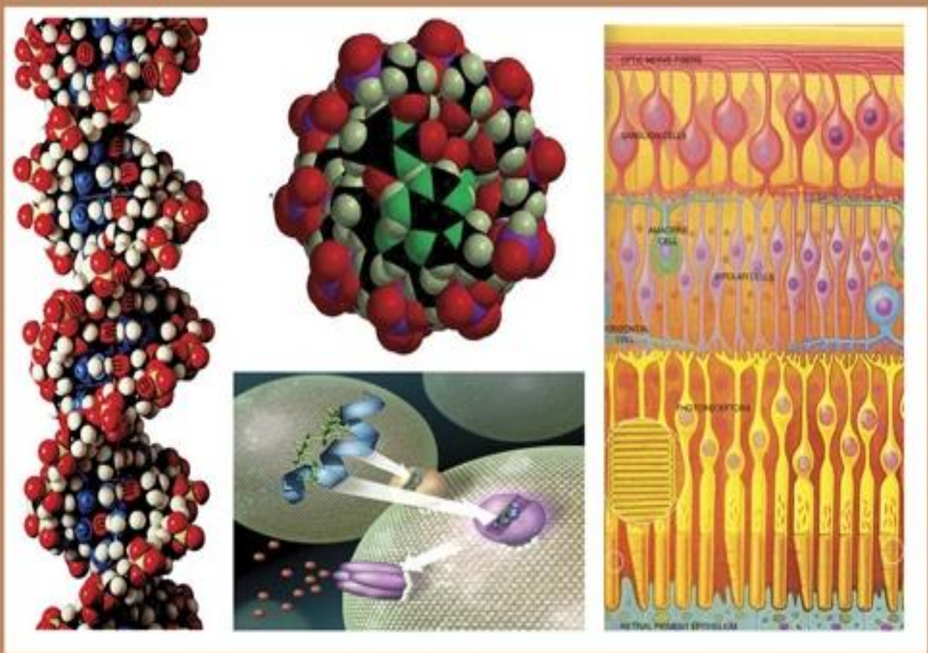
C

EGYPTIAN ACADEMIC JOURNAL OF

BIOLOGICAL SCIENCES

PHYSIOLOGY & MOLECULARBIOLOGY



ISSN
2090-0767

WWW.EAJBS.EG.NET

Vol. 14 No. 1 (2022)

.

Citation: *Egypt.Acad.J.Biolog.Sci. (C.Physiology and Molecular biology) Vol. 14(1) pp257-264 (2022)*

DOI: 10.21608/EAJBSC.2022.228237

Egypt. Acad. J. Biolog. Sci., 14(1):257-264 (2022)

Egyptian Academic Journal of Biological Sciences
C. Physiology & Molecular Biology
ISSN 2090-0767
www.eajbsc.journals.ekb.eg

Cardiac Autonomic Changes in Shift Workers as Assessed by Time-Domain Measures of Short-Term Heart Rate Variability

Vijayabaskaran Shanmugavaradharajan*[1], Pavitra Vyshnavi Yogisparan and Damodaran Vasu[2]

1. Department of Physiology, PSG Institute of Medical Sciences and Research,
2. Institute of Community Medicine, Madras Medical College, Chennai, Tamil Nadu, India – 600003.

*E. Mail: vbkr70@gmail.com

ARTICLE INFO

Article History
Received:22/2/2022
Accepted:30/3/2022
Available:31/3/2022

Keywords:
Shift work;
Cardiac autonomic activity; HRV;
Time domain measures;

