Progesterone mediates the late positive potentials evoked by affective pictures in high neuroticism females

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Abstract
**Background**: Neuroticism, which is a personality trait characterized by the tendency to experience negative affect, is associated with premenstrual negative emotion changes. The present ERP study intended to investigate how neuroticism and the menstrual cycle influence the evaluation of emotion as a function of the tested levels of ovarian hormones.

**Method**: Forty-two healthy females with regular menstrual cycles were grouped by neuroticism (N): 16 were included in the high-N group, and 26 were included in the low-N group. Each female performed an emotion evaluation task in the early follicular phase, late follicular phase and luteal phase while the ERPs, hormone samples and Pleasure-Arousal-Dominance (PAD) mood ratings were measured.

**Results**: The PAD and behavioral data did not differ between the two groups during the three phases. However, the mean amplitude of the Late Positive Potentials (LPP, 300–1000 ms post-stimulus) of ERPs was significantly larger in the high-N group than that in the low-N group. Moreover, the interaction between the group and phase was significant 2000–4000 ms post-stimulus: for the high-N group, the LPP of the luteal phase was the largest, followed by the
late follicular phase and the early follicular phase; whereas the LPP of the luteal phase was the largest, followed by the early follicular phase and the late follicular phase for the low-N group. More importantly, the LPP (300–4000 ms post-stimulus) evoked by positive pictures from the central or parietal area was significantly negatively correlated with the progesterone level in the early follicular phase.

Conclusions: The present study provides electrophysiological evidence showing that both the menstrual cycle and neuroticism modulate the LPP evoked by emotional pictures. Furthermore, the negative correlation between progesterone and the amplitude of the LPP suggests that the effect of the menstrual cycle on the LPP may be primarily a function of progesterone. These findings suggest that the LPP evoked by emotional pictures for high and low neuroticism females change throughout the menstrual cycle and that this change is in part mediated by progesterone.

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1. Introduction

Females often experience negative mood prior to menstruation. Neuroticism, which is a personality trait characterized by the tendency to experience negative affect (Eysenck, 1967) and influences emotion processing (Canli et al., 2001; Reynaud et al., 2012; Servaas et al., 2014), has been found to be associated with premenstrual negative emotion changes. In an early landmark study, high neuroticism women were found to consistently be more restless, irritable, fatigued, fearful and depressed during the premenstrual phase than during other phases of the menstrual cycle, and they were also hypersensitive to various stimuli (Benedek and Rubenstein, 1939). Females with premenstrual syndrome (PMS) also scored significantly higher in neuroticism than healthy females (Hallman et al., 1987). A later study found that the neuroticism scores of females who suffer from premenstrual dysphoric disorder (PMDD) were higher and that the premenstrual mood disorder was related to high scores on the neurotic scale (Ramos et al., 2003). Neuroticism could also account for a significant amount of variation in the negative premenstrual affect both before and after controlling for the baseline (follicular) symptom levels (Ross et al., 2001). Furthermore, the following two studies provide the evidences for relationships among neuroticism, negative premenstrual affect and genetics. An Australian twin study examining additive genetic influence on PMS found the genetic correlations of 0.62 between reported SMS and neuroticism (Treloar et al., 2002). Women with PMDD also displayed higher levels of neuroticism-related personality traits (e.g. psychic trait anxiety) than healthy controls, and PMDD patients with at least one copy of the short allele of the 5-HTTLPR polymorphism scored higher on psychic trait anxiety than PMDD patients who were homozygous for the long allele (Gingnelli et al., 2010).

In addition, the menstrual cycle has been demonstrated to impact mood and emotion processing (for review see Farage et al., 2008). Compared to the follicular phase, negative emotions increased during the luteal phase both in healthy, non-PMDD women (Gonda et al., 2008) and in PMDD women (Reed et al., 2008). Ovulating women were found to be more accurate in their social cognitive judgments and interpersonal perception compared to women during menstruation (Macrae et al., 2002). Furthermore, females in the follicular phase recognized emotional faces more accurately than females in the menstruation or the luteal phase (Pearson and Lewis, 2005; Derntl et al., 2008a; Guapo et al., 2009). Besides the above behavioral studies, event-related potentials (ERPs), as indicators of the perceptual process with excellent temporal resolution, are used to reflect the time course of emotion processing during the menstrual cycle. Some studies have found that the menstrual cycle modulated the late ERP components. For example, P3, which seems to reflect attention and memory processes in the frontal and temporal/parietal cortices (Polich, 2007), was largest in response to babies and male models when the progesterone level was high (Johnston and Wang, 1991). Moreover, the late positive potential or component (LPP or LPC), occurring between 300 and 1200 ms after stimulus onset, which was larger in amplitude to emotional than to neutral stimuli, especially arousing emotional stimuli (Olofsson et al., 2008), was also modulated by the menstrual cycle. The LPC (peaking 550–600 ms post-stimulus) showed a larger peak during the ovulatory phase for sexual stimuli (i.e. nude men), which suggested increased sexual desire and deeper emotional processing (Krug et al., 2000). The LPP (750–1000 ms post-stimulus) evoked by facial expressions were larger during the periovulation phase than during the premenstrual phase (Zhang et al., 2013b). Moreover, the LPP (300–1000 ms post-stimulus) evoked by affective pictures were larger during the late follicular phase than during the luteal phase (Zhang et al., 2013a). Therefore, the late ERP components may be electrophysiological indicators of the effect of the menstrual cycle on emotion processing.

The modulation of emotion processing by the menstrual cycle may be related to the accompanying fluctuation in ovarian hormones, especially estrogen and progesterone. The menstrual phase and the early follicular phase of the menstrual cycle are characterized by low levels of both progesterone and estrogen. The estrogen levels rapidly increase late in the follicular phase, peaking one day before ovulation. The progesterone levels steadily increase during the luteal phase and peak mid-luteal phase, in parallel with a second estrogen peak. The late luteal phase is characterized by declines in both the estrogen and progesterone levels, which reach baseline shortly before the onset of menstruation (Farage et al., 2008). Research has shown an increase in the behavioral ratings of pleasantness to emotional pictures when estrogen levels were high (Wang and Johnston, 1993), while women have been found to experience more negative emotions when estrogen levels declined or were low (Collins et al., 1985; Cockerill et al., 1994).
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