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Comparison of Photoplethysmographic Signal Features Between Healthy and Sleep Apnea Patients During Five Sleep Stages

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The diagnosis of sleep apnea is mainly based on polysomnographic system and the diagnostic process is time-consuming, complicated and uncomfortable. It is an urgent need to make the diagnosis process convenient and comfortable. In this paper, we compared finger photoplethysmographic (PPG) signals of healthy and sleep apnea patients in five sleep stages by Gaussian function. PPG signals were obtained by polysomnographic system from 17 healthy subjects and 70 sleep apnea patients in Shandong Provincial Hospital. The 10 successive cardiac cycles signal, which did not include the sleep apnea events, was intercepted and normalized during each sleep stage. Each data segment was fitted by three Gaussian functions and obtained a total of 9 parameters for 3 functions (each function has 3 parameters). As for the healthy, means of 9 Gaussian parameters in 5 sleep stages were compared respectively and means for patients were treated similarly. Gaussian parameters of healthy were also compared with those of sleep apnea patients in 5 sleep stages respectively. The results showed there were no significant statistical differences among 5 sleep stages within healthy group or patient group, but there were significant statistical differences among healthy patients and sleep apnea patients in 5 sleep stages for Gaussian parameters W_1 , W_3 and C_1 . This study could be an easy operated and comfort way to diagnose sleep apnea.

Keywords: Sleep Apnea, Gaussian Function, Sleep Stage, Photoplethysmographic (PPG).

1. INTRODUCTION

Polysomnography is considered as the standard method for diagnosing sleep apnea. However, its diagnostic process is time-consuming, complicated, expensive and uncomfortable. Therefore, the research for a convenient, comfortable and cost-effective method is a common problem for sleep medicine. In recent years, non-contact measurements or devices have been introduced for investigating sleep apnea. Thermal infrared imaging is used to detect nasal airflow, vibration/sound sensors is used to monitor the sound of airflow and breathing movement and radio-frequency architecture which transmits low-power radio-frequency energy is also used to detect movement and respiration. These non-contact measurements have many advantages such as convenient and comfortable. If these sensors are blocked or placed incorrectly, nasal airflow or movements

are not detected. Furthermore, limb movements, body position or noise can interfere with the results.

Pulse signal contains various information of the human body and can be easily obtained. Making full use of the characteristics of the pulse waveform can simplify the diagnostic process of sleep disorders. The relationship between pulse rate variability (PRV) and heart rate variability (HRV) is researched recently by calculating the peak to peak interval (PPI).^{7,8} Lin et al. have reported that PRV corresponds well with HRV to healthy subjects, and Liu et al. have demonstrated that PRV can substitute HRV for sleep apnea patients during sleep. The change of pulse wave amplitude (PWA) has also been researched for sleeping patients by Habarubio et al., and significant differences of PWA are found between non-sleep events and sleep events. As characteristics of the pulse waveform, PPI and PWA can be obtained easily and be used for real-time calculation. However, only local features of the waveform were used in previous studies and the features' quality is relatively poor when pulses are

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Table I. The number of data segments intercepted during each sleep stage for 87 subjects enrolled.

Subject's basic inform	Sleep stage					
Number of people	W	R	N1	N2	N3	
17	Healthy	16	13	17	17	15
70	Patient	64	45	55	56	46

Table II. Two-way analysis results of variance (ANOVAs) with patient types as main factor and sampling sleep stages as sub-factor. F/P values were given.

