

Correlation Study in HRV Fluctuations During Four Sleep Stages

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ABSTRACT

The research has studied the correlation between sleep stages and heart rate variability (HRV) based on the experiment, and it found that the heart rate, sympathetic nervous system and parasympathetic nervous system of autonomic nervous system presented strong adjusting effects in four sleep stages.

KEYWORDS: *sleep stages; heart rate variability (HRV); autonomic nervous system*

Date of Submission: 12-10-2018

Date of acceptance: 27-10-2018

I. INTRODUCTION

Heart rate variability (HRV) reflects changes in sympathetic and parasympathetic activity in the autonomic nervous system [1-2]. The correlation between sleep stages and autonomic nervous system activity is analyzed from the HRV. According to the different changes of Electroencephalogram (EEG), Electrooculogram (EOG) and Electromyogram(EMG) in sleep process, sleep can be divided into NREM and REM stages, and NREM stage can be further divided into Light stage (including N1 stage and N2 stage) and SWS stage (including N3 stage and N4 stage)[3-7]. According to the clinical experience of long-term professional training doctors and the data recorded by the polysomnographic (PSG), each sleep stage shows different physiological characteristics.

In order to reduce the patient's high physiological and psychological load during PSG sleep recording, researchers have attempted to distinguish sleep stages using heart rate and other relevant physiological signals, and achieved certain research results [8-15]. However, due to the large number of factors affecting heart rate changes and the complex nature of heart rate changes, some substantive physiological laws have not yet been revealed.

Based on these questions, in order to analyze the relevance of sleep staging and autonomic regulation from the perspective of HRV, this paper proposes a study of the relationship between sleep duration and heart rate. By analyzing the parameters of HRV, we analyze the changes in HRV during the Wake, N1, N2, SWS and REM stages, it uses HRV to study the neurological activity under different sleep stages and understand the changes in the neurological function during sleep.

II. GENERAL SOLUTION AND EXPERIMENTAL DATA

At the Sleep Center of the Sixth Hospital Affiliated to Sun Yat-sen University, this experiment was performed using a Philips Respironics Inc. (Amsterdam, Netherlands). The sleep physiological signals recorded by PSG mainly include 2-leads ECGs, 6-leads EEGs, 2-leads EOGs and 1-lead EMG, in which nasal heat, nasal pressure, chest breathing, abdominal breathing, pulse, blood oxygen, body movements, snoring and other signals were also recorded. After the PSG recording is completed, the signals are automatically staged by the computer software, and then the experts' interpretation of the software calibration results of sleep staging and respiratory events are performed manually. The sampling rate of the central electrical signal is 500 Hz, and the ECG signals during sleep stages through 2 electrocardiograph electrodes are obtained during the whole night's sleep recording of PSG, and the recording time is generally about 8 hours. At last, the recorded signals will be divided into consecutive segments every 30 seconds, and the doctors performed sleep staging on these segmented data. Fig. 1 shows the details of data collection and experimental equipment.



Fig. 1. Photos of the clinical experiment: (a) expert pasting electrodes on subjects; (b) sleep-breathing monitoring of subjects; (c) experimental equipment list; (d) channel list of Alice 5 PSG, Philips, Inc.; (e) PSG computer monitoring screen.

In this experiment, the sampling rates of EEG, EOG, and EMG were all 500 Hz. A higher sampling rate will reduce the speed and efficiency of the algorithm, so the sampled signal is down-sampled by 250 Hz in order to reduce the computational complexity of the data. The Figure 2 shows some of typical PSG recordings indicating various sleep stages, respectively.

