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Cardiovascular Reactivity to Acute Mental Stress in Post Ovulatory Females

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ABSTRACT

Background: Female hormones fluctuate with the phases of menstrual cycle. Estrogen, which has attributes in cardio-protection, is secreted less during luteal phase. In post-ovulatory phase, days 1-2 before menstruation has minimal female hormone influence due to less secretion. Mental stress subjected at this phase might enhance sympathetic activation which in long run may precipitate cardiovascular diseases. Hence, to explore the autonomic activity to mental stress during this phase of menstrual cycle the study was undertaken.

Methods: Thirty apparently healthy young postovulatory female medical students of B. P. Koirala Institute of Health Sciences, Nepal of age 19.93 (± 0.91) years with BMI of 20.70 kg/m^2 (± 2.49) kg/m^2 were recruited for the present study. Their short term heart rate variability (HRV) of 5 min was recorded during rest at sitting position. Then each subject was given a mental stress (nine questions selected from MENSA workout questionnaire) for 5 min. During the stress, HRV was recorded simultaneously. Data was statistically analyzed using Friedman test followed by multiple comparisons. The $p<0.005$ was considered statistically significant.

Results: Mental stress significantly decreased RMSSD ($p= 0.001$), NN50 ($p= 0.001$) and PNN50 ($p=0.001$) in time domain and HF nu ($p=0.012$) in frequency domain parameters of HRV.

Conclusions: Young healthy post ovulatory females responded to acute mental stress by withdrawing cardiac parasympathetic activity.

Keywords: Female; HRV; mental stress

INTRODUCTION

Mental stress increases heart rate and blood pressure,[1] which are directly proportional to stress level and reactivity.[2] Further, greater reactivity and late recovery from stress have been related to future cardiovascular risks.[3]

Females seem less likely to have cardiovascular diseases (CVD) owing to estrogen.[4] We set out to show that our understanding of the stress response is fundamentally altered once sex differences are taken into account. This is achieved by comparing the heart rate variability (HRV Yet, recent studies have stated that menstrual cycle is one of the potential modulators of the autonomic nervous system reactivity to stress.[5] It is postulated that hypothalmo-pituitary-adrenal axis response is higher in luteal phase.[6] This cardiovascular reactivity to stress can be appraised by employing Heart rate variability (HRV).[7] Less studies have been done in luteal phase especially 1-2 days prior to menstruation when female sex hormone secretion is minimal.[8] Mental stress subjected at this phase might enhance sympathetic activation which, in long run, may precipitate CVD. Hence, to explore the autonomic activity to mental stress during this phase of menstrual cycle, this study was done.

METHODS

An observational study was conducted in 30 young healthy post ovulatory female medical students of B. P. Koirala Institute of Health Sciences (BPKIHS), Dharan, after obtaining ethical approval from the Institutes Review Board. An informed written consent was obtained from all of the enrolled subjects. The participants were 19.93 ± 0.91 years and had BMI of 20.70 ± 2.49 kg/m^2. Study samples enrolled were without any history of cardiovascular diseases, diabetes, and psychiatric illness

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or currently under medication for any diseases. Subjects with irregular menstrual cycles or who are subjected to any gynecological treatment were excluded from the study.

In this study, the acute mental stress executed was in the form of nine problem solving questions from the MENSA workout questionnaire.[9] Mensa is the largest and oldest high IQ society in the world. It is a non-profit organization open to people who score at the 98th percentile or higher on a standardized, supervised IQ or other approved intelligence test. However, the Mensa workout quiz is provided for entertainment purposes and was devised by Dr. Abbie Salny. These nine questions were selected on a random basis from "MENSA workout" questionnaire which included a total of 30 questions.

The female subjects who agreed to participate in the study were asked to note down their menstrual calendar for 2 months along with a note of their basal body temperature. Those females who have the same menstrual calendar for the 2 months were recruited for the study. The ovulation day of female participants were estimated according to their menstrual calendar, and were called for the recording in the post ovulatory phase. Most of the subjects had a 28-30 day menstrual cycle and hence were called on 11/ 12/ 13th day after ovulation. This day was chosen as physiologically there would be less release of female hormones during this phase of menstrual cycle (1-2 day prior to menstruation).

The selected subjects visited the neurocardiology laboratory, Department of Basic and Clinical Physiology, BPKIHS between 10 am- 12 noon. The day before the test, the subjects were instructed to have a light breakfast 2 hours before the recording. On arrival, they were allowed to rest for 15 min and then their resting BP, HR and RR were recorded in a sitting position in a non-dominant arm. Their resting short term HRV for 5 min was recorded using polar S810i HRM (Heart rate monitor).