ABSTRACT

Background: The global prevalence of shift work is estimated to be around 20%. Due to its untimely work schedule shift work affects the sleep-wake cycle and increases cardiovascular risk. Autonomic dysfunction is one of the explanatory links that has been proposed. Here, we strived to gather evidence regarding this association by assessing the cardiac autonomic activity of shift workers using Heart Rate Variability (HRV). **Materials and methods**:30 shift workers and 30-day workers were enrolled for the study as per the set criteria and subjected to Time-domain analysis of short-term HRV. By appropriate statistical methods, Time-domain indices between shift workers and day workers were compared based on their gender and Body Mass Index (BMI) and individual HRV measures were correlated with BMI. **Results**: Shift workers had a significantly lower RMSSD [Square Root of the Mean of the Sum of the Squares of the Differences between adjacent NN (normal-to-normal) intervals] (p- .004) and pNN50 (number of pairs of adjacent NN intervals differing more than 50 milliseconds divided by the total number of NN intervals) (p- .015) when compared to the day workers. Shift working males had a reduced RMSSD (p- .012) and pNN50 (p- .03). Shift workers showed a negative correlation between their BMI and time-domain measures SDNN (Standard Deviation of all NN intervals) (r-0.020) and RMSSD (r-0.005). **Conclusion:** Our study shows that shift work exposure is detrimental to cardiac autonomic activity and especially males are at a higher risk. Obesity in shift workers increases the risk.

INTRODUCTION

Shift work is generally defined as work that adheres to a work schedule that deviates from the normal daylight working hours (7/8 am to 5/6 pm). In other words, shiftwork consists of non-standard working hours which are irregular, and unusual (IARC, 2010*)*. Prevalence of shift work is globally similar and the available data suggest that around 18% to 20% are involved in this grueling alternative schedule (McMenamin, 2007) (Paoli, 2001) (KUBO, 2014). In this modern era, shift work has attained paramount importance as it provides round-the-clock service to the end-user, but on the negative side puts the employees on an untimely work schedule (Härmä&Kecklund, 2010). As it tampers with the sleep/wake cycle and circadian patterns in the human body, shift work is found to be a major risk factor for health disorders that are psychoneurotic, cardiovascular, gastrointestinal, and even cancerous in nature (Costa, 2010).

Citation: *Egypt.Acad.J.Biolog.Sci. (C.Physiology and Molecular biology) Vol. 14(1) pp257-264 (2022)*
DOI: 10.21608/EAJBSC.2022.228237

The risk of cardiovascular disorders (CVD) in shift workers is found to be high and it has been linked so far by physiological mechanisms such as autonomic dysfunction, inflammatory changes, dyslipidemia, and hyperglycemia (Puttonen *et al.,* 2010). It has been shown that autonomic dysfunction affects the cardiovascular system by increasing blood pressure levels and heart rate fluctuations that are aggravated by emotional or physical stress (Garland, 2009).

Any clinical and subclinical autonomic imbalance or dysfunction can be detected by Heart Rate Variability (HRV) fairly and accurately (Guo *et al.,* 2013). HRV analyses the beat-to-beat changes in the heart rate and reflects cardiac autonomic activity as the heart rate is continuously modulated by the changes in the sympathetic as well as the vagal activity (Electrophysiology, 1996). Christensen *et al,* have shown that any alteration in the HRV may be considered an indication or a risk factor for impending cardiac disease (Christensen *et al.,* 1999).

HRV can be analyzed by time domain and frequency domain methods. Time-domain method infers from the changes in the time interval between two successive normal to normal complexes (NN). The time-domain measures we have taken into account here are the Standard Deviation of all NN intervals (SDNN), Square Root of the Mean of the Sum of the Squares of the Differences between adjacent NN intervals (RMSSD), the number of pairs of adjacent NN intervals which differ more than 50ms in the entire recording (NN50), and the number of pairs of adjacent NN intervals differing more than 50 milliseconds in the entire recording divided by the total number of NN intervals (pNN50) (Electrophysiology, 1996)).

Of these measures, SDNN measures of total variability while RMSSD, NN50, and, pNN50 reflect heart rate variations of high-frequency nature (Electrophysiology, 1996). Literature shows that the time domain measures, especially SDNN and RMSSD are valuable in assessing autonomic function (Kang *et al.,* 2016).