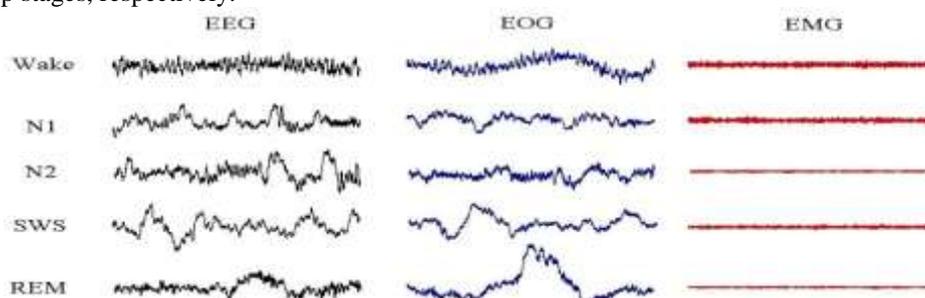


Fig. 2. Typical oscillogram of EEG, EOG and EMG in sleep stages of Wake, N1, N2, SWS and REM from our data

In this study, all-night polysomnographic (PSG) sleep recordings were obtained from 18 healthy subjects, of which 14 were males and 4 were females, ranging from 28 to 52 years old (mean=39.1±7.4 years). These measurements were approved by the ethics committee of the 6th Affiliated Hospital of Sun Yat-Sen University. The sleep quality and medical history were recorded by interview, and all subjects reported no history of neurological or psychological disorders. The all-night PSGs were recorded in the Sleep-disordered Breathing Center of the 6th affiliated hospital of Sun Yat-Sen University (by Alice 5 PSG, Philips, Inc.). There was also no outside interference during data collection, and no medications were utilized to cause sleep. The specific demographics, sleep structure, and apnea-hypopnea index (AHI) of the subjects are shown in Table 1.

Tab.1 Demographic, sleep structure and AHI of subjects

subject	sex	age	AHI	Wake/ALL	N1/Sleep	N2/Sleep	N3/Sleep	R/Sleep
1	M	36		14.25	24.87	50.65	15.71	8.77
2	M	67		16.52	18.19	47.14	14.99	19.68
3	M	28	5.7	28.24	13.99	71.63	10.07	4.31
4	M	36	0.8	5.33	12.93	56.29	8.14	22.63
5	M	40	3.7	13.15	19.44	42.60	23.50	14.46
6	M	59		16.05	14.30	50.18	13.93	21.58
7	M	43		19.77	9.06	60.27	10.63	20.05
8	M	36	0.6	5.52	15.68	51.13	7.48	25.72
9	M	73		15.53	19.59	54.08	12.51	13.82
10	F	60		6.85	16.02	48.40	12.81	22.77
11	F	48	0.7	25.41	14.94	53.58	17.04	14.44
12	M	45	3.2	24.57	32.58	50.68	6.94	9.80
13	M	56		13.40	38.34	38.91	4.04	18.71
14	M	64	1.8	3.26	13.84	54.49	5.36	26.31
15	M	59	3.2	4.90	17.65	52.31	7.35	22.69
16	F	62		13.62	19.93	52.69	4.65	22.74
17	F	57	0.3	21.32	2.05	43.53	25.67	28.75
18	M	30		34.94	49.65	41.90	4.75	3.70

in which, AHI is the summation of apnea and hypopnea times per hour of sleep. The evaluation criteria of OSAS is: normal, AHI < 5; mild, AHI 5-20; moderate, AHI 21-50; severe, AHI ≥ 50. M is male, F is female, All is the number of sleep stages and Sleep=N1+N2+SWS+REM.

In the experiment, ECG electrodes were placed as following, one was on the right and left of the second intercostal space in the chest, and one was placed on the left clavicular line and the rib arch. The classic II lead electrodes were placed on the right upper limb and left lower limb, and it can also be placed on the trunk, using the placement method in which the right shoulder and left hip are connected in parallel. When the electrocardiographic event is discriminated, enlarging the recorded pattern contributes to the judgment of arrhythmia. In order to reduce interference, standard ECG electrodes were used in this experiment, which would be superior to EEG electrodes in recording.