Measured parameters of Gaussian functions	Patient types	Sleep stages	Patient types× sleep stages
H_k			
H_1	3.95/0.049*	0.94/0.44	1.67/0.16
H_2	15.91/<0.001***	0.18/0.95	1.27/0.28
H_3	19.12/<0.001***	1.52/0.20	1.62/0.17
W_k			
W_1	65.86/<0.001***	0.58/0.58	0.66/0.62
W_2	36.22/<0.001***	084/0.50	0.99/0.42
W_3	87.23/<0.001***	0.37/0.83	0.22/0.93
C_k			
C_1	92.07/<0.001***	0.75/0.56	0.57/0.68
C_2	61.64/<0.001***	1.11/0.35	0.90/0.47
<i>C</i> ₃	39.48/<0.001***	0.91/0.46	0.66/0.62

Notes: Patient types—Healthy and sleep apnea patients; sleep stages—Five sleep stages of W, R, N1, N2 and N3; *P < 0.05, $^{***}P$ < 0.001.

weak or disturbed. Recently, Curve fitting was used to quantitatively analyze the morphological changes of pulse waveform. 10-12 Gaussian function is a common function for fitting analysis. 13, 14 It is reported that three Gaussian functions are optimal for fitting artery waveforms with low absolute error. 15

According to the 2007 American Academy of Sleep Medicine (AASM) Manual, sleep is divided into rapid eye movement (REM) period and non-rapid eye movement (NREM) period, in which NREM period is divided into N1, N2 and N3 sleep stages based on sleep depth. In addition, we studied the waveforms of the tester's awake period. For the convenience of expression, there are five stages mentioned in this paper, referred to as: W (wake), R (REM), N1, N2 and N3 stages. In this paper, we use three Gaussian functions to reconstruct finger PPG for 17 healthy subjects and 70 sleep apnea patients during the five sleep stages. We have two aims: (1) To investigate whether there are significant differences for Gaussian parameters in five sleep stages within healthy group and patient group. (2) To investigate whether there are significant differences for Gaussian parameters among healthy patients and the sleep apnea patients during five sleep stages.

2. METHODS

2.1. Subjects

Ninety-three subjects were enrolled in this study. None of the subjects smoked or drank for a week before participating in the test. Seventeen of them (10 man and 7 female) were healthy,

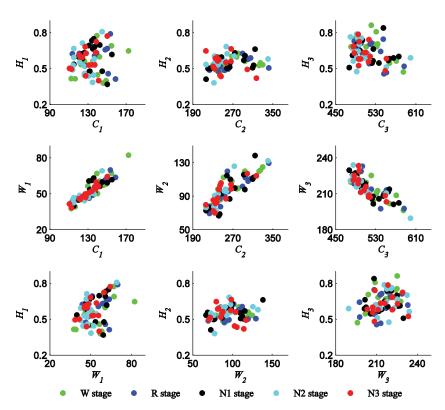


Fig. 1. The relationship among Gaussian parameters in 5 sleep stages within healthy group.

seventy (49 man and 21 female) were sleep apnea patients and six (1 man and 5 female) were unclear diagnosis. Our study included only 87 healthy and sleep apnea patients. Ethical permission was received from the ethical committee of Shandong Provincial Hospital and all subjects gave their informed consent.

2.2. Data Acquisition and Processing

All tests were done at the sleep medicine center of Shandong Provincial Hospital. Instruments used in this testing are the Alice 5 Sleepware Polysomnographic System manufactured by Philips. Multi-channel signals included EEG, ECG, PPG, etc. were synchronously recorded for 8 hours on average at night at sampling frequency 100 Hz. Five sleep stages of W, R, N1, N2, and N3 were automatically identified by the Alice 5. Data used in this paper were subjects' finger PPG signals which obtained by the Alice 5. A 30-second PPG signal, which did not include the sleep apnea events, was intercepted during each sleep stage for each subject. Among 93 subjects, 6 subjects' recordings were excluded because of unclear diagnosis. Not every subject's sleep contains five sleep stages. Some participants only had N1 stage, while others did not have N3 stages, and even some had only wake stage. Table I shows the number of data segments intercepted during each sleep stage for 87 subjects. Each data segment was processed according to our previous method. 16 In short, each data segment was first filtered and marked the foot points for each pulse period, and then 10 successive cardiac cycles signal was selected from each data segment, and finally was normalized to 10 single-cycle signals with 1-unit amplitude and length of 1 000