Only a few works of literature involving HRV are available that trace the association between shift work and cardiac autonomic modulation and many of them made use of the frequency domain measures (Amelsvoort *et al.,* 2001). Also, the results were found to be contradictory and variable in explaining the disease pathway (Amelsvoort *et al.,* 2001) (Järvelin-Pasanen *et al.,* 2013). Even the ones that used time-domain measures were of western origin and do not provide a regional perspective (Hulsegge *et al.,* 2018) (Bernardes Souza et al., 2014). Hence, in this study, by comparing the time-domain measures of short-term HRV between shift workers and day workers, we aimed to assess the impact of shift work on the cardiac autonomic activity.

MATERIALS AND METHODS

Ours is a cross-sectional, observational study. After getting approval from the Institutional Human Ethics Committee (Project No.14/113), the study was conducted in our tertiary care hospital. A total of 60 participants were used for the study. Study subjects were recruited from the hospital staff as per the set criteria. Thirty permanent day workers and thirty shift workers of age between 20 - 35 years were included as study participants. Shift workers were identified as per the defined criteria (IARC, 2010). Informed consent was obtained from the participants and complete confidentiality was ensured. Individuals with hypertension, bronchial asthma, cardiac issues, thyroid disorders, and pregnancy were not included as subjects as these are known to affect HRV.

Subjects were taken to the Research laboratory was HRV analysis. They were instructed to refrain from smoking, caffeine intake for at least 2 hours, and alcohol intake for at least 36 hours before the recording. They were also advised to have adequate sleep (at least 8 hours) on the previous night and a normal breakfast on the day of recording. The assessment was done in a supine position with the subject lying on a couch in a dimly lit, quiet room that had an ambient temperature of about 20 to 25 °C.

Before the recording, the procedure was properly explained to the subjects and they were asked to rest briefly for about 5 minutes on the couch to rid of the anxiety. After the necessary rest, HRV was recorded for 5 minutes. An electrocardiogram (ECG) in Lead II was recorded for 320 seconds at a sampling rate of 1,024 Hz, using a computerized student's physiograph, three-channel (INCO, Chennai). The recording was analyzed using NIVIQURE-HRV software (Niviqure Meditech Private Limited, Bangalore) and time-domain measures were extracted.

The collected data were subjected to statistical analysis by SPSS version 24. Continuous variables were represented in the mean ± SD form and categorical variables by their frequency. For comparison of the two groups, the independent sample t-test and Mann Whitney U test were employed. To find out the association between two continuous variables, Spearman and Pearson correlation tests were used. The p-value, less than or equal to 0.05 was taken as significant.

RESULTS

Sixty subjects were recruited in this cross-sectional study out of which 30 were day workers who acted as controls and the remaining 30 were shift workers, with an equal number of males and females in each group.

Table 1 shows, the comparison of data between shift workers and day workers. When time domain parameters of shift workers RMSSD (p=0.004) and PNN50 (p=0.015) were found to be significantly reduced when compared to the day workers (Table-1).

Table 2 shows, the comparison of data between male shift workers and male day workers Here, male shift workers showed a significant reduction in RMSSD (p=0.012), NN50 (p=0.06), and pNN50 (p=0.03) when compared to the male day workers (Table-2).

Table 3 shows, the comparison of data between female shift workers and female day workers When females alone were compared, there was no significant difference in time domain measures (Table-3). However, there is a significant difference in their BMI (p=0.002).

Table -4 shows the comparison of shift workers with day workers based on their BMI. In the BMI >23 group, shift workers showed a significant reduction in RMSSD (p=0.04), NN50 (p=0.04), and pNN50 (p=0.02), while in the BMI <= 23 category shift workers showed a significant reduction in RMSSD (p=0.02) alone when compared to the day workers.

As shown in Table 5, sub-group analysis revealed, in the BMI <=23 group, male shift workers had a significant decrease in RMSSD (p=0.046) alone. However, the groups consisting of males with BMI >23, females with BMI <=23 and >23 did not show any statistical difference between shift workers and day workers. In a separate subgroup analysis, a comparison between male shift workers and female shift workers revealed a significant difference (p=0.045) in NN50 alone.