HRV is commonly analyzed by frequency domain and time domain. In frequency domain, the LF power component of HRV (0.04–0.15 Hz) reflects the activity of the sympathetic nervous system (SNS), while the HF power component (0.15–0.4 Hz) reflects the activity of the parasympathetic nervous system (PNS). The LF component is sensitive to stress in general (either physical or mental, but in general is higher for mental stress), the LF/HF ratio indicates autonomic balance (for any kind of activity).[10]

Time-domain is another standard clinical parameter of HRV.[10] Time-domain analysis measures variation in HR over time or the intervals between successive normal cardiac cycles. Time-domain analysis of recording data involves simple calculations of mean normal-to-normal (NN) intervals and the variance between NN intervals. One of the simplest time-domain analysis variables is the standard deviation of the NN interval (SDNN; i.e., the standard deviation of NN). The root mean square of the successive differences (RMSSD), number of interval differences of successive NN intervals greater than 50 ms (NN50), and proportion derived by dividing NN50 by the total number of NN intervals (pNN50) are derived from the difference between adjacent NN intervals. These variables are impacted by the PNS, as they reflect beat-to-beat changes. Among these, RMSSD is a more stable parameter.[10]

Acute mental stress was given by showing each question in the Laptop screen (Dell) of 12 inches. These questions were displayed for a period of 5 min. Their BPs, HR and RR were recorded during the stress. BP and HR were recorded at 2nd and 4th minute. RR were recorded at the 5th min. Short term HRV was continuously recorded during the stress period. A rest of 5 min was allowed for recovery and their BPs, HR, RR and HRV were recorded as explained earlier during the recovery.

The data collected were entered in Microsoft Excel and was statistically analyzed using statistical software SPSS version 17 (SPSS INC., Chicago, ILL, USA). Repeated measures of ANOVA followed by the Bonferroni test was used to analyze cardiorespiratory measures. Whereas, HRV was analyzed using Friedman test followed by multiple comparisons. All data were considered as statistically significant at $p<0.05$.

RESULTS

Acute mental stress increased the cardiorespiratory variables in young healthy post-ovulatory females (Table 1). At the end of 4 min of recovery, all the cardiorespiratory variables were comparable to resting state except for SBP which continued to decrease.

Acute mental stress decreased the time domain measures of HRV (RMSSD, NN50 and PNN50). Even at 5 min of recovery, these variables were comparable to mental stress state. The recovery SDNN, NN50 and PNN50 variables were significantly reduced than the resting states, except for RMSSD which was found to be comparable to resting states (Table 2). In the frequency domain, only HF power decreased significantly during mental stress (Table 2).

Table 1. Comparison of cardiorespiratory variables in young healthy post-ovulatory females during rest, mental stress and recovery.

Variables	Female (n=30)(mean ± SD)					p value									
	Rest	Mental stress (task)		Recovery from mental stress		p1	p2	p3	P4	P5	P6	P7	P8	P9	P10
		2 min	4 min	2 min	4 min										
SBP (mmHg)	103.93±7.75	112.13±10.57	111.67±10.52	102.60±8.73	100.67±7.92	0.001	0.001	1.000	0.014	0.001	0.001	1.000	0.001	0.001	0.163
DBP (mm Hg)	71.53±4.75	79.20±7.33	81.80±7.69	70.87 ± 5.91	70.87±5.84	0.001	0.001	1.000	1.000	0.001	0.001	0.67	0.001	0.001	1.000
PR (bpm)	79.67±11.37	85.93±14.32	83.10±14.23	78.90±12.45	77.23±11.18	0.004	0.126	1.000	1.000	0.007	0.001	0.749	0.141	0.043	1.000
RR(cycles/min)	14.70±2.41		16.73±.89		14.63±3.39		0.011		1.000						0.005

SBP=systolic blood pressure (mm Hg), DBP=diastolic blood pressure (mm Hg), PR=pulse rate (bpm), RR=respiratory rate (per min). The $p<0.05$ was considered statistically significant, NS=statistically non-significant, p1=between rest and 2 min of mental stress (task), p2= between rest and 4 min of mental stress (task), p3=between rest and 2 min of recovery from mental stress, p4=between rest and 4 min of recovery from mental stress, p5=between 2 min of mental stress (task) and 2 min of recovery from mental stress, p6=between 2 min of mental stress (task) and 4 min of recovery from mental stress, p7=between 2 min of mental stress (task) and 4 min of mental stress (task), p8= between 4 min mental stress (task) and 2 min of recovery from mental stress, p9= between 4 min of mental stress (task) and 4 min of recovery from mental stress, p10= between 2 min of recovery from mental stress and 4 min of recovery from mental stress.

