

Acceleration Plethysmography (APG) Correlate with Moods in Nursing Workers with Fatigue and Stress after Work

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Abstract

Purpose: Fatigue or stress in the workplace is a serious problem. The purpose of this study is, in order to understand characteristics of fatigue and stress, to assess the correlation between the physiological and psychological fatigue of healthy nurses during normal work.

Methods: 51 healthy nurses and 24 controls were recruited. Participants were randomly allocated two groups: the new nursing worker (NNW) group with less than 3 years of working (n=25) and the expert nursing workers (ENW) group with more than 3 years of working (n=26). We examined nurses' physiology: Acceleration Plethysmography (APG) and Blood Pressure (BP) and psychology: Visual Analogue Scale (VAS) and Mood Inventory Scale (MIS) before and after a normal workday.

Results: The VAS increased significantly, in all groups. In the NNW group, we observed that LF/HF ratio, Low frequency (LF), and BP increased significantly as compared to ENW group and the controls. In the ENW group, HF decreased slightly and DBP decreased significantly. The autonomic activity correlated significantly with the MIS for all nurses.

Conclusion: Nursing workers were characterized by increased sympathetic components in the NNW group and decreased parasympathetic components in the ENW group. These findings may help nurses and other workers reduce fatigue, cope with stress, and prevent illness. Physiological indicators may provide an objective assessment of nurse fatigue, and the MIS test may alternative for physiological tests to detect fatigue more quickly and easily. We hope this study will contribute towards addressing the issues related to workers' mental health in the workplace.

Keywords: Acceleration Plethysmography (APG) • Stress • Fatigue • Mood inventory scale • Nursing worker

Introduction

Workplace fatigue impacts workers' physical and mental health [1]. Large scale sociological investigations reveal that more than 50% adults suffer from fatigue [2]. Fatigue not only impairs concentration and work efficiency, but, in worst cases, it can lead to sickness and death [3]. In recent years, Japan's aged society faces a chronic shortage of nurses and other care staff members. The profession of nursing, not only due to the problem of aging society, but also due to the epidemic of COVID-19 pandemic and the occurrence of clusters in facilities for the elderly, is physically and mentally stressful. Long working hours and interpersonal challenges increase this fatigue, causing many to leave the work force. Nursing is a demanding and stressful profession worldwide, and nurses suffer from physical illness, mental disorder, and emotional exhaustion more than other health practitioners in the general population [4,5]. In particular, the turnover rate of less than 3 year, which has a short working period, is higher than that of other occupations [6-8]. Therefore, in order to improve the physical and mental health of nurses and reduce the decrease in labor, understanding

nursing fatigue, especially new nurses (NNW) who are stressful and have a high turnover rate, compared to expert nurses (ENW) and other occupations is important.

Many people think that feeling of figure expressed as "tired" can be overcome by "spirit", and it is difficult to make an accurate evaluation. The phenomenon of fatigue is recognized by everyone, and it is an unquestionable fact that it has a quantitative nature. Fatigue can be classified as physical and mental. Physical fatigue, also known as peripheral fatigue, results from repeated muscle actions. By contrast, mental fatigue represents a failure to complete mental tasks that require self-motivation and internal cues in the absence of demonstrable cognitive failure or motor weakness [9]. And fatigue can have various effects on autonomous functions such as cardiac function and hemodynamics [10,11]. Thus, mental fatigue decreases the sufferers' work efficiency in daily life. Previous studies have consistently demonstrated the decrease in sympathetic nervous activity due to mental stress [12,13]. Mental fatigue not only increases sympathetic nervous activity but it also decreases parasympathetic nervous agility [14-18]. In general, it is a question of whether fatigue is evaluated as a subjective sensation by recognizing reaction, and time delay, increased false reaction, and multiple attention difficulties. The difficulty in measuring and evaluating fatigue as a medical subject may be due to its delay as another medical research area. Questionnaires typically used to evaluate subjective fatigue [19-21] fail to achieve objectivity, while physiological studies of fatigue fall short of capturing its subjective feeling.