In the correlation analysis, shift workers had a significant negative correlation between their BMI and HRV parameters, SDNN (r -0.020) and RMSSD (r -0.005). Similarly, day workers also showed a significant negative correlation between their BMI and SDNN (r -0.002). However, when they are grouped based on their gender and analyzed, male shift workers showed a significant negative correlation between their BMI and HRV parameters RMSSD (r -0.014) and NN50 (r -0.014) while female shift workers had a significant negative correlation between their BMI and SDNN (r -0.039) alone. Male and female day workers did not show any correlation between their BMI and HRV parameters.

Table 1: Comparison between Shift workers and Day workers

	Numbers	Shift workers Mean ± SD	Day Workers Mean ± SD	Significance (p value) ┼
Age	30	27.67±4.48	27.63 ± 4.31	.98
BMI	30	22.39±2.71	24.5±3.98	.02
SDNN	30	51.95±25.13	53.01 ± 17.29	.85
RMSSD	30	34.93±12.49	47.62±19.49	.004*
NN50	30	50.93±43.95	74.17±49.83	.06
pNN50	30	18.06±14.18	28.56±17.92	.015*

* $p < 0.05$; ┼ -Independent t test

Table 2: Comparison between Shift workers (Male) and Day workers (Male)

	Numbers	Shift workers Mean ± SD	Day Workers Mean ± SD	Significance (p-value) ┼
Age	15	28.40± 4.64	27.53±3.98	0.59
BMI	15	23.8±2.30	23.9±4.1	0.94
SDNN	15	57.74±30.86	59.43±18.14	0.86
RMSSD	15	33.27±10.86	50.15± 21.94	0.012*
NN50	15	33.07±27.92	62.07±48.94	0.06
pNN50	15	15.26±12.3	28.93±19.41	0.03*

* $p < 0.05$; ┼ - Mann Whitney U test

Table 3: Comparison between Shift workers (Female) and Day workers (Female)

	Numbers	Shift workers Mean ± SD	Day Workers Mean ± SD	Significance (p value) ┼
Age	15	26.93 ±4.35	27.73±4.76	.64
BMI	15	20.99±2.38	25.1±3.9	.002*
SDNN	15	46.15±16.86	46.59±14.2	.94
RMSSD	15	36.6±14.1	45.08±17.09	.15
NN50	15	68.8±50.4	86.27±49.36	.35
pNN50	15	20.87±15.75	28.2±16.98	.23

* $p < 0.05$; ┼ - Mann Whitney U test

Table 4: Comparison between Shift workers and Day workers with BMI <=23 and > 23

BMI		Numbers		Shift workers Mean ± SD	Day Workers Mean ± SD	Significance (p value)
		Shift workers	Workers Days			
>23	SDNN	12	19	49.05±20.81	50.23±12.92	.85
	RMSSD	12	19	33.06±10.56	43.03±13.09	.04*
	NN50	12	19	38.92±29.78	69.37±41.95	.04*
	pNN50	12	19	14.61±10.14	25.08±12.31	.02*
<=23	SDNN	18	11	52.81±29.63	57.82±22.94	.64
	RMSSD	18	11	36.03±14.64	55.54±26.17	.02*
	NN50	18	11	58.50±53.64	82.46±62.57	.29
	pNN50	18	11	20.29±17.11	34.58±24.4	.09

* $p < 0.05$; ┼ - Mann Whitney U test

Table 5: Comparison between Shift workers (Males, Females) and Day workers (Males, Females) with BMI <=23 and > 23