2.3. Curve Fitting

In this paper, Gaussian function used to analyze PPG signals. Gaussian function is defined as follows: 12, 15

$$f_k(n) = H_k \times \exp\left(-\frac{2(n - C_k)^2}{W_k^2}\right)$$

Each Gaussian functions has three parameters: H_k ($0 < H_k < 1$), W_k ($0 < W_k < 1000$), and C_k ($1 < C_1 < C_2 < C_3$), correspond to the peak height, the time support and the peak position respectively. The subscript k indicates different Gaussian functions with k = 1, 2, 3 and n is the length of Gaussian function with $n = 1, 2, \ldots, 1000$. Previous studies demonstrated that it is enough to model arterial pressure waveforms by three Gaussian functions. In this paper, three Gaussian functions were used to fit PPG signals as fitting kernels and there were total 9 parameters for three Gaussian functions.

2.4. Statistical Analysis

The overall means of healthy were compared with overall means of patients in 5 sleep stages respectively. Two-way analysis of variance (ANOVAs) was performed to investigate for Gaussian parameters among healthy patients and the sleep apnea patients during 5 sleep stages. It is considered to be statistical significance when P < 0.05.

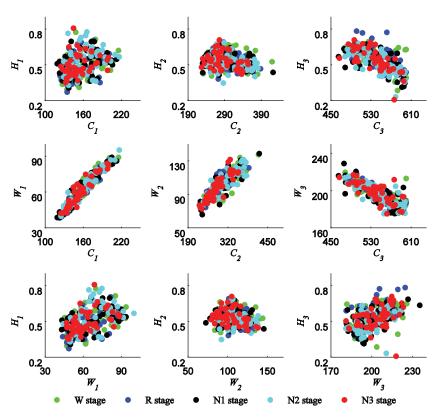


Fig. 2. The relationship among Gaussian parameters in 5 sleep stages within sleep apnea patient group.

Table III. Overall means and SDs of nine parameters of Gaussian functions in 5 sleep stages for healthy patients and sleep apnea patients.

Patient	Sleep	H_k			W_k			C_k		
types	stage	H ₁	H_2	H_3	<i>W</i> ₁	W_2	W_3	C ₁	C_2	C_3
Healthy	W	0.54 ± 0.11	0.55 ± 0.04^{b}	0.68 ± 0.10 ^a	53.78 ± 11.53^b	101.14 ± 14.53	215.38 ± 9.55^a	135.12 ± 15.50 ^b	266.43 ± 34.54^{b}	518.83 ± 31.51 ^b
	R	0.61 ± 0.10^{a}	0.53 ± 0.05^b	0.63 ± 0.10	55.01 ± 8.57^{b}	97.72 ± 17.86^b	213.80 ± 10.25^a	137.11 ± 14.47^{b}	267.90 ± 35.49^b	524.58 ± 27.92
	N1	0.59 ± 0.11	0.55 ± 0.06	0.63 ± 0.09^{a}	52.73 ± 7.19^b	95.45 ± 19.92^{b}	214.06 ± 9.49^a	133.04 ± 10.69^{b}	262.08 ± 32.22^{b}	521.15 ± 30.50^b
	N2	0.55 ± 0.11	0.56 ± 0.06	0.63 ± 0.09^{a}	49.19 ± 6.05^{b}	92.92 ± 16.42^{b}	216.65 ± 10.07^a	127.27 ± 9.15^b	248.19 ± 27.14^{b}	506.79 ± 29.04^b
	N3	0.58 ± 0.10	0.54 ± 0.07^{b}	0.63 ± 0.08	50.48 ± 6.81^{b}	92.39 ± 14.55^{b}	216.42 ± 8.95^{a}	129.53 ± 10.76^b	250.79 ± 26.89^b	507.25 ± 20.45^b
Sleep	W	0.54 ± 0.10	0.59 ± 0.07^a	0.59 ± 0.09^b	66.13 ± 13.31^a	106.97 ± 15.25	201.41 ± 11.43^{b}	159.78 ± 21.87^a	300.01 ± 41.23^a	545.67 ± 37.05^a
apnea	R	0.53 ± 0.10^{b}	0.58 ± 0.07^a	0.62 ± 0.09	64.71 ± 13.15^a	109.63 ± 12.66^a	201.65 ± 10.76^b	157.10 ± 21.90^a	300.43 ± 37.75^{a}	542.83 ± 30.44
	N1	0.55 ± 0.10	0.58 ± 0.06	0.57 ± 0.10^{b}	65.43 ± 14.51^a	107.55 ± 17.56^a	202.32 ± 11.59^{b}	158.22 ± 24.27^a	301.19 ± 47.87^a	542.40 ± 37.97^{a}
	N2	0.57 ± 0.12	0.56 ± 0.07	0.56 ± 0.09^{b}	67.32 ± 14.67^{a}	110.56 ± 15.45^a	202.58 ± 11.27^{b}	159.52 ± 22.03^a	306.49 ± 42.78^{a}	544.46 ± 33.60^a
	N3	0.55 ± 0.09^{b}	0.58 ± 0.07^a	0.59 ± 0.10	62.90 ± 11.87^{a}	105.16 ± 14.69^{a}	204.06 ± 10.67^{b}	153.28 ± 19.05^{a}	287.50 ± 34.13^{a}	538.72 ± 31.48^{a}