Pulse waves contain a lot of information about hemodynamics from the heart to peripheral blood vessels. In the volume pulse wave, the pulsation generated at the origin of the aorta propagates to the peripheral artery site, and the volume change of the peripheral artery is recorded accordingly [22]. Digital plethysmogram (DPG) is a measurement of blood flow fluctuations from changes in the absorbance of haemoglobin at the fingertips. Acceleration plethysmogram (APG) is an improvement of the DPG waveform

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to a second derivative waveform for quantitative analysis of pulse waves. It is mainly used as a test that reflects peripheral vascular hemodynamics and autonomic nervous function. The APG waveform is composed of the five components, a,b,c,d, and e. The a-a interval of APG has the same physiological significance as the autonomic nerve analysis by the R-R interval of the electrocardiogram [23]. It has become possible to evaluate autonomic nervous function more easily. Autonomic nerve fatigue may cause chronic fatigue syndrome (CFS) [24-28], multiple sclerosis (MS) [29-31], and primary biliary cirrhosis [32]. These reports suggest that changes in autonomic nervous activity are related to the mechanisms underlying fatigue. However, this relationship has been demonstrated only in patients with specific diseases, but not in healthy subjects.

Fatigue is not only a symptom common to such specific diseases, but it is also observed in healthy individuals [33,34]. Recent research using 30 minutes of fatigue inducing mental tasks has shown decreased parasympathetic activity and increased sympathetic activity even in healthy volunteers [10]. Similarly, a comparison of autonomic activity and mental fatigue after eight hours of fatigue inducing mental tasks (corresponding to a normal workday for healthy adults) has indicated decreased parasympathetic activity (HF) and increased autonomic function (LF/HF ratio) [11]. However, the study did not examine mood, only the visual analogue scale (VAS) for subjective fatigue. There is a feeling of fatigue after work and an effect on autonomous function. However, there are very few reports that examine the relationship between after work fatigue and autonomic nerves for stressful nurses. It can be assumed that the new nurses are different from the expert nurses in terms of sensitivity and tolerance to stress and how to deal with them. These may also make a difference in how fatigue after work is felt and how it affects autonomous function. Comparing NNW group with ENW group, it may be possible to evaluate the unique characteristics of newcomers.

Our study aims to advance current research by (1) by examining and comparing the fatigue characteristics of the new nursing worker (NNW) group and the expert nursing worker (ENW) group of control after 8 hours of work to clarifying similarities and differences, and (2) comparing the psychological mood test and the physiological fatigue test of nurses.

Methods

Participants and research design

We recruited 51 nurses (44.67 ± 10.82 years) working in six elderly care institution and 24 non-nursing workers (40.33 ± 11.65 years) of control group. Participants were randomly allocated two groups: the new nursing workers (NNG) group with less than 3 years of working and the expert nursing workers (ENW) group with more than 3 years of working. The cities where workers are big city; Tokyo 23-ku (2), local city; Fukushima city (2), mountain village area; Samegawa village, Fukushima prefecture (2).

For All participants, nursing workers and controls (non-nursing workers), we confirmed health through medical checkups and preliminary interviews. Then, we were excluding candidates with suspicion of physical or mental instability.

The work of nurses and controls was set to day shift, and the working hours were set to 8 hours. We measured the participants' (nurses and control) physical and mental conditions before (7:45-9:30 am) and after (17:00-19:00 pm) their working day. We gauged their autonomic nervous system at rest in sitting position using APG (Arttett, Umedica, Osaka), and then their systolic and diastolic blood pressure, and heart rate using a sphygmomanometer (HEM-6300, Omron Health Care, Kyoto) on their upper arm. We measured APG and BP twice in three minutes both before working and after working. We adopted the stable recorded data that showed the least deviation from the baseline [35]. After each physiological examination, we administered VAS and MIS questionnaires.

Ethics committee and ethical consideration

This study examined the nurses' physiology and moods, with the approval of the Medical College Ethical Review Board. Both orally and in writing, we explained the study contents, privacy policy, and right to withdraw, to receive participants' consent.

