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Research article

THE EFFECT OF PHASE OF MENSTRUAL CYCLE ON SYMPATHETIC SKIN RESPONSE AMONG HEALTHY YOUNG INDIAN WOMEN

[1]David Pansy, [2]Das Subhasis, [3]Suganthi B, [4]Lyall Shalin, [5]Krishnamurthy N, [6]Veliath Susheela

[1]Assistant Professor, Department of Physiology, Pondicherry Institute of Medical Sciences, Puducherry.
[2]Associate Professor, Department of Physiology, Pondicherry Institute of Medical Sciences, Puducherry
[3]Tutor, Department of Physiology, Pondicherry Institute of Medical Sciences, Puducherry.
[4]Assistant Professor, Department of General Surgery, Pondicherry Institute of Medical Sciences, Puducherry.
[5]Professor, Department of Physiology, Pondicherry Institute of Medical Sciences, Puducherry.
[6]Professor and Head, Department of Physiology, Pondicherry Institute of Medical Sciences, Puducherry.
Email address: docpansy@gmail.com

ABSTRACT: This descriptive study was undertaken to investigate the influence of menstrual cycle on sympathetic skin response (SSR) during different phases of menstrual cycle in young healthy Indian women. A comparison of SSR latencies and amplitudes were done in the follicular, ovulatory and mid luteal phases of menstrual cycle. Fifty women in age group of 18 – 25 years having regular menstrual cycles were chosen for this study. After confirming the regularity of menstrual cycle, SSR was performed on them. The recording was done under standardized conditions using standardized procedure. Amplitude of SSR was found to vary in the three phases, but the differences were statistically not significant. Latency of SSR was found to be greatest in the follicular phase (1.54 ± 0.22 s) and least in the mid-luteal phase (1.35 ± 0.18 s). Statistically significant differences were found between mean SSR latency in the follicular phase and the other two phases ($p < 0.01$). This study concludes that SSR is enhanced during the mid-luteal phase in women with regular menstrual cycles indicating sympathetic dominance.

Keywords: Follicular phase, mid-luteal phase, sympathetic skin response

INTRODUCTION

Sympathetic skin response (SSR), which represents sudomotor activity, results from the activation of a polysynaptic reflex (Elie & Guiheneuc, 1990). The effectors of the reflex arc and the most probable generators of the potential change are the activated eccrine sweat glands with cholinergic innervation. The method of SSR recording was introduced into practice in electrophysiological laboratories by Shahani et al (1984) and later by (Knezevic and Bajada 1985). The SSR latency and amplitude are dependent on the body temperature and the relation is linear. This is most probably caused by a change in the conduction velocity of postganglionic non-myelinated fibers and by the effect of neuroglandular secretion (International Federation of Clinical Neurophysiology, 1999). Stability of the room temperature (around 26°C) and a 15-20 minutes stay of the person to be examined in a room with this temperature prior to examination are sufficient to prevent this effect. In clinical neurological practice evaluation of the SSR is used particularly in the diagnosis of autonomic disorders in patients with peripheral neuropathy. Most frequently SSR is used for diagnosis of lesions of the thin unmyelinated fibers in diabetic neuropathy (Levy et al, 1992; Miralles et al, 1995; Soliven et al, 1987) and uremic neuropathy (Watahiki et al, 1989; Ozcan et al, 1996; Wang et al, 1994). The test has been used in such varied disorders with peripheral as well as central sympathetic involvement such as carpal tunnel syndrome (Solders, 1986), multiple sclerosis (Caccia et al, 1993), Parkinson's disease and Parkinsonian syndrome (Yokota et al, 1991; Braune et al, 1997), surgical or chemical sympathectomy (Fusina et al, 1999) and nerve regeneration after surgical procedures (Lefaucher et al, 1996). Needless to say, this list is by no means exhaustive, but these examples demonstrate the varied use of the test in clinical practice. In fact, SSR has been reported as the most sensitive method for assessing peripheral sympathetic nerve function (Jazayeri et al, 2003).