Notes: Different lowercase letters indicate significant difference among healthy patients and the sleep apnea patients at same sleep stage by T test at P < 0.05; a indicates a significant increase and b indicates a significant decrease.

3. RESULTS

3.1. Overall Means and SDs of Parameters of Gaussian Functions in Five Sleep Stages for the Healthy Patients and the Sleep Apnea Patients

Table II presented the statistical results of 9 Gaussian parameters among 5 sleep stages for healthy patients and the sleep apnea patients. According to the results of "sleep stages" shown in Table II, there were no statistical differences among 5 sleep stages within healthy group or patient group. The results of "Patient types × Sleep stages" showed there were no statistical differences in the interactions among healthy patients and sleep

apnea patients. Figures 1 and 2 showed the relationship among Gaussian parameters in 5 sleep stages for healthy patients and sleep apnea patients respectively. From Figures 1 and 2 we can see that there were no significant differences in the distribution of parameters in 5 sleep stages of healthy subjects or patients.

Table III shows overall means and SDs of 9 Gaussian Parameters of three Gaussian functions in 5 sleep stages for healthy patients and sleep apnea patients. The results of Table III showed that the overall means of parameters W_1 , C_1 and C_2 in 5 sleep stages, parameters W_2 and C_3 in 4 sleep stages (for W_2 , except stage W; for C_3 , except stage R) for sleep apnea patients were

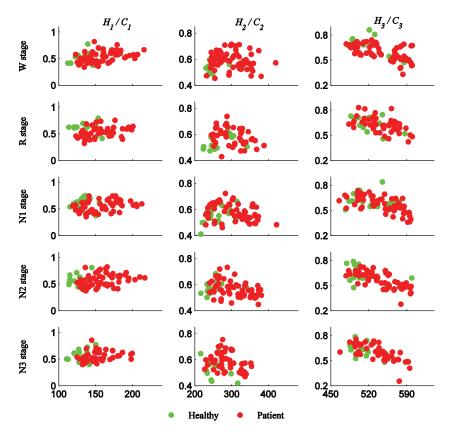


Fig. 3. Comparison of Gaussian parameters H_k/C_k among healthy and sleep apnea patients in 5 sleep stages.

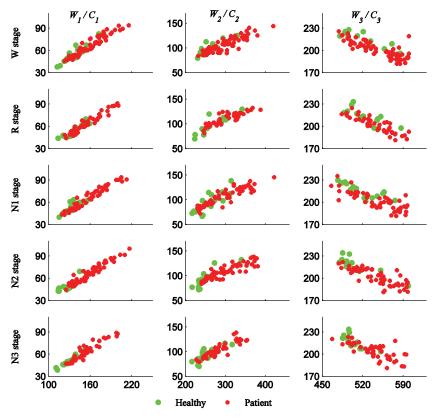


Fig. 4. Comparison of Gaussian parameters W_k/C_k among healthy and sleep apnea patients in 5 sleep stages.

significantly higher than those of healthy patients; while for parameter W_3 , the overall means of sleep apnea patients were significantly lower than those of healthy patients in 5 sleep stages. As for parameters H_1 , H_2 and H_3 , the overall means of sleep apnea patients were significantly larger or smaller than those of the healthy patients at some stages.