Accelerated Plethysmography (APG)

Photoplethysmography was used to measure changes in the absorption of light by hemoglobin, related to blood flow volume. We used APG [2,36-38] to evaluate autonomic function, using a pulsimeter (Artett, U-Medica, Osaka) with a sensor positioned on the tip of the ventral side of the index finger. The pulsimeter automatically analyzed the APG wave form consisting of four waves in systole (a-d) and one in diastole (e). The output of the pulsimeter sensor was preprocessed by an analogue filter (2nd order, low pass filter with 23 Hz of cutoff frequency). The data were recorded using an analogue to digital converter (3.3 volt to 10 bit) with a real time sampling rate of 1,000 samples per second. These digital data were processed with a 67th order finite impulse response filter using the Hanning window, interpolated to sub-millisecond order. Frequency analyses for pulse interval variation were diagnosed with fast Fourier transformation.

Resolution ability for power spectrum was 0.001 Hz. For the frequency analyses, the total power was calculated as the power within a frequency range of 0-0.4 Hz. We classified frequency range of 0.04-0.15 Hz as low frequency component power (LF), and high frequency (HF) as the frequency range of 0.15-0.4 Hz. The HF is vagally mediated [39-41], whereas the LF originates from a variety of sympathetic and vagal mechanisms [39,42]. The low frequency component power/high frequency component power ratio (LF/HF) reflects autonomic function [18].

Questionnaires

Visual Analog Scale (VAS): VAS is an abbreviation for Visual Analog Scale and is also called a visual evaluation scale. The purpose is originally to measure the intensity of pain, but to measure the degree of fatigue [43]. We asked subjects to record their fatigue on a visual analogue scale (VAS) based on Japanese Fatigue Society guidelines, rating their fatigue from 0 (no fatigue) to 100 (complete exhaustion).

Mood Inventory Scale (MIS): We used the Sakano's Mood Inventory scale, with confirmed reliability and validity in its Japanese version [44]. The Sakano's Mood Inventory comprises five groups (tension and excitement, feeling refreshed, fatigue, depressive mood, and anxiety) with eight questions in each, totaling 40 items, using a 4-point Likert scale. The total score for each factor ranges from 8 to 32, with higher scores indicating greater conformity. In this study, tension and excitement, feeling refreshed, and fatigue, were used, but depressive mood and anxiety were not used. It was not used with Depressive Mood and Anxiety in this study because there were no significant changes or correlations.

Statistical analysis

Statistical analysis was performed using Stata IC 15 (Light Stone Inc.). P values less than 0.05 were considered statistically significant. Baseline characteristics of nominal data (gender, age, working city) were compared using the chi-square test and t-test for independent samples for nurses' engaged years. The pulse rate and the VAS value for fatigue are shown as the Mean \pm SD. We evaluated the difference between before work and after work and between the groups with a repeated measure ANOVA, t-test and used Spearman's correlation analysis to compare (VAS value, MIS Scale) with fatigue and LF/HF ratio.

Results

Nurses' parameters of the groups

Table 1 shows the demographic characteristics of the participants. There was a significant difference in engaged years between NNW and ENW.

The NNW is a nursing worker who has been working for less than 3 years and is mainly engaged in the care of patients. The ENW are expert nurses who have been working for more than 3 years, including nurses engaged in

managerial positions and counselling services. There was no difference in age, gender, working city among the three groups.

Table 1. Baseline characteristics of participants with Nursing Worker and Controls.

Age, Working Period; Mean (SD), Gender, Working City; Mean (%)			
	New -Nursing Worker n=25	Expert-Nursing Workers n=26	Control n=24
Age (year)	43.96 (9.30)	45.38 (12.34)	40.33 (11.65)
Working period (year)	1.23 (0.65)	16.19 (8.69) **	-----
Gender			
Male (%)	11 (44%)	7 (27%)	8 (32%)
Female (%)	14 (56%)	19 (73%)	16 (68%)
Working City			
Tokyo 23-ku (%)	5 (%)	8 (%)	5 (%)
Fukushima city (%)	13 (%)	11 (%)	11 (%)
Samegawa village (%)	7 (%)	7 (%)	8 (%)
New Nursing worker (NNW) group: less than 3 years of nursing worker, Expert Nursing worker (ENW) group: more than 3 years nursing worker, Control: non-nursing workers. *Different between the groups for working period (independent t-test, p<0.01), Gender and Working City (Chi-square test, p<0.01). † p>0.05, ** p>0.01			

Physiology tests

Table 2 shows the autonomic nervous activity measured by APG and BP before and after work. Repeated measure ANOVA analysis revealed significant differences between groups. LF/HF and LF increased significantly from the baseline after work (p<0.01), in the NNW, and which was different from ENW and Control. Systolic blood pressure (SBP) and diastolic blood

pressure (DBP) increased significantly (p<0.05), in the NNW, and which was different from ENW and Control. BP decreased significantly, (p>0.05), in the NNW, and which was different from ENW. Systolic blood pressure (SBP) and were reduced, significantly (p<0.01), in ENW, and which was different from NNW and Control. Diastolic blood pressure (DBP) was increased significantly (p<0.01), in control, and which was different from NNW and ENW.