III. HRV FEATURE EXTRACTION METHOD

3.1 Process of HRV extraction

Frequency-domain analysis of HRV quantitatively reflects the modulation of the sympathetic and parasympathetic nervous systems of the heart. Therefore, in this experiment, frequency domain analysis was used to analyze the HRV during sleep.

In this experiment, two ECG signals were selected for the experimental study of sleep HRV in the 28-lead PSG signal obtained. In general, a guided ECG signal is sufficient for assessment of HRV. However, when the sleep stage is switched or when body movement is occurred during the awake stage and some other sleep events is occurred, if a certain ECG sensor signal falls off, another ECG signal may be used as an alternative signal. The flow chart of HRV feature extraction of this experiment is shown in Figure 3.

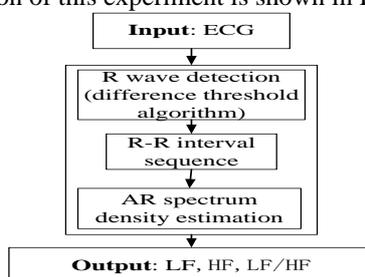


Fig.3 Flow chart of HRV analysis in sleep stages

3.2 HRV extraction algorithm

This paper mainly uses the spectral analysis method (frequency domain analysis method) in the linear analysis method. Because the frequency domain analysis method describes the distribution of energy of complex heart rate fluctuation signals in different frequency bands, the various physiological factors are separated by appropriate amounts of analysis, and thus compared with the time domain analysis method, the result reveals higher accuracy and sensitivity [1-2, 16-18].

The basic steps of spectral analysis are followed by [1-2, 16-18]:

- (1) R wave identification was performed to obtain a heart rate map;
- (2) The HRV spectrum can be obtained by spectral analysis of the heart rate chart.

3.3 Frequency-domain analysis of HRV

Through the methods above, autoregressive (AR) transformation was performed on consecutive R-R interval values, and the HRV power PSD (spectral density estimate) and the power spectrum density (energy density) was obtained on the horizontal axis and the ordinate axis. According to the previous research, the spectrum components were divided into the following parts [1-2, 16-19]:

- (1) Total power (TP): frequency band ≤ 0.4 Hz;
- (2) Low frequency power (LF): frequency band 0.04~0.15 Hz;
- (3) High frequency power (HF): frequency band 0.15~0.4 Hz;
- (4) Ultra-low frequency power (ULF): frequency band ≤ 0.003 Hz;
- (5) Extremely low frequency power (VLF): frequency band 0.003~0.04 Hz.

LF mainly reflects the sympathetic tone, while HF mainly reflects the parasympathetic tone. TP reflects the total tension of the sympathetic and parasympathetic nerves. In addition, LF/HF reflects the autonomic balance index and is one of the most important indicators of autonomic dysfunction.

Many commercial software have their own frequency domain analysis of HRV. The power spectrum unit mainly adopts ms^2/Hz , which reflects the R-R interval variation [1-2, 16-18]. However, the former one reflects a higher sensitivity of the frequency spectrum change than the latter one. In addition, some experts have also proposed to standardize LF and HF to remove the influence of total power. The standard processing method is as follows:

$\text{LFnorm} = 100 \times \text{LF} / (\text{TP} - \text{VLF})$, unit: dimensionless;

$\text{HFnorm} = 100 \times \text{HF} / (\text{TP} - \text{VLF})$, unit: dimensionless;

$\text{LF/HFnorm} = \text{LFnorm} / \text{HFnorm} = \text{LF} / \text{HF}$, unit: dimensionless.

3.4 Sleep staging method

In order to eliminate the EEG fluctuations caused by local sports and other issues caused by sleep mis-judgment, some stages still need to be managed separately, and these unrealistic and disturbed stages are filtered far beyond the average heart rate. Through the matlab, the heart rate was obtained, and the HRV of each sleep stage was calculated by the R-R interval.

