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SHORT COMMUNICATION

Association between subjective and cortisol stress response depends on the menstrual cycle phase



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Summary The relation between the physiologic and subjective stress responses is inconsistently reported across studies. Menstrual cycle phases variations have been found to influence the psychophysiological stress response; however little is known about possible cycle phase differences in the relationship between physiological and subjective stress responses. This study examined the effect of menstrual cycle phase in the association between subjective stress and physiological response. Forty-five women in either the follicular ($n = 21$) or the luteal phase of the menstrual cycle were exposed to a psychosocial stress task. Salivary cortisol, cardiovascular, and subjective stress were assessed throughout the experiment. Results revealed a significant group difference in the association between peak levels of cortisol and post task subjective stress. In women in the follicular phase a negative association was observed ($r^2 = 0.199$, $p = 0.04$), while this relation was positive in the group of women in the luteal phase ($r^2 = 0.227$, $p = 0.02$). These findings suggest a possible role of sex hormones in modulating the cortisol stress response function in emotion regulation.

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Social evaluative threat is one of the most potent laboratory stressors, inducing physiological and emotional responses (Campbell and Ehlert, 2012). The stress response is characterized by synchronized activation of the fast-reacting sympathetic adrenal medullary system (SAM) quickly releasing noradrenaline and the hypothalamic-pituitary-adrenal axis

(HPAA), culminating in a slower cortisol response (Andrews et al., 2013). Parallel to the physiological responses, social threat induces strong subjective responses (Campbell and Ehlert, 2012). Past research has successfully identified factors associated with the modulation of both the subjective and neuroendocrine stress responses (Kudielka et al., 2009). However, there has been little consensus regarding the coherence between the neuroendocrine and subjective stress responses, suggesting a complex relationship (Campbell and Ehlert, 2012; Andrews et al., 2013).

Both gender and menstrual cycle phase in women are important modulators of the physiological stress response (Kajantie and Phillips, 2006). Compared to the follicular

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phase (characterized by rising levels of circulating estrogens), many studies found the luteal phase (characterized by high circulating levels of estrogens and progesterone) to be associated with increases in physiological responses to stress, although this is not consistently observed (Kirschbaum et al., 1999; Childs et al., 2010; Felmingham et al., 2012). Interestingly, most of the studies investigating the association between the subjective and neuroendocrine stress responses failed to control for possible effect of gender and/or cycle variations (Campbell and Ehlert, 2012).

A recent study tested the associations between the physiological and emotional stress responses in a large population. This study revealed a positive association between autonomic and subjective stress responses, but a negative association between cortisol levels and subjective stress (Het et al., 2012). It was proposed that the autonomic response might contribute to the stress-related emotional arousal whereas the later cortisol response would exert mood protective effects (Het et al., 2012). These associations were present in both men and women, however the authors did not report on possible effect of menstrual cycle phase variations. Interestingly, another recent study showed that variations in the menstrual cycle phase influenced the association between cortisol stress response and emotional memory. Specifically, women in mid-luteal phase (days 18–24) demonstrated a positive association between cortisol stress response and recall for threatening stimuli, which was not observed in other phases (Felmingham et al., 2012). This recent finding showed that in times of stress, the association between the cortisol response and emotional experiences differs across the menstrual phase, and that during the luteal phase, specifically the cortisol response seems to enhance, instead of dampen, threat processing.

Thus, the present study aimed to look at the relation across subjective, cardiovascular, and neuroendocrine stress responses in women across cycle phases. Based on the most recent findings investigating the relation between cortisol and threat processing, we hypothesized that women in follicular phase would show a negative relationship between cortisol release and subjective stress response, while this association may be either absent or inverted (i.e. positive) for women in the luteal phase of their menstrual cycle.

1. Methods

1.1. Participants

Forty-five women, (age 21.4 ± 2.46) were recruited via classified ads at McGill University. Exclusion criteria for the study were medication use, prior or present neurological or psychiatric illness, smoking, body mass index ≥ 27 or ≤ 18 , substance abuse, amenorrhea and/or use of contraceptive medication during the past 6 months and menstrual cycle length >25 or <35 . Menstrual cycle phase was assessed based on self-report measures. All subjects were questioned twice in regard to their menstrual cycle phase, during recruitment and on the day of testing. Females were either tested in the follicular phase of their cycle (2–12 days post menses onset, $n = 21$) or in the luteal phase (17–30 days post menses onset, $n = 24$). Days of testing were also adjusted according to the subject's cycle length. The Douglas Hospital Research Ethics Board approved the study. All subjects gave written informed consent.

1.2. Procedure

Subjects were tested between 2 and 6 pm. Participants waited for one hour, during which they completed questionnaires. Participants were then exposed to a modified version of the Trier Social Stress Test as previously explained in Duchesne et al. (2012). In brief, participants were exposed to a previously developed 10-min mock job interview in front of a gender mixed panel of two evaluators (Duchesne et al., 2012). Following stress exposure, subjects remained in the laboratory for another 50 min, were debriefed, and sent home.

1.3. Stress measures

Neuroendocrine, cardiovascular, and subjective measures of stress were measured throughout the experiment in 10-min intervals starting from 10 min prior to task onset for a total of eight sampling times. Cortisol was measured from saliva using salivettes (Sarstedt Inc., Quebec City, Canada). Salivettes were stored at -20°C until analysis. Samples were analyzed using a time-resolved fluorescence immunoassay. Blood

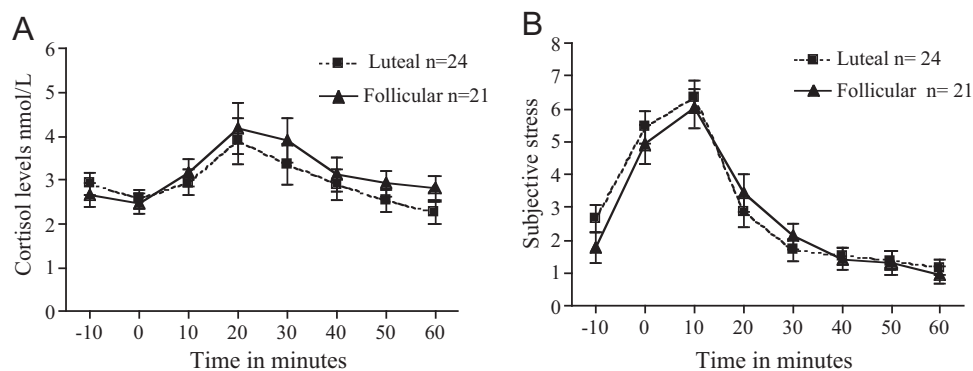


Figure 1 Salivary cortisol (A) and perceived stress (B) across the experiment in groups of women in the luteal and follicular phase of the menstrual cycle.

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