Table 2. Autonomic activities before (baseline) and after the working (8hr).

Mean (SD)							
	New-Nursing Worker		Expert- Nursing Worker		Control		p
	Before	After	Before	After	Before	After	
LF/HF	2.18(1.52)	5.59(5.54) **	2.80(2.41)	3.12(3.34)	4.35(3.16)	3.91(4.45)	+++
LF(ms2)	426.84(611.94)	921.68(789.52) **	463.77(544.62)	389.88(603.83)	1064.26(976.16)	935.92(885.95)	+++
HF(ms2)	241.50(207.41)	241.44(169.35)	195.67(153.81)	156.58(198.04)	290.36(212.11)	366.92(289.12)	
BPM	80.9(8.44)	76.65(7.20) **	77.30(8.76)	77.00(9.96)	76.93(11.71)	75.42(9.84)	++
SBP	119.83(10.62)	123.46(10.92) †	129.73(14.34)	124.00(11.97) **	119.58(13.87)	121.50(13.86)	+++
DBP	79.29(10.20)	82.54(7.33) **	85.15(11.81)	85.55(10.85)	79.12(12.58)	82.76(11.71) **	+++
New Nursing worker (NNW) group: less than 3 years of nursing worker, Expert Nursing worker (ENW) group: more than 3 years nursing worker, Control: non-nursing workers. LF: low-frequency component power, HF: high-frequency component power, LH/HF ratio: low-frequency component power/high-frequency component power ratio, BPM: Pulse Rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, Values are presented as the mean and SD (paired-t-test). *p>0.05, **p>0.01. †difference between NNW and ENW (+p<0.05, ++p>0.01), †difference between NNW and Control (~p<0.05, ^^p>0.01), ▲ difference between ENW and Control (▲ p<0.05, ▲▲ p>0.01).							

Questionnaire

Table 3 shows questionnaire evaluation before and after work. Repeated measure ANOVA analysis revealed significant differences between groups. The VAS value of fatigue increased significantly in all groups compared to

before work (p<0.01), but there was no difference between the groups. The Tension and Excitement items of MIS had significantly increased (p<0.01), in ENW, and which was different from NNW and Control. The Feeling Refreshed of MIS showed significant decreases (p<0.01), in ENW, but there was no difference between the groups.

Table 3. Questionnaire before (baseline) and after the working (8-hr).

Mean (SD)							
	New-Nursing Worker		Expert- Nursing Worker		Control		p
	Before	After	Before	After	Before	After	
VAS value	4.01(1.78)	5.05(1.37) **	5.05(1.37) **	5.44(2.11) **	4.15(1.48)	4.99(1.45) **	

Mood Inventory							
Tension Excitement	12.63(4.16)	12.75(4.45)	13.15(16.13)	13.67(6.46) **	13.30(6.32)	14.22(6.82) **	++**
Refreshing Mood	18.51(4.94)	17.75(5.30)	18.38(4.63)	16.44(4.86) **	18.13(4.38)	16.78(4.57) **	
Fatigue Mood	16.43(5.22)	17.00(6.39)	16.59(6.27)	17.34(6.84)	14.91(5.98)	16.87(7.54) **	

New Nursing Worker (NNW) group: less than 3 years of nursing worker, Expert Nursing Worker (ENW) group: more than 3 years of nursing worker, Control group: non-nursing workers. VAS: Visual Analogue Scale. Values are presented as the mean and SD (paied-t-test). *p>0.05, **p>0.01. +difference between NNW and ENW(+p<0. 05, ++ p>0.01), ^difference between NNW and Control (^p<0. 05, ^^p>0.01), ▲ difference between ENW and Control (▲ p<0. 05, ▲▲ p>0.01).