Table 2. Comparison of HRV measures in young healthy post-ovulatory females during rest, mental stress and recovery.

Variables	Female (n=30) median (interquartile range)			P		
	Rest	Mental stress (task)	Recovery from mental stress (task)	p1	p2	p3
Time domain of HRV						
SDNN (ms)	62.25 (43.1 - 72.1)	60.3 (51 - 70.5)	52 (43.38 - 63.88)	0.697	0.077	0.019
RMSSD (ms)	59.7 (36.7 - 72.83)	46.15 (31.05 - 67.85)	49.65 (36.65 - 62.23)	0.004	0.106	0.058
NN50	138.5 (73.25 - 206.5)	114.5 (43.5 - 185.75)	117.5 (61.25 - 185)	0.017	0.388	0.004
pNN50 (%)	39.75 (17.75 - 59.28)	26.05 (10.4 - 48)	30.7 (16.28 - 51.73)	0.002	0.061	0.026
Frequency domain of HRV						
LF power (ms^2)	890 (474.75 - 1269.5)	621 (314.75 - 940)	508 (365 - 912)	0.147	0.711	0.116
LF (nu)	39.55 (29 - 58.08)	41.5 (29.45 - 53.35)	35.45 (25.63 - 51.75)	0.964	0.504	0.313
HF power (ms^2)	1226 (554.75 - 2323)	866.5 (509.25 - 1956.75)	1144 (594.75-1320.25)	0.012	0.168	0.131
HF (nu)	60.4 (41.93 - 70.98)	58.3 (46.53 - 69.53)	64.5 (46.7 - 74.2)	0.991	0.491	0.349
TP(ms^2)	3187.5 (1782.75 - 4616.25)	2660 (1689 - 4997)	2714.5(1521.75-724)	0.299	0.750	0.057
LF/HF	0.66 (0.41 - 1.39)	0.72 (0.43 - 1.15)	0.55 (0.35 - 1.09)	0.596	0.797	0.221

SDNN = standard deviation of RR interval, RMSSD= root mean square of differences of successive RR intervals, NN50 = number of RR intervals that differ by ≥50 ms, pNN50 = percentage of NN50. VLF = very low frequency, LF = low frequency, HF = high frequency, power expressed in ms^2 (millisecond), nu = normalized units, TP= total power. The $p<0.05$ was considered statistically significant. p1=between rest and mental stress (task) p2= between mental stress and recovery p3= between rest and mental stress recovery.

DISCUSSION

Mental stress, in the form of nine MENSA workout questionnaire, in post ovulatory females, showed significant increase in both BP and HR at 2 min. This increase in BP continued till 4th min of the stress whereas, HR decreased at 4th min compared to 2 min. Parasympathetic markers of time domain (RMMSD, NN50 and PNN50) and frequency domain (HF power) decreased during the mental stress. The cardiovascular variables during recovery at 2 min were comparable to the resting state. Moreover, at 4th min of recovery, SBP was even less than the resting state. Again, HRV during recovery, showed decrease in SDNN, NN50 and PNN50 compared to the resting state.

Mental stress increases BP.[11] We measured both systolic and diastolic components of BP. SBP is mainly determined by left ventricular ejection and arterial compliance, whereas DBP is mainly determined by vascular resistance.[1] There was significant increase in both SBP and DBP. It means the pressor response to the stressors involve determinants of both the systolic and diastolic BP. The underlying mechanism must be activation of ß-adrenergic activity by mental stress.[1] This happens to evoke active coping behavior; producing a shift in baseline SBP and HR. All participants were actively engaged in solving the questionnaire which requires active coping behavior, thus, causing abrupt rise in BP and HR.