BMI		Numbers		Shift workers Mean ± SD	Day Workers Mean ± SD	Significance (p value)┼
		Shift workers	Workers Days			
Male <=23	SDNN	4	6	73.84±49.91	71.57±19.98	.92
	RMSSD	4	6	33.91±11.91	64.99±24.03	.046*
	NN50	4	6	23.25±22.01	88.33±63.52	.09
	pNN50	4	6	16.38±17.40	41.82±22.26	.09
Male >23	SDNN	11	9	51.88±21.09	51.34±11.94	.94
	RMSSD	11	9	33.03±11.06	40.26±14.37	.22
	NN50	11	9	36.64±29.89	44.56±28.4	.55
	pNN50	11	9	14.86±10.96	20.34±11.91	.29
Female <=23	SDNN	7	5	45.80±17.42	41.32±13.9	.62
	RMSSD	7	5	36.73±15.85	44.19±26.37	.48
	NN50	7	5	70.25±56.47	75.40±68.05	.87
	pNN50	7	5	21.59±17.58	25.9±26.38	.69
Female >23	SDNN	8	10	47.54±17.8	49.23±14.30	.87
	RMSSD	8	10	36.06±3.54	45.52±12.02	.22
	NN50	8	10	63.0±12.49	91.7±40.41	.26
	pNN50	8	10	17.97±4.62	29.34±11.59	.13

* $p < 0.05$; ┼ - Mann Whitney U test

DISCUSSION

Shift work is a pattern of work that is known to be associated with circadian misalignment (Costa, 2010). It has been shown already that autonomic impairment is associated with sleep restriction (Grimaldi *et al.,* 2016). As it is a sensitive device to gauge autonomic function (Guo *et al.*, 2013), short-term HRV is used to compare the autonomic functions of shift workers and day workers.

To start with, we found a significantly lower RMSSD and pNN50 in shift workers (Table 1). These measures reflect heart rate variability of high frequency in nature (Electrophysiology, 1996), and the reduction implies that the shift workers have reduced cardiovagal activity when compared to the day workers. Moreover, these findings also imply that shift workers have a higher cardiovascular risk (Christensen *et al.*, 1999).

Our findings are ably supported by Souza et al., who showed lifetime shift work exposure decreases cardiac parasympathetic modulation (Bernardes Souza *et al.,* 2014). Our findings also concur with Hulsegge *et al.,* who found a significantly lower cardiovagal activity in shift workers but only in males (Hulsegge *et al.,* 2018). Furthermore, Amelsvoort *et al.,* have also demonstrated an autonomic impairment in shift workers, but an increase in the cardiac sympathetic modulation (Amelsvoort *et al.,* 2001).

However, our findings are contradicted by Järvelin-Pasanen et al., who found a few but insignificant differences between normal and extended shift workers (Järvelin-Pasanen *et al.*, 2013), and Freitas *et al.*, who found no differences between day and night shifts (Freitas *et al.*, 1997).

Our study also revealed that the shift working males have a significantly lower RMSSD, NN50, and pNN50 when compared to the day working males (Table 2). As all these measures are indicative of cardiovagal activity (Electrophysiology, 1996), these findings imply that males when exposed to shift work are more likely to have a decreased parasympathetic modulation. Our study is supported by Hulsegge et al., who found a similar autonomic imbalance in shift working males (Hulsegge *et al.*, 2018).

Our study revealed no significant differences between shift working and day working females (Table 3). This implies that the risk of autonomic impairment due to shift-work exposure is considerably less in females when compared to males. Our finding is again supported by Hulsegge *et al.,* who also found no differences in time domain HRV parameters in female shift workers (Hulsegge *et al.,* 2018).

Shift workers when compared to the day workers, showed a significant reduction in time-domain measures that reflect parasympathetic activity, in both the obese (BMI >23) and non-obese (BMI <=23) groups (Table 4). However, the shift workers belonging to the obese group had alterations in multiple measures indicating that obese shift workers are at a higher risk. This finding is supported by a past study, which found an increase in BMI negatively affects parasympathetic components of HRV (Koenig *et al.,* 2014). Hence, based on our findings we propose that obese shift workers are more prone to develop autonomic dysfunction.