Correlation

Table 4 shows the correlation between physiology and the questionnaire. For all nurses, LF/HF correlated negatively with the MIS Fatigue items (r=-0.32, p<0.05), LF correlated negatively with the MIS Fatigue items (r=-0.36, p<0.01), and correlated positive with the MIS Feeling Refreshed items

(r=0.29, p<0.05). In NNW, LF/HF correlated negatively with the MIS Fatigue items (r=-0.47, p<0.01) (Figure 1). In ENW, LF correlated positively with the MIS Feeling Refreshed items (r=0.52, p<0.01) (Figure 2) and correlated negatively with MIS Fatigue items (r=-0.39, p<0.01) (Figure 3). For Control, HF correlated positively with the MIS Feeling Refreshed item (r=0.30, p<0.05).

Table 4. Correlation between physiology and the questionnaire.

	Correlation coefficient											
	All Nursing Worker			New Nursing worker			Expert Nursing worker			Control		
	LF/HF	LF	HF	LF/HF	LF	HF	LF/HF	LF	HF	LF/HF	LF	HF
Mood Inventory												
Tension Excitement												
Refreshing Mood		0.29*						0.52**				0.30*
Fatigue Mood	-0.32*	-0.36**		-0.47**				-0.39**				
bpm					-0.55**	-0.77**		0.38**				0.66*
SDP												-0.43**
DBP												-0.38**

New Nursing worker (NNW) group: less than 3 years of nursing worker, Expert Nursing worker (ENW) group: more than 3 years nursing worker, Control: non-nursing workers. LF: low-frequency component power, HF: high-frequency component power, LH/HF ratio: low-frequency component power/high-frequency component power ratio, BPM: Pulse Rate, SBP: systolic blood pressure, DBP: diastolic blood pressure. Spearman's correlation analysis (*p>0.05, **p>0.01)

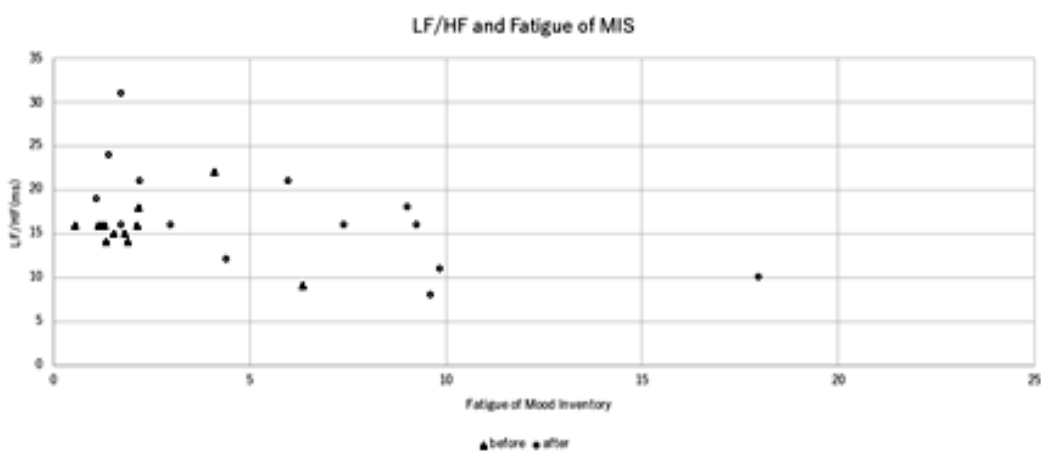


Figure 1. Collation between Fatigue of Mood Inventory (MIS) and autonomic activity. In the NNW group, LF / HF ratio obtain on a wave interval analysis using accelerated plethysmography in all measurement point before and after 8-hr. working. Spearman's correlation coefficients and p-values are shown (r=-0.47, p<0.01).

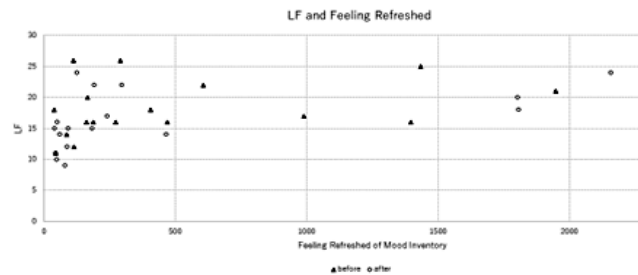


Figure 2. Collation between Feeling Refreshed of Mood Inventory (MIS) and autonomic activity. In the ENW group, Low-frequency component power (LF) obtains on a wave interval analysis using accelerated plethysmography in all measurement point before and after 8-hr. working. Spearman's correlation coefficients and p-values are shown ($r=0.52$, $p<0.05$).