This experiment adopted the clinical data of the Sleep and Respiratory Disorders Treatment Center of the Sixth Hospital Affiliated to Sun Yat-sen University. The sleep center doctors use AASM's clinical interpretation criteria to stage sleep data. The AASM standards differ from the previous R&K standards in terms of interpretation rules [5-7].

IV. EXPERIMENT AND RESULTS

The AR model in the third part was used to obtain various indicators of HRV through the frequency domain analysis algorithm. According to the above calculation process and methods, the following experimental results were obtained. Among them, the statistical results with LF, HF, and LF/HF between each sleep stage and HRV are shown in Tables 2, 3, and 4, respectively.

Tab.2 The mean and standard deviation (S.D.) of LF in Wake, N1, N2, SWS, REM of 18 subjects, and the unit, cycle / minute (CPM)

subject	Wake	N1	N2	SWS	REM
t	mean±S.D.	mean±S.D.	mean±S.D.	mean±S.D.	mean±S.D.
1	139.69±101.02	231.72±129.85	410.93±84.81	673.74±218.95	426.98±290.0
2	1001.3±752.58	904.87±516.34	834.94±339.98	827.32±269.13	1984.9±1327
3	1343.3±930.31	2282.4±1735.5	3306.1±1685.4	4119.7±2161.9	4725.9±2914
4	941.28±376.88	908.89±666.80	913.68±241.12	1269.8±38.88	886.36±988.8
5	3565.3±1047.9	3030.3±1815.4	1685.6±518.91	2292.9±990.88	4649.5±4255
6	1243.3±722.99	1087.0±655.05	661.12±333.40	866.51±141.65	2442.3±2367
7	1758.5±1046.3	1694.3±510.89	1817.7±501.68	1954.8±670.42	2886.7±1315
8	366.82±194.69	788.43±295.24	1002.0±353.02	2235.6±818.86	1892.9±675.3
9	2771.3±2897.6	3900.9±1466.4	2552.0±641.12	2115.0±190.96	7926.4±1203
10	2087.1±3156.1	3874.0±1571.5	3543.3±804.69	1876.7±1564.3	4518.6±1214
11	97.27±64.92	397.03±205.62	210.90±38.83	2235.6±818.86	2539.2±1245
12	8234.6±5349.4	7291.7±6453.8	13867±7342.6	6692.4±2976.8	9026.5±7229
13	3634.2±2852.9	5235.4±2455.6	5575.6±4362.0	6395.6±1278.1	5277.1±4834
14	452.79±242.49	142.31±91.65	293.89±115.33	937.77±145.64	1059.8±888.6
15	5514.9±4381.0	1835.9±1365.0	1143.7±346.47	2589.1±1464.7	5644.4±3518
16	2737.6±6782.0	564.17±236.24	245.06±1532.0	2235.6±818.86	1260.4±505.8
17	815.38±291.01	912.66±495.98	1029.4±221.52	823.96±111.02	1387.6±331.9
18	168.48±108.86	459.49±419.33	299.57±312.74	98.08±59.52	826.06±311.3
mean	2048.5±1738.8	1974.5±1171.5	2188.5±1098.6	2235.6±818.86	3297.9±1967

Tab.3 The mean and standard deviation (S.D.) of HF in Wake, N1, N2, SWS, REM of 18 subjects, and the unit, cycle / minute (CPM)