The menstrual cycle, under the influence of the pulsatile secretion of gonadotropin releasing hormone (GnRH) from the hypothalamus, which controls the secretion of follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary, is divided into a predominantly estrogenic part referred to as the proliferative phase or the follicular phase as opposed to a part with higher progesterone levels referred to as the secretory phase or the luteal phase. The two phases are separated by a period of menstrual bleeding at the start of the cycle and an ovulatory period in the mid-cycle. Many behavioral and psychological changes have been observed in response to hormonal variations during the premenstrual phase, pregnancy and menopause. Additionally, human (Torigoe et al, 1999) and animal (Yao et al, 2009) studies have demonstrated the effects of stress on these hormones and their consequent behavioral manifestations. Most of the behavioral and emotional patterns are exhibited through changes in the autonomic nervous system (ANS). Significant differences in autonomic nervous activity have been found to exist between the follicular and luteal phases of the menstrual cycle (Ter Horst et al, 2012). Sympathetic nervous activity in the luteal phase is significantly greater than in the follicular phase, possibly due to the effect of progesterone (Sato & Miyake, 2004; Sato et al, 1995; Saeki et al, 1997). Conversely, in the follicular phase, which is characterised by increasing estrogen levels, parasympathetic activity has been shown to predominate (ter Horst et al, 2012; Sato & Miyake, 2004; Sato et al, 1995). Estrogen has site dependent inhibitory effect on sebaceous glands (Ryan et al, 1994). Estrogen receptor α (ERα) is restricted to sebaceous glands whereas estrogen receptor (ERβ) is found more in sebaceous as well as eccrine sweat gland (Parchami et al, 2010; Pelletier & Ren, 2004). Sebaceous gland activity is stimulated by androgens but inhibited by estrogen. Subcutaneous administration of estrogen cause both reduction in size and number of sebaceous gland (Ryan et al, 1994). It can therefore be assumed that the levels of the female sex hormones or the phases of the menstrual cycle would have an effect on the measured values of SSR latency and amplitude. However, most of the studies evaluating the effect of ovarian hormones on autonomic function have used cardiovascular autonomic function tests (Muchekehu & Harvey, 2009; Bai et al, 2009; Minson et al, 2000). Only a few studies have attempted to correlate the phases of the menstrual cycle with cutaneous autonomic function (Hirshoren et al, 2002; Mehta & Chakrabarty, 1993; Rossi et al, 2009; Gautam et al, 2011; Ozisik et al, 2005). The results of such studies are mostly inconclusive (Rossi et al, 2009; Gautam et al, 2011; Ozisik et al, 2005). Hence, this study was undertaken with the purpose of evaluating SSR in the three phases of the menstrual cycle.

PARTICIPANTS AND METHODS

This descriptive study was conducted in the Department of Physiology, Pondicherry Institute of Medical Sciences, Pondicherry, from August 2011 to May 2012. Ethical clearance was obtained from institutional Ethics Committee. Informed written consent was obtained from each participant before including them in the study. The participants in this study included young healthy women in the age group of 18-25 years, having normal and regular menstrual cycles. The menstrual cycles of all the participants were charted over two months for regularity. A detailed history was taken and thorough physical examination was conducted to rule out any systemic diseases, autonomic dysfunction, use of oral contraceptives or any drugs that affect autonomic function. Pregnant or lactating women were excluded from the study. Each recruited participant was instructed to report for SSR recordings in the three phases of the menstrual cycle, viz., the early follicular phase which was calculated as the fourth day of the cycle, the ovulatory phase taken as 14 days prior to next cycle & the mid luteal phase which was calculated as the seventh day from the day of ovulation. On each day of the study, the subjects reported at a fixed time in morning after a light breakfast. In the laboratory, after explaining the procedure, anthropometric measures and basal vital parameters were recorded. The skin temperature was recorded from the volar aspect of the forearm using a digital thermometer. Subsequently, the subject was asked to rest in the supine position for 15 min on the couch in order to adapt to the laboratory environment. The ambience of the environment and illumination were maintained constant during the recording of SSR. The instrument used in the study was NCV-EP-EMG machine (RMS EMG.EP MARK II, Recorders and Medicare Systems, Chandigarh). For recording of SSR the low frequency filter setting was 0.2 Hz while high frequency filter was set at 100 Hz. The sensitivity was set at 500μV. Ag-AgCl surface disc electrodes of 1 cm diameter were used for recording. The active electrode was placed on the palmar aspect of the dominant hand, while the reference electrode was placed on the dorsal aspect of the same hand using RMS recording jelly after thorough cleaning of the skin surface. The ground electrode was firmly fixed to the volar aspect of the forearm. SSR was recorded using supramaximal electrical stimulus. It was ensured that the subject did not sleep during the recording. The latency (defined as the time interval between the stimulus & the onset of the SSR wave form) and amplitude (defined as the peak to peak amplitude of the SSR wave) of SSR was noted for each of the recordings.

