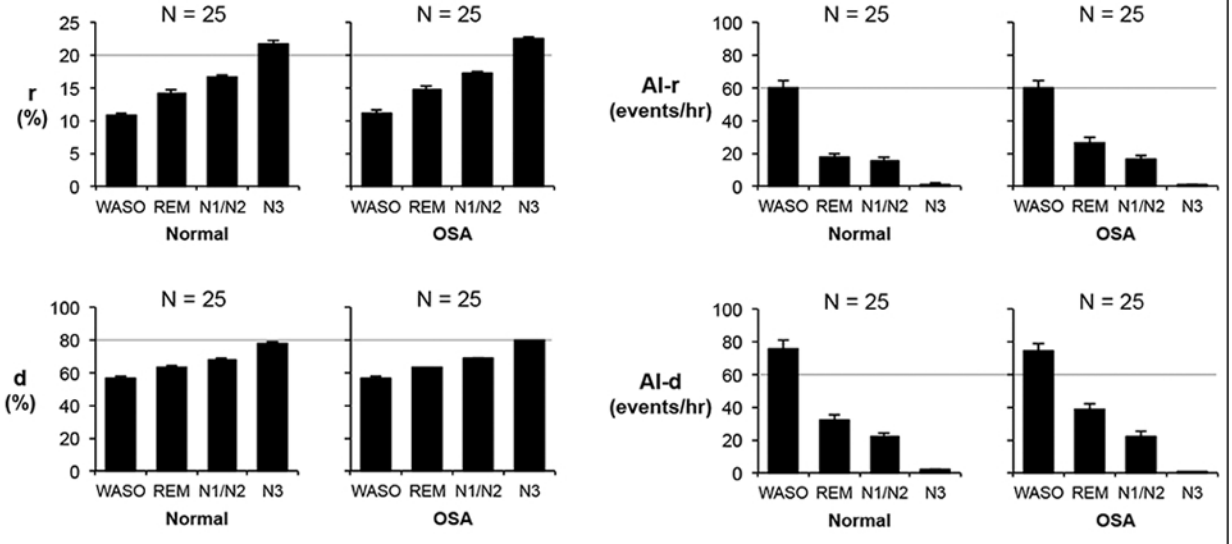
Markers for sleep fragmentation were created by generalizing the conventional definition of EEG arousals. For r(t), the second-by-second time series of r, the ratio of the mean for 3 s (one value per second) to the mean for the preceding 10 s (ten values) was determined, and the process was repeated using successive steps of 3 s, resulting in a time series of approximately 9000 ratios for a typical overnight EEG. Whenever the ratio was increased by more than 100%, the change was counted as an "arousal", and the arousal rate was assessed in specific sleep stages (WASO, N1/N2, REM, N3), and expressed as the number of arousals/hr. A similar procedure was performed for d(t), the time series for d, except that the criterion for an arousal was 50%.

Results



Values of *r* were calculated second-by-second, averaged epoch-by-epoch, and color-coded by sleep stage. Insert shows the sleep-stage-specific mean values. *r* (and *d*) can be interpreted as indicators of sleep depth.

Average data for subcohort 1



As expected, on average, none of the 16 individual markers differed between the groups, indicating that a dynamical statistical analysis was needed to detect the footprint of OSA in the EEG.

Step 1: Classification Accuracy for Five Independent Subcohorts (N = 50/subcohort)

Subcohort No.	Accuracy (%)	Markers											
1	82	2	7	10	11	12							
2	82	1	2	3	4	5	6	7	8	10	12	16	
3	86	1	4	7	8	9	11	12	13	15			
4	88	1	2	4	5	8	9	10	11	14	15	16	
5	90	1	2	3	5	6	7	8	10	11	14	15	16

Key for markers:

1: *r* (WASO)	2: *r* (N1/N2)	3: *r* (N3)	4: *r* (REM)
5: *d* (WASO)	6: *d* (N1/N2)	7: *d* (N3)	8: *d* (REM)
9: AI-*r* (WASO)	10: AI-*r* (N1/N2)	11: AI-*r* (N3)	12: AI-*r* (REM)
13: AI-*d* (WASO)	14: AI-*d* (N1/N2)	15: AI-*d* (N3)	16: AI-*d* (REM)

Five replicate independent dynamical analyses (ABR, LDA) were performed on subcohorts of the SHHS cohort (N = 266) formed by random selection. Classification accuracy (Normal or OSA) determined using the LDA-based biomarker functions was 82–90%. As expected, because of information redundancy among the 16 markers, the number and identity of the markers needed for optimal classification varied among the subcohorts.

Step 2: Classification Accuracy for Non-Selected Subjects

Classification accuracy for the 28 subjects who were not selected in any of the 5 subcohorts was 93%, as assessed using a combination of the five previously determined biomarker functions, indicating that new subjects can be correctly diagnosed based on a comparison of their sleep EEG with EEGs obtained from a standard population.

Conclusion

The presence of OSA can be reliably identified using algorithmic analyses of the sleep-staged EEG and comparing the computer markers with a standard population.

Future Application

Elimination of the need for conventional sleep staging (Fig. 1) would increase the clinical usefulness of ABR-based identification of OSA. One possibility would be to classify sleep epochs using ABR prior to computing the markers (Fig. 2). To facilitate this development, new names were assigned to the four brain states found most useful for the purpose of recurrence analysis: Wake-like Brain Activity ("WABA"), Light-Stage sleep-like Brain Activity ("LISA"), Slow-Wave Sleep-Like Brain Activity ("SWABA"), and REM-like Brain Activity ("REBA"). After algorithmically staging sleep based on the four ABR brain states, the 16 ABR markers could be computed and used to identify the presence of OSA.

