Development and Validation of a Continuous EEG-Based Marker for Sleep Depth

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Abstract

Physiologically-based markers that represent sleep depth on a continuous time scale are needed. Attempts to develop such markers based on EEG amplitude/frequency properties have been unsuccessful. We developed a novel nonlinear method based on quantification of the dynamical pattern (recurrence) in the EEG. Our goals were to establish the new marker's normal phenotype, and to show that it was altered in patients with a sleep disorder.

Scored PSGs (R&K) from 8 healthy medication-free subjects (EEGs from Fz–Cz) and 8 subjects with OSA (C3–O1) were obtained from the PhysioBank (essentially all overnight EEGs in the archive). The sleep-stage structure of the subjects with OSA was abnormal. All EEGs analyzed were sampled at 100 Hz.

Brain electrical activity manifested in the EEG was quantified by means of recurrence analysis (RA), employing the variable termed *percent recurrence* (R). R, which quantifies extent to which the EEG is governed by law rather than chance, captures information in the EEG that cannot be obtained using conventional methods such as spectral analysis. The physiological meaning of increased R can be expressed as increased regulation, order, determinism, or law-governed activity. Increased R can also be interpreted as decreased chaos, or disorder. Details of RA are given elsewhere.

The EEGs were analyzed second-by-second. For each hour in the PSG, 1 hour × 60 minutes × 60 sec = 3600 values of R were computed and averaged epoch-by-epoch, resulting in 120 values of average R per hour for the EEG.

When recurrence analysis was applied to the EEGs recorded from normal subjects during sleep, the expected cyclic macro-architectures (3–5 cycles) was seen. A consistent relationship was found, from subject to subject, between the magnitude of R

and sleep stage such that R(N3)>R(N2)>R(N1)>R(W), and R(REM) ≈ R(N1). In the subjects with OSA, the sleep cyclic structure manifested in R in the subjects with normal sleep was reduced or absent. On average, R was significantly lower in OSA subjects during REM and N3 sleep ($P<0.05$).

Epoch-by-epoch changes in R computed from the EEG exhibited the macro-architecture of normative sleep, indicating R's criterion validity as a continuous marker for normal sleep. Sleep structure as visualized using R was fundamentally altered in subjects with OSA, particularly in those with more severe disease. Mean R was reduced in association with OSA ($P < 0.05$), indicating that the reduction in EEG complexity that occurred during normal sleep did not occur in subjects with disordered breathing.

The recurrence marker R captured the temporal activity of the sleep EEG, and thereby provided continuous quantitation of brain electrical activity during sleep. Pending verification based on PSGs recorded and staged under AASM rules, recurrence markers, which emphasize the continuous nature of sleep, may be a useful complement to sleep staging, which emphasizes sleep discontinuity.

Introduction

Physiologically-based markers that represent sleep depth on a continuous time scale are needed. Attempts to develop such markers based on EEG amplitude/frequency properties have been unsuccessful. We developed a novel nonlinear method based on quantification of the dynamical pattern (recurrence) in the EEG. Our goals were to establish the new marker's normal phenotype, and to show that it was altered in patients with a sleep disorder.

Methods

Patients

Scored PSGs (R&K) from 8 healthy medication-free subjects (EEGs from Fz–Cz) and 8 subjects with OSA (C3–O1) were obtained from the PhysioBank (essentially all overnight EEGs in the archive) (1). The sleep-stage structure of the subjects with OSA was abnormal (Table 1). All EEGs analyzed were sampled at 100 Hz.

Recurrence Analysis

Brain electrical activity manifested in the EEG was quantified by means of recurrence analysis (RA), employing the variable termed *percent recurrence* (R). R, which quantifies extent to which the EEG is governed by law rather than chance, captures information in the EEG that cannot be obtained using conventional methods such as spectral analysis. The physiological meaning of increased R can be expressed as

increased regulation, order, determinism, or law-governed activity. Increased R can also be interpreted as decreased chaos, or disorder. Details of RA are given elsewhere (2).

The EEGs were analyzed second-by-second. For each hour in the PSG, 1 hour × 60 minutes × 60 sec = 3600 values of R were computed and averaged epoch-by-epoch, resulting in 120 values of average R ($\bar{R}$) per hour for the EEG (Fig. 1).