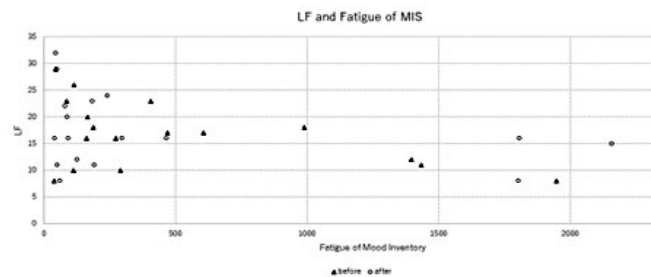


Figure 3. Collation between Fatigue of Mood Inventory (MIS) and autonomic activity. In the ENW group, Low-frequency component power (LF) obtains on a wave interval analysis using accelerated plethysmography in all measurement point before and after 8-hr. working. Spearman's correlation coefficients and p-values are shown ($r=-0.39$, $p<0.05$).

Discussion

Our study showed that, after 8 hours of work, autonomic activity, LF and LF/HF ratio in the NNW group with less than 3 years of the working more changed significantly as compare among the groups. In other words, fatigue increased objectively. It must be mentioned, but after 8 hours of work, it cannot be denied that there is also the influence of the circadian rhythm. However, nursing labor requires considerable physical and mental additions. Therefore, the effects of inducing fatigue and affecting autonomic nervous function are fully expected. The present finding that mental fatigue affects the sympathetic nervous system (increased LF/HF ratio) is consistent with previously reported results [45], in which fatigue inducing mental tasks increased sympathetic activity and decreased parasympathetic activity [46,47]. The VAS was increasing significantly in common in all groups, it was replicated previous studies [10,11]. It was suggested by previous reports and this report that labor causes subjective fatigue.

However, the results of this study differed in the characteristics of nursing workers, especially depending on the engaged years. The difference that the NNW group had an increased sympathetic component and the ENW group had a decreased parasympathetic component is a new finding of the present study. □

In addition to feeling of fatigue on the VAS, as a characteristic of after work fatigue in nursing workers, in the NNW group's fatigue after work is characterized while on physiological tests, the LF/HF ratio and LF increased, and BP was significantly higher for both SBP and DBP. Psychologically, there was a slight increase in the MIS Tension and Excitement Mood, and the Refreshing Mood was slightly reduced, although it increased or reduced and was not significant. Also, the negative association of the LF/HF ratio with the Fatigue item of MIS.

It is said that LF reflects the sympathetic nerve, HF reflects the parasympathetic nerve, and the LF/HF ratio reflects the autonomic function. In the objective evaluation, sympathetic nerve activity increases, the autonomic nerve is out of balance, and in the subjective evaluation, tension and excitement of MIS tends to increase slightly. Since these characteristics are significantly different from those of the ENW group and the control group, special attention should be paid to the balance between sympathetic

nerve activity and autonomic nerves to calm tension and excitement, and the balance of autonomic nerves as a countermeasure against fatigue caused by the NNW group. It is expected that the method of taking will be effective, and there is one possibility of recovery.

In the ENW group, although not significant, HF and DBP slightly decreased, the MIS Refreshing Mood was slightly reduced. Also, the positive association of the LF with Feeling Refreshed item of MIS, the negative association of the LF with the Fatigue item of MIS.

If anything, the parasympathetic component is decreasing, the psychologically refreshing mood is decreasing, and ENW group is not particularly significantly different from the control group, so as a measure against fatigue and stress in ENW group and other occupations. If you feel tired from work, you can expect an effect by focusing on parasympathetic nerve activity and relaxing.

For nurses as a whole, the negative association of the LF/HF ratio with the Fatigue item Sakano's Mood Inventory, the positive association of the LF with the Feeling Refreshed item of MIS, and the negative association of the LF with the Fatigue items of MIS. Focusing on parasympathetic nerve activity and promoting relaxation in nursing labor regardless of the length of service and in other occupations will help recovery from fatigue and will be one of the important measures.