Many past studies have shown that mental stress increases HR as well.[12] In our study mental stress did increase the HR by 7.8% (p1=0.004, Table 1) at 2 min of stress but by the 4th min, there was only 1.3% (p2=0.126, Table 1) increase in HR. The results from this study therefore confirm that the effect of stress on cardiac dynamics substantially differ with duration of exposure to mental stress in females. The initial rise in HR could be an immediate response to mental stress mediated due to sympathetic neural discharge or activation of adrenergic hormones.[1] The gradual decrease in HR could be due to effect of estrogen on the action of catecholamines.[3] Ueyama et al. (2008) had hypothesized that estrogen reduce the sympathoadrenal outflow of stress hormones from the central nervous system thus, protecting the heart from the effects of stress.[13] Since this study was done in post ovulatory females, the menstrual phase where the effect of estrogen is minimal. This minimal estrogen level might be responsible for this effect. Further research is needed to explore more in this area.

In the present study, the BP and HR measurements and the stress tests were applied at a fixed time in the morning (10:00-12:00 h). Using a fixed time rather than a random time was important as Shea et al,[14] had evaluated the circadian rhythm of BP in healthy subjects and had observed that the timing of the endogenous circadian peak in BP occurs in the evening, whereas, the lowest circadian BP occurs early in the morning. Thus, these changes seen in our study were unrelated to the circadian rhythms in cortisol, catecholamines and the neural control of HR.

The acute mental stress affected the power spectral and time domain of HRV. In our study the HF component decreased significantly from the resting value, indicating that the stress was induced in the participants. On the other hand, HF power represents the influence of respiration on heart rate and is assigned to parasympathetic activity[15] and is characterized by the respiratory sinus arrhythmia (RSA).[10] When highly frequent parasympathetic modulation occurs, it increases HR.[10,15] This is what probably must have happened during the mental stress to cause increase in HR. There was no significant change in other frequency domain parameters during this stress. Whereas, in other studies no change in power spectral analysis are reported[16] and in some there was decrease in LF component.[4,17]

In a study done by Collins (2005) et al, LF/HF ratio was used as a sympathetic measure and the HF power as parasympathetic activity to assess job strain. They found that the ratio was significantly elevated and the HF power reduced in the high strain group on workdays.[18] In our study, the HF power decreased significantly whereas, LF/HF ratio increased but was not significant. Thus, the females responded to this stress by parasympathetic withdrawal without concomitant activation of sympathetic nervous system.[10] Berntson et al,[19] Paritala,[20] and Taelman et al,[21] have also shown that in females cardiovascular responses induced by mental stress may be driven by a cardiac parasympathetic modulation alone. This could be due to the effect of estrogen which is thought to contribute to activate the parasympathetic nervous system.[4, 5,13]

A 'female-specific stress response' has been suggested by Taylor et al,[22] who hypothesized that females exhibit a tend-and-befriend response in which they employ social coping methods to combat stress. This tend-and-befriend response is driven by the action of estrogen and oxytocin.[22] It is characterized by a smaller increase in HR, and an increase in HF[4] whereas, in our study there was an increase in HR with decrease in HF.

In time domain measures, RMSSD, NN50 and PNN50 decreased from a resting value during mental stress. There might have been changes in breathing pattern during mental stress thus reducing the HF and RMSSD components, indicating reduction in HRV.[21,23]

Systolic and diastolic blood pressures have been reported to increase with computer work and to remain significantly elevated during a resting period following mental work.[16,17] On contrary, our study showed the cardiorespiratory parameters of recovery from mental stress at 2 min were comparable to the resting states. This reflects that the females recovered from mental stress within 2 min of recovery time. This is supported by HRV findings in frequency domain. It showed that autonomic control of the heart returned to resting conditions within 5 minutes of recovery from the mental stress. The findings are in line with studies done by Satya A. Paritala.[20] Whereas, SDNN, NN50 and PNN50: all time domain measures of HRV were decreased during recovery. The SDNN reflects all the cyclic components responsible for variability in the period of recording, therefore it represents total variability. Such prolonged stress related activation in the cardiovascular system has been linked to increased risk of cardiovascular disease.[24] Thus, the included female subjects who had recovery cardiovascular variables similar to resting states after mental stress showed reduced heart rate variability which is an indication of increased susceptibility to future CVDs.

CONCLUSIONS

Acute mental stress induced increased cardiovascular response by causing withdrawal in parasympathetic activity in young healthy post ovulatory female medical students. Their cardiovascular variables returned to resting state within 5mins of recovery. The underlying mechanism was by further decreasing parasympathetic activity and inducing sympathetic activity. Thus, resulting an overall decrease in HRV. These indicate that parasympathetic reserve of females at post ovulatory phase (2-4 days before menstruation) is reduced and susceptibility to CVD is greater.

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