Table 1. Sleep data for OSA and normal subjects.

	Time in Bed (min)	Percent Sleep Stage				
		Awake	**REM**	**N1**	**N2**	**N3**
OSA	366 ± 9.8	28.0 ± 15.0*	7.5 ± 4.0*	19.5 ± 5.3*	38.0 ± 20.0	7.3 ± 6.8*
Normal	482 ± 63	7.3 ± 2.3	17 ± 9.4	7.9 ± 3.7	47.0 ± 10.0	21.4 ± 3.9
						*P < 0.05

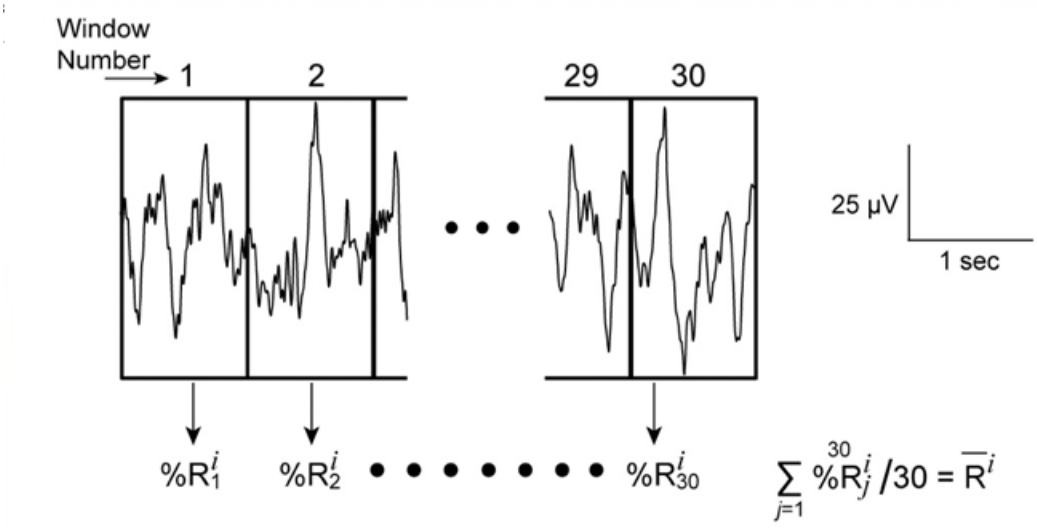

Fig. 1. Application of recurrence analysis to the *i*th epoch in the sleep EEG. Percent recurrence ® is computed second by second and averaged over each 30-second epoch. $\bar{R}^i$ is the average percent recurrence for the *i*th epoch (1 second window).

Results

When recurrence analysis was applied to the EEGs recorded from normal subjects during sleep, the expected cyclic macro-architectures (3–5 cycles) was seen (Fig. 2). A consistent relationship was found, from subject to subject, between the magnitude of R and sleep stage such that R(N3)>R(N2)>R(N1)>R(W), and R(REM) ≈ R(N1). In the subjects with OSA, the sleep cyclic structure manifested in R in the subjects with normal sleep was reduced or absent (Fig. 3). On average, R was significantly lower in OSA subjects during REM and N3 sleep (P<0.05) (Fig. 4).