3.2. Comparison of Gaussian Parameters Among Healthy Patients and Sleep Apnea Patients in Five Sleep Stages

Figures 3–5 show relationships among Gaussian parameters for healthy patients and sleep apnea patients in 5 sleep stages. The results of "patient types" in Table II showed there were significant statistical differences among healthy patients and sleep apnea patients in 5 sleep stages for Gaussian parameters. From the results of Table III, we can see there were significant statistical differences in parameters W_1 , W_3 and C_1 in 5 sleep stages among healthy patients and sleep apnea patients, and 95% CI of W_1 , W_3 and C_1 (showed in Table IV) for healthy were not coincident with the patient's in 5 sleep stages.

4. DISCUSSION

In this study, we used three Gaussian functions to decompose finger PPG (not include the sleep apnea events) for 17 healthy subjects and 70 sleep apnea patients during 5 sleep stages. We compared 9 parameters obtained by three Gaussian functions among 5 sleep stages for each subject and among healthy patients

and sleep apnea patients during 5 sleep stages. Two-way analysis of variance (ANOVAs) with patient types as main factor and sampling sleep stages as sub-factor for 9 Gaussian parameters were calculated respectively. Statistical results (see Table II) showed there were no significant statistical differences in 9 parameters among 5 sleep stages for healthy subjects, and no statistical differences among 5 sleep stages for sleep apnea patients. However significant statistical differences in 9 parameters appeared in 5 sleep stages among healthy patients and sleep apnea patients. Table III showed that the overall means of parameters W_1 , C_1 and C_2 for sleep apnea patients were significantly higher than those of healthy patients in 5 sleep stages; while patient's W_3 parameters were small than those of healthy patients in 5 sleep stages. It could be seen from Table IV that 95% CI of W_1 , W_3 and C_1 for healthy were not coincident with the patient's in 5 sleep stages respectively.

Although Polysomnography is considered the standard method for diagnosing sleep apnea, its diagnostic process is uncomfortable and time-consuming. Take our research as an example: the average testing time was 8 hours at night in this study; seventeen of the 87 testers were diagnosed as healthy, but they all experienced sleep disorder during their sleep; seventy were diagnosed as sleep apnea patients and ten of them only had wake stage in whole night. Therefore, the research for a convenient and comfortable method is an urgent problem to be solved. Noncontact measurements have been introduced to research sleep apnea, however they have some limitations. Although improvements are done, such as correction of index or introduction of

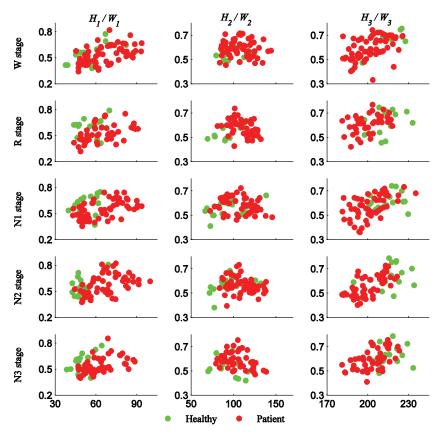


Fig. 5. Comparison of Gaussian parameters H_k/W_k among healthy and sleep apnea patients in 5 sleep stages.

new methods, ^{17, 18} algorithm development and further testing are facing problems in the future.