RESULTS

Sixty-five healthy female participants were initially recruited for this study. Out of these 65 participants, ten women had irregular menstrual cycles, four women did not come for regular follow up and one participant conceived during the study period. All the remaining 50 participants in whom the study could be completed belonged to the age group 18 to 25 years (Mean: 19.60 ± 1.75 years). The three main parameters studied, i.e. the skin temperature, latency of SSR and amplitude of SSR were subjected to multivariate tests. Repeated measures ANOVA (RMANOVA) was applied using a linear model. An initial Wilk's Lambda multivariate statistic was done. If the Wilk's Lambda test was found to be significant ($p < 0.0167$), Mauchly's test of sphericity was performed on each of the models. The assumption regarding sphericity was deemed to be met if the probability of Mauchly's test statistically was > 0.05. Subsequently, the Greenhouse-Geisser correction was applied to determine whether there was any statistically significant difference among the means of each parameter in the three phases of the menstrual cycle. Additionally, if significant difference among the means was established, a post-hoc Bonferonni correction was done with the pair-wise comparisons of the mean values of each parameter in the three phases of the menstrual cycle. Table 1 shows the mean skin temperature and SSR amplitude values in the three phases of the menstrual cycle. Multivariate analysis of the mean values of skin temperature and amplitude showed no statistically significant difference in the three phases of the menstrual cycle. Descriptive statistics related to SSR latency is given in Table 2 and Figure 1.

Table 1: Mean skin temperature and SSR amplitude values in the three phases of the menstrual cycle

Phase of menstrual cycle	Skin temperature (ºC)	SSR amplitude (mV)
	Mean ± SD	Mean ± SD
Follicular	29.62 ± 0.76	0.294 ± 0.19
Ovulatory	29.90 ± 0.83	0.329 ± 0.42
Mid luteal	29.87 ± 0.98	0.270 ± 0.19

Table 2: Mean SSR latency values with inter-quartile range (in seconds) in the three phases

SSR latency		Follicular phase	Ovulatory phase	Mid-Luteal phase
Median		0.3	0.3	0.2
Percentiles	**25th**	0.175	0.1	.175
	75th	0.3	0.348	0.3