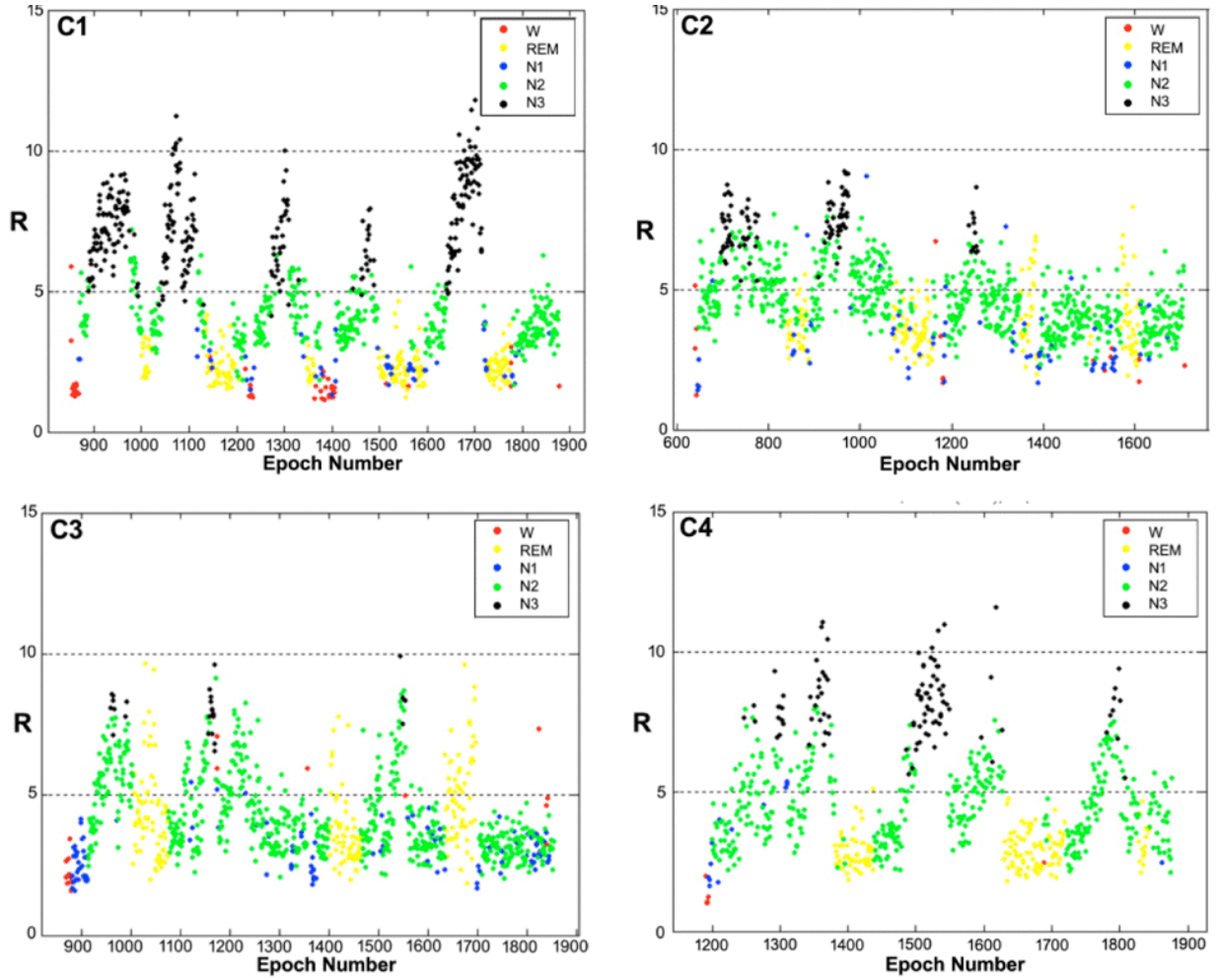

Figure 2. (continued on next page)