Previous researches have showed that pulse rate variability (PRV) and pulse wave amplitude (PWA) could be used to simplify the diagnosis of sleep disorders. Lin et al.⁷ and Liu et al.⁸ both studied the relation among PRV and HRV by PPG, however Lin et al. researched healthy subjects sitting quiet or after exercising and Liu et al. researched sleep apnea patients during sleep by data containing sleep apnea event. Habarubio et al.⁹ compared the differences of PWA of sleeping patients among nonsleep events and sleep events. Sleep events usually occur during

sleep and need longer detection time. Our results indicate that Gaussian parameters obtained from PPG in wake stage are not significantly different from those obtained in sleeping (in stage of R, N1, N2 and N3), so Gaussian parameters W_1 , W_3 and C_1 obtained from PPG in wake stage can be used to diagnose sleep disorders, which means diagnostic process can be comfortable, simple and short.

Our researches have some limitations. First, sample size is small. Second, healthy subjects were relatively young (28 ± 11 years old), while the patients were either young or old (the oldest is 85 years old). It has been reported that age affects

Table IV. 95% CI of nine parameters of Gaussian functions in 5 sleep stages for healthy patients and sleep apnea patients.

Sleep		H_k			W_k			C_k		
stage	State	H ₁	H_2	H ₃	H ₁	H_2	H ₃	H ₁	H_2	H_3
W	Healthy	0.48-0.60	0.53-0.57	0.63-0.73	47.63–59.92	93.40-108.88	210.29–220.47	126.86-143.38	248.02-284.84	502.04-535.62
	Patient	0.51-0.56	0.58-0.61	0.57-0.61	62.80-69.45	103.16-110.78	198.55-204.26	154.32-165.25	289.71-310.31	536.41-554.92
R	Healthy	0.54-0.67	0.50-0.57	0.56-0.69	49.83-60.19	86.93-108.51	207.61-219.99	128.36-145.86	246.45-289.34	507.71-541.45
	Patient	0.510-0.56	0.56-0.60	0.60-0.65	60.76-68.67	105.82-113.43	198.42-204.88	150.52-163.69	289.09-311.77	533.69-551.97
N1	Healthy	0.54-0.65	0.52-0.58	0.58-0.67	49.04-56.43	85.21-105.70	209.18-218.95	127.54-138.53	245.51-278.64	505.47-536.83
	Patient	0.52-0.58	0.56-0.60	0.55-0.60	61.51-69.35	102.80-112.29	199.19-205.46	151.66-164.78	288.25-314.13	532.13-552.66
N2	Healthy	0.49-0.61	0.53-0.60	0.59-0.69	46.09-52.30	84.48-101.36	211.48-221.83	122.57-131.98	234.24-262.14	491.86-521.72
	Patient	0.54-0.60	0.55-0.58	0.53-0.58	63.33-70.32	106.90-114.75	198.60-204.41	153.62-165.42	295.03-317.95	535.46-553.45
N3	Healthy	0.52-0.64	0.50-0.58	0.58-0.68	46.71-54.25	84.33-100.45	211.47-221.38	123.57-135.49	235.90-265.68	495.92-518.58
	Patient	0.52-0.58	0.56-0.60	0.56-0.62	59.37–66.42	100.80–109.53	200.89–207.23	147.62–158.93	277.37–297.64	529.37-548.07

Note: The result was marked red when 95% CI for healthy were not coincident with the patient's.

pulse shape characteristics at the finger PPG.^{19–21} Finally, sleep events occupied most of the sleep for some heavy apnea patients and the interval was less than 5 minutes between signals without apnea events and apnea event, so PPG we obtained from some heavy apnea patients may be affected by apnea events.

5. CONCLUSION

We compared 9 Gaussian parameters among 5 sleep stages for healthy patients or sleep apnea patients and compared 9 Gaussian parameters among healthy patients and sleep apnea patients during 5 sleep stages. Our results showed that there were no significant statistical differences among 5 sleep stages for healthy patients or for sleep apnea patients, while there were significant statistical differences among healthy patients and sleep apnea patients during 5 sleep stages for parameters W_1 , W_3 and C_1 . Our study will help simplify sleep apnea diagnosis.

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