This finding suggests that subjective evaluation by questionnaire might be a valid index of evaluation of autonomic activity. Then, the MIS test may alternative for physiological tests to detect fatigue more quickly and easily. These findings will contribute to the development of effective stress coping methods. It can lead to coping and prevention of stress not only for nurses but also for fatigued workers. This finding suggests that subjective evaluation by questionnaire might be a valid index of evaluation of autonomic activity. And it can help manage and prevent stress, not only for nurses, but also for tired workers.

Stressful mental fatigue affects not only mental but physical bodily functions as well. Increased sympathetic activity and decreased parasympathetic activity suggest autonomic hypervigilance. The prefrontal cortex (PFC) and anterior cingulate cortex (ACC) play an important role in the regulation of autonomic nervous activities [11]. The PFC normally

inhibits sympathy excitatory subcortical circuits [48-50], while the ACC regulates parasympathetic activity [51,52]. Several studies have reported that prolonged mental tasks lasting an hour or longer gradually reduced brain activity related to mental task processing [53,54]. Our study suggests that nursing work entails continuous activation of the PFC, and that acute mental tasks might temporarily cause the PFC and ACC to dysfunction, increasing sympathetic and decreasing parasympathetic activities [55-61]. Neuroimaging studies may be required to confirm this hypothesis.

Conclusion

Our results provide evidence that nurses' fatigue increases sympathetic activity and autonomic function and is also related to mood. After work fatigue of the NNW group was that the LF/HF ratios and LF increased, blood pressure increased significantly for both SBP and DBP, and the Tension and Excitement component of MIS increased slightly. In the ENW group, HF decreased slightly and DBP decreased significantly. MIS's Refreshing Mood was down slightly. In particular, the characteristics of nurses differed depending on the working years, and the difference was that the NNW group had an increased sympathetic component and the ENW group had a decreased parasympathetic component. Knowing the differences in the characteristics of fatigue between new and specialist nurses is expected to lead to disease prevention and reduction of turnover by taking measures against stress in response to each. The nurses' subjective psychological state after work affects their autonomous function, so physiological indicators may provide an objective assessment of nursing fatigue. In addition to, Sakano's MIS scales correlate with physiological indicators; hence, Sakano's Questionnaire may be an alternative to physiological test when assessing nursing fatigue and can be tested more quickly and concisely. These findings may lead to stress coping and prevention not only for nurses but also for workers with fatigue. We hope this study will contribute towards addressing the issues related to workers' mental health in the workplace.

Limitations

The present study has several limitations. First, we should be noted that fatigue is not only physiological and psychological, but also under the influence of human circadian rhythms. Second, our study included only a small number of participants, limited to nursing care facilities (fix facilities). Third, our study's cross-sectional correlations cannot clarify cause and effect relationships. To generalize our results, studies involving a larger number of participants with better cause and effect analyses are essential.

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Declarations

We declare that manuscript is original, has not been published before and is not currently being considered for publication elsewhere. We know of no conflicts of interest associated with this publication, and there has been no significant financial support for this work that could have influenced its outcome. We have confirmed the availability to the "minimal dataset" required for reproduction and development. As corresponding author, I confirm that the manuscript has been read and approved for submission by all the named authors.

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Conflict of Interest

All authors declare that they have no conflicts of interest.

Ethics Approval

This study was conducted with the approval of the Fukushima Medical University Ethics Committee according to guidelines.

Consent to Participate

Both orally and in writing, we explained the study contents, privacy policy, and right to withdraw, to receive participants' consent.

Consent for Publication

All authors contributed to and have approved the final manuscript.

Availability of Date and Material

We have confirmed the availability to the "minimal dataset" required for reproduction and development.

Author's Contributions

Miki Ishizuka, Shin-ichiro Katsuda, and Akihiro Hazama designed the study and wrote the protocol. Miki Ishizuka managed the literature searches and wrote the first draft of the manuscript. Miki Ishizuka performed statistical analyses under technical supervision by Shin-ichiro Katsuda, and Akihiro Hazama. Shin-ichiro Katsuda, and Akihiro Hazama helped with interpretation of data.

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