Also, non-obese male shift workers (Table 5) showed a significant reduction in RMSSD than the non-obese male day workers. However, obese male shift workers did not exhibit any significant change. This may be explained by the fact that obesity-induced HRV changes may mask the shift exposure effect.

In our study, among the shift workers, there was a significant difference in HRV measures between males and females. This difference between genders is supported by Ramaekers *et al.*, but they found a decrease in sympathetic modulation in healthy females (Ramaekers, 1998). However, we found reduced cardiovagal activity in males who are exposed to shift work. This finding again reiterates the hypothesis that males are more prone to develop autonomic dysfunction due to shift work exposure (Hulsegge et al., 2018). Our study also shows a significant negative correlation between HRV parameters and BMI in shift workers, especially in men. This finding is supported by Hulsegge *et al.*, (Hulsegge *et al.*, 2018), and Koenig *et al.*, (Koenig *et al.,* 2014), who showed that the shift work exposure and obesity can precipitate autonomic dysfunction and the risk is higher in men when compared to women.

Hence, as per our study findings, we hypothesize that shift work precipitates autonomic imbalance, the reasons being circadian misalignment and sleep restriction (Grimaldi *et al.,* 2016). Males are more prone to this effect and this can be explained by their decreased vagal activity during waking (Elsenbruch *et al.*, 1999).

On the limitations part, the cross-sectional nature of the study design and a smaller sample size prevents us from gathering more evidence. A larger population sample followed up periodically through a longitudinal study might be needed to reveal more information on the effects of shift exposure.

Conclusion

Based on our findings, we conclude that shift work exposure is detrimental to cardiac autonomic activity, and shift working males are at a higher risk for cardiovascular complications when compared to females. Obesity in shift workers increases the risk by precipitating autonomic imbalance.

REFERENCES

Amelsvoort, L., Schouten, E., Maan, A., Swenne, K., &Kok, F. (2001). 24-Hour Heart Rate Variability in Shift Workers: Impact of Shift Schedule. *Journal Of Occupational Health,* 43(1), 32-38. https://doi.org/10.1539/joh.43.32

Bernardes Souza, B., MussiMonteze, N., Pereira de Oliveira, F., Magalhães de Oliveira, J., Nascimento de Freitas, S., & Marques do NascimentoNeto, R. et al. (2014). Lifetime shift work exposure: association with anthropometry, body composition, blood pressure, glucose and heart rate variability. *Occupational And Environmental Medicine,* 72(3), 208-215. https://doi.org/10. 1136/ oemed-2014-102429

Christensen, J., Toft, E., Christensen, M., &

Schmidt, E. (1999). Heart rate variability and plasma lipids in men with and without ischaemic heart disease. *Atherosclerosis,* 145(1), 181-186. https://doi.org/10. 1016/ s0021-9150(99)00052-0

Costa, G. (2010). Shift Work and Health: Current Problems and Preventive Actions. *Safety And Health At Work,* 1(2), 112-123. https://doi. org/ 10.5491/shaw.2010.1.2.112

Electrophysiology, T. (1996). Heart Rate Variability. *Circulation,* 93(5), 1043-1065. https://doi.org/10. 1161/ 01.cir.93.5.1043

Elsenbruch, S., Harnish, M., & Orr, W. (1999). Heart Rate Variability During Waking and Sleep in Healthy Males and Females. *Sleep,* 22(8), 1067-1071. https://doi.org/10.1093/sleep/22.8.1 067

Freitas, J., Lago, P., Puig, J., Carvalho, M., Costa, O., &Falcão de Freitas, A. (1997). Circadian heart rate variability rhythm in shift workers. *Journal Of Electrocardiology*, 30(1), 39-44. https://doi.org/10.1016/s0022-0736 (97)80033-7

Garland, E. (2009). Pure autonomic failure. Amazon.com. Retrieved 20 February 2022, from https://www. amazon.com/Autonomic-Nervous-System-autonomic-Neurology-ebook /dp/B019ZU7M4M