subject	Wake	N1	N2	SWS	REM
	mean±S.D.	mean±S.D.	mean±S.D.	mean±S.D.	mean±S.D.
1	30.10±12.72	133.09±73.70	229.30±46.58	227.59±72.07	152.66±133.3
2	156.81±88.82	313.34±163.42	295.97±127.20	282.24±89.34	614.45±602.0
3	253.51±190.69	506.41±325.07	944.48±349.44	1044.1±434.36	951.62±376.2
4	178.12±62.59	360.36±254.18	427.80±74.47	282.03±69.02	542.50±250.3
5	946.76±401.72	859.50±392.56	687.41±257.94	934.99±378.61	1216.7±742.6
6	299.76±131.02	443.53±124.24	312.41±132.96	341.46±48.59	611.84±450.1
7	526.52±279.02	819.18±272.04	709.29±238.09	595.42±153.88	732.07±346.0
8	78.86±40.22	341.28±103.57	381.36±104.88	728.99±248.21	222.60±1177
9	359.92±227.31	1389.5±467.08	801.88±83.58	805.88±30.14	2171.9±427.0
10	668.41±784.87	1299.7±569.30	1078.3±138.61	599.14±346.68	1261.2±524.6
11	43.22±25.33	191.28±85.56	108.37±20.21	728.99±248.21	791.77±316.2
12	2272.1±1739.1	2103.1±1314.0	3805.8±1610.8	2049.7±1111.8	2680.8±1390
13	1049.1±588.41	2054.2±615.96	1869.9±611.26	2007.6±239.11	1337.4±688.1
14	88.56±42.23	102.03±34.58	148.62±39.51	229.93±44.43	373.05±395.6
15	1900.2±1175.6	742.12±497.68	570.81±216.60	1025.4±629.30	1749.0±842.7
16	814.61±1691.1	371.61±105.22	758.43±179.19	728.99±248.21	888.64±748.7
17	173.26±74.96	336.25±163.82	423.79±46.56	445.75±39.44	452.23±85.91
18	44.98±12.32	221.60±200.77	171.15±158.11	63.76±36.31	350.94±137.0
mean	549.16±420.45	699.34±320.15	762.50±246.44	728.99±248.21	905.08±535.2

Tab.4 The mean and standard deviation (S.D.) of LF/HF in Wake, N1, N2, SWS, REM of 18 subjects, and the unit, cycle / minute (CPM)

subject	Wake	N1	N2	SWS	REM
	mean±S.D.	mean±S.D.	mean±S.D.	mean±S.D.	mean±S.D.
1	4.44±2.36	1.75±0.23	1.81±0.27	2.97±0.36	3.13±1.13
2	6.21±3.03	2.57±0.81	2.85±0.23	2.93±0.21	3.61±1.24
3	6.58±4.79	4.26±1.60	3.62±1.63	4.00±1.65	4.66±1.67
4	5.35±1.09	2.98±1.09	2.12±0.35	4.53±0.80	1.65±1.65
5	5.17±4.72	3.31±1.15	2.63±0.72	2.58±0.75	3.52±1.78
6	4.84±3.70	2.32±0.89	2.19±0.64	2.53±0.18	3.74±1.03
7	3.72±1.90	2.18±0.53	2.70±0.67	3.21±0.68	4.26±1.58
8	5.08±3.40	2.36±0.66	2.65±0.65	3.01±0.71	3.35±0.80
9	6.05±4.23	2.89±0.74	3.17±0.64	2.63±0.22	3.70±0.42
10	2.69±0.95	3.05±0.69	3.37±1.03	2.65±1.11	4.34±2.37
11	2.16±0.24	2.05±0.29	1.96±0.24	3.01±0.71	3.40±1.48
12	4.14±2.25	3.21±0.91	3.59±1.06	3.45±0.99	3.11±0.98
13	3.15±1.38	2.51±0.56	2.79±1.70	3.18±0.49	3.66±1.62
14	5.42±2.28	1.33±0.62	1.97±0.51	4.26±1.25	3.26±1.56
15	3.28±2.50	2.34±1.04	2.10±0.41	2.83±1.49	3.15±1.01
16	2.99±1.06	1.58±0.59	2.98±1.32	3.01±0.71	1.74±0.80
17	5.33±2.49	2.62±0.54	2.43±0.43	1.85±0.19	3.11±0.75
18	3.66±2.11	2.07±0.32	1.72±0.30	1.57±0.27	2.37±0.41
mean	4.46±2.47	2.52±0.74	2.59±0.71	3.01±0.71	3.32±1.24

The statistical results of Tables 2, 3, and 4 above are further summarized to obtain the statistical results in Table 5 below.