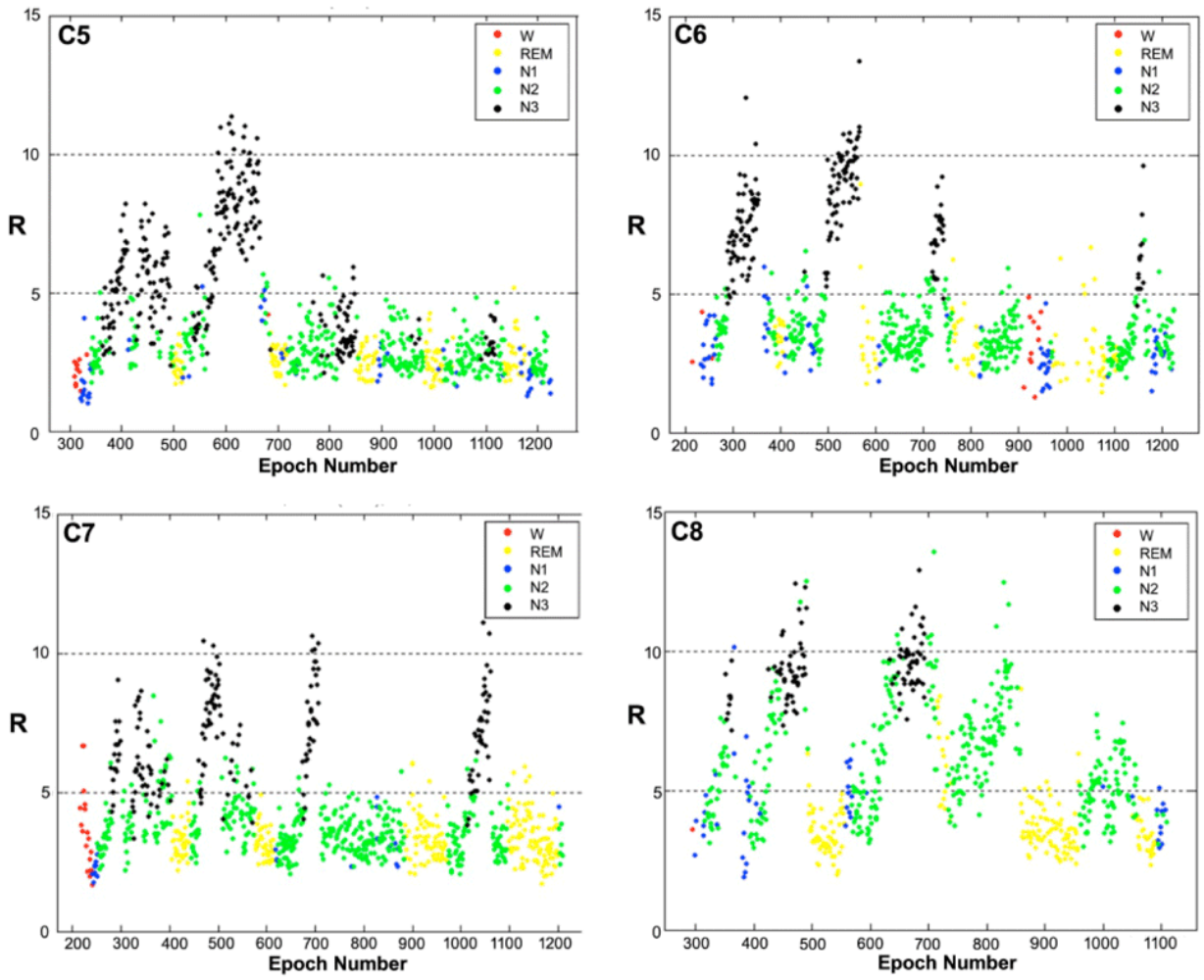

Figure 2. Recurrence analysis of sleep-staged EEGs from normal subjects. Percent recurrence (R) was computed using successive one-sec intervals of the overnight sleep EEG from 8 clinically normal subjects (C1–C8). R was averaged epoch-by-epoch (resulting in one value of $\overline{R}$ for each sleep epoch) and color-coded by sleep stage. Each point represents the average value of R for one 30-sec EEG epoch.