Grimaldi, D., Carter, J., Van Cauter, E., &Leproult, R. (2016). Adverse Impact of Sleep Restriction and Circadian Misalignment on Autonomic Function in Healthy Young Adults. *Hypertension*, 68(1), 243-250. https://doi.org/10. 1161/ hypertensionaha.115.06847

Guo, Y., Palmer, J., Strasser, F., Yusuf, S., &Bruera, E. (2013). Heart rate variability as a measure of autonomic dysfunction in men with advanced cancer. *European Journal Of Cancer Care,* 22(5), 612-616. https://doi.org/10.1111/ecc.12066

Härmä, M., &Kecklund, G. (2010). Shift work and health – how to proceed?. *Scandinavian Journal Of Work, Environment & Health,* 36(2), 81-84. https://doi.org/10.5271/sjweh.2902

Hulsegge, G., Gupta, N., Proper, K., van Lobenstein, N., IJzelenberg, W., & Hallman, D. et al. (2018). Shift work is associated with reduced heart rate variability among men but not women. *International Journal Of Cardiology,* 258, 109-114. https://doi.org/10.1016/j.ijcard.2018 .01.089

IARC (2010). IARC monographs on the evaluation of carcinogenic risks to humans, volume 98, Painting, Firefighting, and Shiftwork. Ncbi.nlm.nih.gov. Retrieved 20 February 2022, from https://www.ncbi.nlm.nih.gov/book s/NBK326814/.McMenamin, T. (2007). A time to work: recent trends in shift work and – Pro Quest. Proquest.com. Retrieved 20 February 2022, from https://www. proquest.com/docview/235645198? accountid=14656&pq-origsite= summon

Järvelin-Pasanen, S., Ropponen, A., Tarvainen, M., Karjalainen, P., & Louhevaara, V. (2013). Differences in Heart Rate Variability of Female Nurses between and within Normal and Extended Work Shifts. *Industrial Health*, 51(2), 154-164. https://doi.org/10. 2486/ indhealth.ms1368

Kang, J., Kim, J., Hong, S., Lee, C., & Choi, B. (2016). Heart Rate Variability for Quantification of Autonomic Dysfunction in Fibromyalgia. *Annals Of Rehabilitation Medicine,* 40(2), 301. https://doi.org/10.5535/arm.2016.40 .2.301

Koenig, J., Jarczok, M., Warth, M., Ellis, R., Bach, C., Hillecke, T., & Thayer, J.

(2014). Body mass index is related to autonomic nervous system activity as measured by heart rate variability — A replication using short term measurements. *The Journal Of Nutrition, Health & Aging*, 18(3), 300-302. https://doi.org/10.1007/s12603-014-0022-6

KUBO, T. (2014). Estimate of the Number of Night Shift Workers in Japan. *Journal Of UOEH*, 36(4), 273-276. https://doi.org/10. 7888/juoeh.36.273

McMenamin, T. (2007). Shift Work and Flexible Schedules. Retrieved 20 February 2022, from https://www.bls.gov/opub/mlr/2007/article/time-to-work-recent-trends-in-shift-work-and-flexible-schedules.htm.

Paoli, P. (2001). Third European Survey on Working Conditions 2000. Eurofound. Retrieved 20 February 2022, from https://www.eurofound.europa.eu/publications/report/2001/working-conditions/third-european-survey-on-working-conditions-2000..

Puttonen, S., Härmä, M., &Hublin, C. (2010). Shift work and cardiovascular disease – pathways from circadian stress to morbidity. *Scandinavian Journal Of Work, Environment & Health*, 36(2), 96-108. https://doi.org/10.5271/sjweh.2894

Ramaekers, D. (1998). Heart rate variability and heart rate in healthy volunteers. Is the female autonomic nervous system cardioprotective?. *European Heart Journal*, 19(9), 1334-1341. https://doi.org/10.1053/euhj.1998.1084