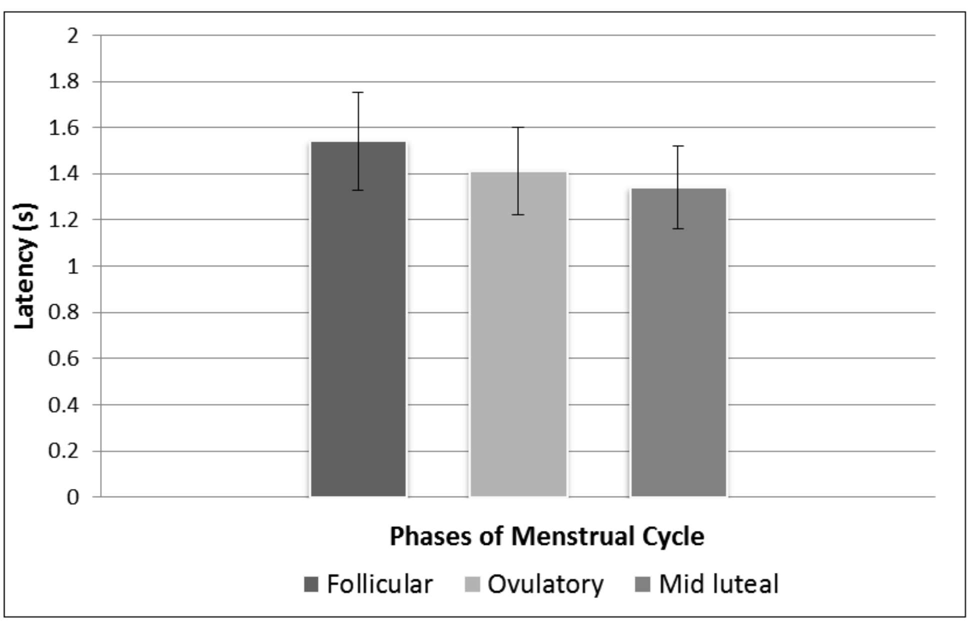

Figure-1: Latency of SSR (Mean ±SD, in s) different phases of Menstrual Cycle

Mean SSR latency was observed to be highest in the follicular phase (1.54 ± 0.22 s) and lowest in the mid-luteal phase (1.35 ± 0.18 s). RMANOVA performed on the mean values of SSR latency in the three phases showed that there was statistically significant difference ($F = 13.631$, $p < 0.001$) in mean latencies of SSR measured at three different phases of menstrual cycle. The subsequent pair-wise comparison with Bonferroni correction is represented in Table 3. Thus, RMANOVA with pair-wise comparison revealed that there was statistically significant difference between the mean latencies of the follicular and ovulatory phases ($p = 0.006$), and also between the follicular and mid-luteal phases ($p = 0.000$). However, between the ovulatory and mid-luteal phases of the menstrual cycle, mean latency of SSR showed no significant difference ($p = 0.248$).

Table 3: Pair-wise comparison of SSR latency in different phases of menstrual cycle

Pair-wise comparison of Phases of menstrual cycle	Significance
Follicular phase **vs.** Ovulatory phase	0.006
Ovulatory phase **vs.** Mid-luteal phase	0.248
Follicular phase **vs.** Mid-luteal phase	0.000

DISCUSSION

Hormonal variations in the different phases of the menstrual cycle are known to affect autonomic function. The female sex hormones are also known to act directly on the eccrine sweat glands via site specific receptors. However, most studies investigating the effect of the menstrual cycle on autonomic function have been conducted on cardiovascular autonomic function and sudomotor function has rarely been studied. In the present study, the mean skin temperature, as measured from the volar aspect of the forearm was found to be comparable in the three phases of the menstrual cycle. Thus any differences in the amplitude and latency of SSR observed in the three phases of the menstrual cycle cannot be attributed to changes in skin temperature. SSR amplitude was found to be highest in the ovulatory phase and least in the mid-luteal phase. However, this difference was statistically not significant. Latency of SSR was longest in the early follicular phase and shortest in the mid-luteal phase. There were statistically significant differences between the SSR latency in the early follicular phase and that in the ovulatory and mid-luteal phases. While the results noted with SSR amplitude are inconclusive, the findings related to SSR latency suggest an increased sympathetic activity during the mid-luteal phase as compared to the early follicular phase in women with regular menstrual cycles, an effect probably brought about by increased level of progesterone as suggested by earlier studies. The hormonal changes during the luteal phase of the menstrual cycle would probably bring about a reversal of the normal estrogen-induced inhibitory effect on the sweat glands, thus leading to an increase in their activity manifested by a reduction in the latency of SSR. This observation is similar to those by other researchers (Bai, 2009; Minson, 2000; Hirshoren, 2002) regarding the effect of the menstrual cycle on autonomic function, in studies which have not involved the recording of SSR. However, the findings of this study do not conform with the conclusions of other studies where peripheral sudomotor function was not found to be affected by female sex hormones (Rossi, 2009; Gautam, 2011; Ozisik, 2005).

CONCLUSION

Based on the findings of this study it can be concluded that SSR latency does decrease in the mid-luteal phase of the menstrual cycle, as compared to the early follicular phase and the ovulatory phase. Thus, in clinical practice, SSR values recorded from women should be analyzed keeping in mind the variations due to the hormonal effects.

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