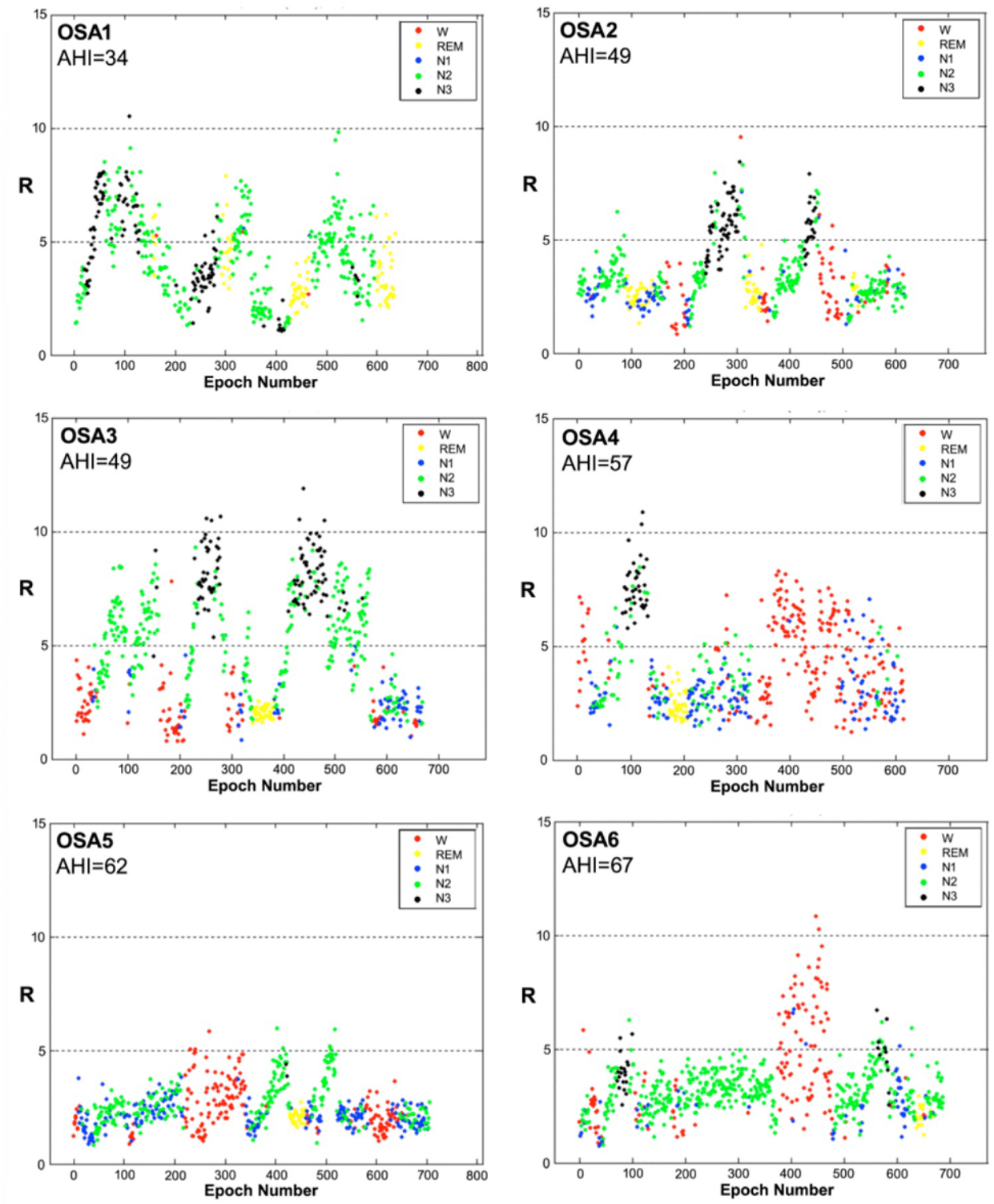

Figure 3. (continued on next page)