Tab.5 The mean and standard deviation (S.D.) of heart rate(HR), LF, HF, and LF / (HF+LF) in Wake, N1, N2, SWS, REM of 18 subjects, and the unit, cycle / minute (CPM)

characteristic parameter	statistic	Wake	N1	N2	SWS	REM
HR	mean	72.50	66.58	64.45	64.33	68.14
	±S.D.	±4.45	±2.09	±1.32	±1.61	±1.74
LF	mean	2048.50	1974.50	2188.50	2235.60	3297.90
	±S.D.	±1738.80	±1171.50	±1098.60	±818.86	±1967
HF	mean	549.16	699.34	762.50	728.99	905.08
	±S.D.	±420.45	±320.15	±246.44	±248.21	±535.20
LF/HF	mean	4.46	2.52	2.59	3.01	3.32
	±S.D.	±2.47	±0.74	±0.71	±0.71	±1.24
LF/(HF+LF)	mean	0.78	0.69	0.70	0.73	0.74
	±S.D.	±0.10	±0.07	±0.06	±0.04	±0.06
HF/(HF+LF)	mean	0.22	0.31	0.30	0.27	0.26
	±S.D.	±0.07	±0.07	±0.06	±0.04	±0.06

The average heart rate showed an inequality relationship is Wake> REM> N1> N2> SWS in each sleep period. This rule is basically similar to the correlation between sleep stage and respiratory rate, indicating that sleep staging and cardiopulmonary signals are basically consistent. The average heart rate changes from NREM to REM are significantly increased, and the conclusion is consistent with the results obtained from previous studies [20-21].

Heart rate variability LF and HF were not significantly different in each sleep stage, indicating that LF and HF signals were more fluctuating during sleep and the regulation was more complicated. The heart rate and LF/HF ratios showed extremely significant differences. It shows that the heart rate, the balance of the autonomic nervous system have a significant characteristic that switching with sleep stages, indicating a more clear feature and regulation.

The LF response is the regulation of sympathetic nerves, and the experiments indicated that REM>SWS>N2>>Wake>N1. In the sleep stage, the sympathetic regulation in the REM phase was the strongest, and the sympathetic regulation in the REM phase was significantly stronger than in the NREM phase. The HF reaction is parasympathetic, and the experiments draw a conclusion that REM> N2> SWS> N1> Wake. It shows that in the REM period, the parasympathetic regulation function is also the strongest one and is consistent with the regulation of LF. Experiments have proved that the REM period is the most active period of sleep heart and lung events. However, some adjustments in the NREM and Wake phases of HF are precisely the opposite with the regulation of LF. It also shows that in the above two sleep stages, the sympathetic and parasympathetic nerves in the autonomic nervous system may sometimes be antagonistic to each other.

LF/HF quantifies the balance of sympathetic and parasympathetic nerves in the autonomic nervous system. The rule of Wake> REM> SWS> N2> N1 is experimentally obtained, which proves that the autonomic balance of REM and Wake periods are poor. This is because in both sleep stages, the sympathetic and

parasympathetic nerves are actively working and the state of regulation is relatively disordered. However, in the NREM period, this balance is stabilized by the weakening of the regulatory effect, and the $LF/(LF+HF)$ also reflects the balance of the autonomic nervous system. The experimental results show that $Wake > REM > SWS > N2 > N1$. The heart rate variability and the statistical parameter values of $LF/(LF+HF)$ basically show the same pattern as LF/HF , which can also be seen from the mathematical derivation of the formula. The $HF/(LF+HF)$ expresses the balance of the autonomic nervous system from the opposite direction. The experimental results show that $N2 > N1 > SWS > REM > Wake$. This inequality shows the opposite rule to $LF/(LF+HF)$.