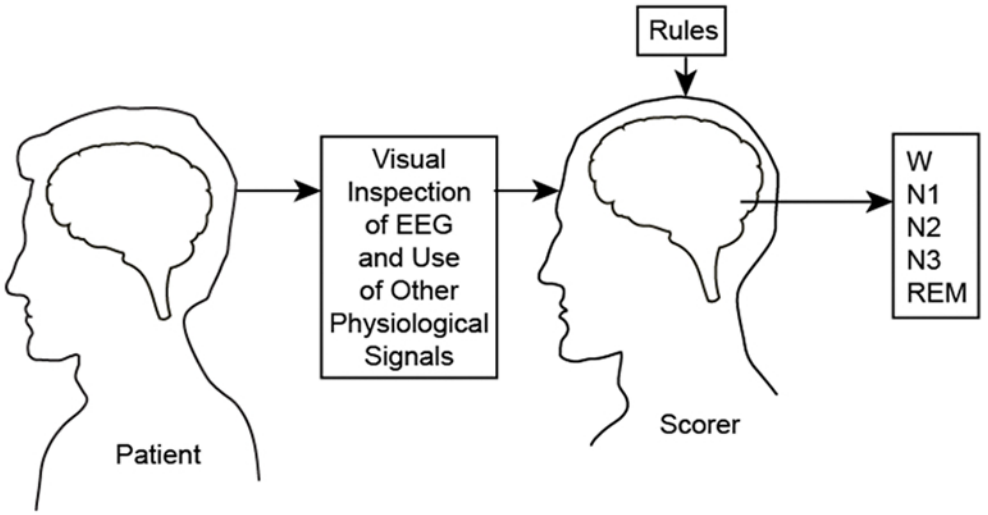


Fig. 1. Conventional procedure for staging sleep. Consecutive 30-second epochs of the PSG are assigned to one of five mutually independent stages based on predetermined rules for interpreting individual signals in the PSG.

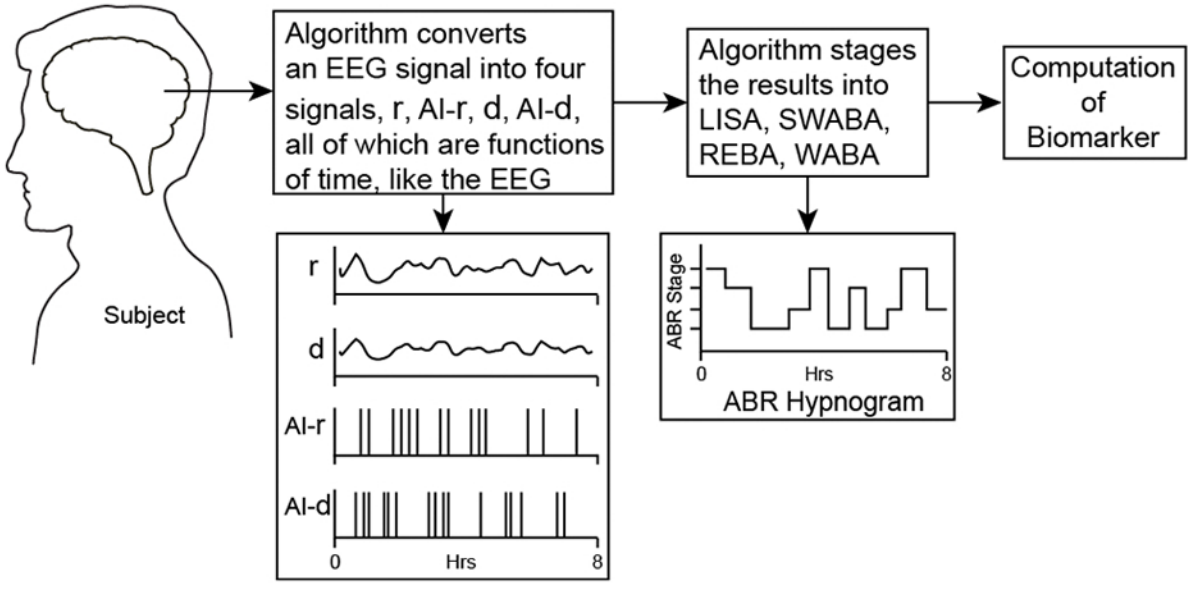


Fig. 2. Algorithmic determination of sleep stages for purposes of diagnosing clinical disorders. In this example, a raw EEG tracing is subjected to two different mathematical machines (computational constructs). From these computations, ABR states can be assigned. Patterns within each ABR state and dynamic changes of these patterns can be used to construct a biomarker value for OSA.

References

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Abbreviations

ABR	Analysis of brain recurrence	LDA	Linear discriminant analysis
r	ABR variable "recurrence"	NSRR	National Sleep Research Resource (https://sleepdata.org)
d	ABR variable "determinism"		
AI	Arousal index	OSA	Obstructive sleep apnea
AI-*r*	AI computed from r(t)	PSG	Polysomnogram
AI-*d*	AI computed from d(t)	SHHS	Sleep Heart Health Study
BMI	Body mass index	WASO	Wake after sleep onset
EEG	Electroencephalogram		