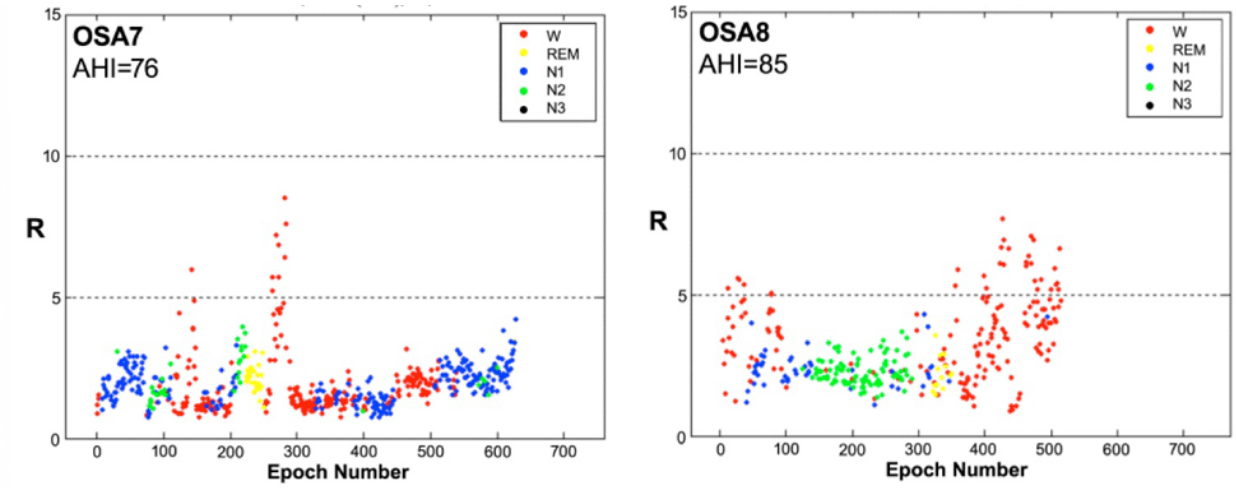

Figure 3. Recurrence analysis of sleep-staged EEGs from subjects with obstructive sleep apnea (OSA). Percent recurrence (R) was computed using successive one-sec intervals of the overnight sleep EEG from 8 clinically normal subjects (C1–C8). R was averaged epoch-by-epoch (resulting in one value of $\bar{R}$ for each sleep epoch) and color-coded by sleep stage. Each point represents the average value of R for one 30-sec EEG epoch.

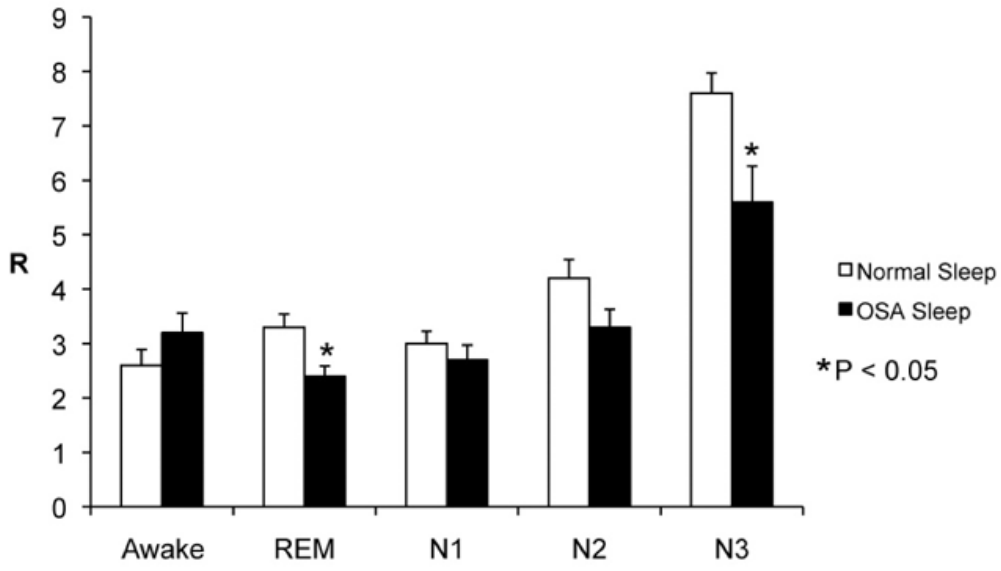

Fig. 4. Percent recurrence (R) of brain electrical activity during sleep. Mean ± SD. N=8 for each group.

Discussion

Epoch-by-epoch changes in R computed from the EEG exhibited the macro-architecture of normative sleep (Fig. 2), indicating R's criterion validity as a continuous marker for normal sleep. Sleep structure as visualized using R was fundamentally altered in subjects with OSA, particularly in those with more severe disease (Fig. 3). Mean R was reduced in association with OSA ($P < 0.05$) (Fig. 4), indicating that the reduction in EEG complexity that occurred during normal sleep did not occur in subjects with disordered breathing. The recurrence marker R captured the temporal activity of the sleep EEG, and thereby provided continuous quantitation of brain electrical activity during sleep. Pending verification based on PSGs recorded and staged under AASM rules, recurrence markers, which emphasize the continuous nature of sleep, may be a useful complement to sleep staging, which emphasizes sleep discontinuity.

References

1. http://www.physionet.org/physiobank/database/sleep-edf/

2. Carrubba S, Kim PY, McCarty DE, Chesson Jr. AL, Frilot II C, Marino AA. Continuous EEG-based dynamic markers for sleep depth and phasic events. J. Neurosci. Meth. In Press 2012. http://dx.doi.org/10.1016/j.jneumeth.2012.04.018

Abbreviations

AHI	Apnea/hypopnea index
EEG	Electroencephalogram
OSA	Obstructive sleep apnea
PSG	Polysomnogram
R&K	Rechtschaffen and Kales
RA	Recurrence analysis
R	Percent recurrence; RA variable computed per sec from the EEG
$\bar{R}$	R averaged over a 30-sec epoch