V. DISCUSSION

The body's autonomic nervous system can be divided into two parts: sympathetic and parasympathetic, which jointly control the activities of internal organs and glands, and each organ receives both sympathetic and parasympathetic regulation of the two nervous systems. The role of both is mutual antagonism. The sympathetic nervous system enhances the activity of organs, and the parasympathetic nervous system weakens the activity of organs. The above five statistical parameters of heart rate variability reflect the change of heart rate variability with sleep stage switching from the frequency domain of heart rate variability. It draws the conclusion that the HR-phase heart rate variability (mean and standard deviation) was significantly greater than the NREM variability [1-2]. It shows that the regulation mechanism of the autonomic nervous system in the REM period is more complex, and coincides with the physiological phenomenon with high complexity in the clinical REM cardiovascular regulation system. For example, the mean values of LF and HF of all the subjects are greater than the NREM period in the REM period, which indicates that both LF and HF showed positive regulation during the REM period. Since LF reflects the activity of sympathetic regulation, the REM period corresponds to a larger value. It shows that from the NREM phase to the REM phase, the activity of the sympathetic nervous system increases. From the basic knowledge of physiology, it makes the activity of the sympathetic nervous system enhanced, and accelerates the heart rate, contract the muscles, and contract the peripheral blood vessels., but at the same time, because HF reflects the activity of parasympathetic regulation, the enhancement of parasympathetic nerve activity will bring about a decrease in heart rate, weakened myocardial contraction and muscle relaxation, and maintain the body in a protective and stable state [1-2]. The sympathetic and parasympathetic interweaving effects act together in the REM phase. The sympathetic modulation enhances the parasympathetic contraction modulation and ultimately achieves a dual effect. Therefore, the LF/HF heart rate variability parameters obtained in this experiment are consistent with the actual physiological phenomenon. The physiologic characterization of the heart and lungs in the REM period is relatively turbulent and the autonomic nervous system is poorly balanced. In addition to the REM period, the light period during the NREM period and the SWS period generally fall asleep. The effect of LF and HF is just the opposite. Both sympathetic and parasympathetic regulation are weakened and the sleep state tends to be stable, and the balance of the autonomic nervous system is better.

Analysis of heart rate variability during sleep staging has been applied in short-term sleep and the sleep period involved is not comprehensive enough [8-11]. Most literature compares the characteristics of heart rate variability among healthy individuals and OSAS populations with different disease levels, which proves that the significant differences between healthy and OSAS patients and autonomic disorders [12-15]. According to the current literature review, sleep staging is only a stage indicator, which means using the sleep period as a scale to measure the differences in heart rate variability between healthy and OSAS populations on a scale [22-26]. The relevant research about the changes in the variability of the sleep stage center rate in the most basic healthy population, and autonomic regulation in sleep stages, sleep and heart rate variability systems is still deficient. This topic has a basic reference significance for the law of comparative study of HRV between OSAS and healthy people. It clarifies the characteristics of the HRV of a healthy population with changes in the stage of sleep, which is conducive to a fundamental understanding of the mechanism of autonomic regulation during sleep and provides statistical basis for more extensive research.

VI. CONCLUSION

In this chapter, the statistics and correlation analysis of sleep stage and heart rate variability were conducted. The experimental study shows that with the switch of the sleep period, the sympathetic, parasympathetic and autonomic nervous system balance rules. were both higher in the REM stage than in the NREM stage. When the sleep state changed from the NREM stage to the REM stage, the activity of autonomic nerves gradually increased and the balance gradually worsened. Analysis and study of sleep period and heart rate variability, mainly from the aspect of nerve regulation, help to clarify the relevant laws of staging and sleep mechanism.

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YanJun Zhang* "Correlation Studyin HRV Fluctuations During Four Sleep Stages " *The International Journal of Engineering and Science (IJES)*, , 7.10 (2018): 32-38