Psychological Effect of the Menstrual Cycle on an Emotional Go/Nogo Task and Its Relation to Plasma Oxytocin and Prolactin Levels

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Abstract
Many previous studies have suggested that the natural menstrual cycle of healthy women influences facial emotion processing. We investigated the effect of facial expression as the emotional distractor on behavioral inhibitory processes in the follicular and luteal phases. In addition, we focused on oxytocin and prolactin levels, which are known to fluctuate in the menstrual cycle and are suggested to have neuropsychological effects on child facial emotion processing. Sixteen healthy women with natural menstrual cycles participated in the experiment once each in their follicular and luteal phases. Following blood sampling for hormone analysis, task performance was measured by electroencephalogram while they performed an emotional Go/Nogo task using angry and neutral faces of children as distractors. Event-related potentials (Nogo-N2 and Nogo-P3) were calculated from the electroencephalogram. The results showed that Nogo-N2 latency was delayed by the angry faces only in the luteal phase. The change rate of Nogo-N2 latency from the follicular to luteal phases was positively correlated with the change rate of the prolactin levels. Regarding task performance and Nogo-P3, fluctuations with menstrual cycles were not observed. Our findings suggest that the distractive effects of children's angry faces on the inhibitory processes fluctuate during the menstrual cycle only in the promoter levels, which are associated with the variation of serum prolactin concentrations within menstrual cycles.

Keywords: menstrual cycles, behavioral inhibition, facial processing, electroencephalogram

Introduction

Many women experience psychological fluctuations with their menstrual cycles. Previous studies suggest that menstrual cycles are associated with the psychological processes occurring at the presentation of emotional faces (Derntl, Kryspin-Exner, Fernbach, Moser, & Habel, 2008; Osório, de Paula Cassis, Machado de Sousa, Poli-Neto, & Martín-Santos, 2018; Pearson & Lewis, 2005). It is also known that task performance of behavior inhibition decreases when facial expressions are presented at the same time. In that situation, facial expressions act as distractions, which cause low performances of behavioral inhibition. For example, it is reported that angry faces caused prolonged response times and decreased task sensitivity (Pacheco-Unguetti, Acosta, Lupiáñez, Román, & Derakshan, 2012). It is thought that this is because anger expressions are processed with priority and compete with processes for behavioral inhibition.

Behavioral inhibition is thought to be an important ability for child caregiving behavior. A previous study reported that impulse control disability of mothers was a risk factor for child maltreatment (Tachibana et al., 2017). Other studies of mothers suggest that some hormones will modulate a part of psychological functions related to cognition of infants and children. Oxytocin is thought to modulate neural activities to children's faces. It is reported that the administration of oxytocin enhanced the allocation of attention towards children compared with adults (Rutherford et al., 2017). It is also suggested that prolactin has effects on caregiving behavior via modulating emotional processes related to child emotion expression (Hashemian, Shafigh, & Roohi, 2016). These oxytocin and prolactin levels fluctuate in the menstrual cycle; oxytocin concentration rises in the follicular phases compared with luteal phases (Salonia et al., 2005), and prolactin concentration is known to rise in the luteal phases.

A Go/Nogo task is a psychological experiment task for investigating behavioral inhibition. It was also demonstrated that Go/Nogo tasks with emotional distractors (emotional Go/Nogo task) are effective in testing emotional bias on behavioral inhibitory control (Schulz et al., 2007). Both task performance and event-related potentials calculated from electroencephalograms are useful indexes of behavioral inhibition. The event-related potentials reflect very small voltages generated in the brain in response to stimuli and can be elicited by a wide variety of sensory, cognitive, or motor events, including behavioral inhibition. Nogo-N2 and Nogo-P3 are known as event-related potentials reflecting inhibitory processes in the brain. Nogo-N2 is a negative peak potential appearing in the time window between 200 to 300 ms after stimulus onset. Nogo-P3 is a positive peak potential appearing in the time window around 300 to 500 ms after stimulus onset. Both are thought to be reflect inhibitory processes in the frontal area including the anterior cingulate cortex (Albert, López-Martín, & Carretié, 2010; Albert, López-Martín, Tapia, Montoya, & Carretié, 2012; Bokura, Yamaguchi, & Kobayashi, 2001; Buodo, Sarlo, Mento, Messerotti Benvenuti, & Palomba, 2017; Chen, Jia, & Woltering, 2018; Liu, Xiao, & Shi, 2018; Schoenberg et al., 2014; Stein, Fey, Koenig, Oehy, & Moggi, 2018; Zhang & Lu, 2012).

This study tested the idea that distractive effects of children's faces on behavioral inhibition would fluctuate during the menstrual cycle via psychological fluctuations within menstrual cycles. The experiment was conducted at two points of the

menstrual cycle, the follicular and luteal phases. An emotional Go/Nogo task with children's angry face was used for testing the distractive effects of the children's facial expressions. The task performance, Nogo-N2 and Nogo-P3, during the task were calculated. The concentration of oxytocin and prolactin levels were measured in each experiment. Oxytocin and prolactin associations with the fluctuations of the distractive effects of child facial expressions were also tested.

Methods

Participants

Eighteen Asian females (seventeen Japanese and one Korean living in Japan for twenty-seven years) participated in this study. The mean age (SD) was 27.3 (4.68) years. They participated in the experiment at two points in their natural menstrual cycles. Their menstrual cycles were estimated by basal body temperature and concentrations of ovarian hormones (estrogen and progesterone). A participant was excluded from all analysis because of their non-natural menstrual cycle. In addition, a participant was excluded from the electroencephalogram analysis because of the lack of electroencephalogram data. Informed written consent was obtained from all participants as approved by the Ethics Committee of Kyushu University (Approval Number 276).

Procedures

In the experiment, they participated in blood sampling to measure serum concentrations of oxytocin and prolactin. Then, they performed an emotional Go/Nogo task for measuring the distractive effects of children's facial expressions on behavioral inhibition. The emotional Go/Nogo task included the following four trials: angry-Go (35%), angry-Nogo (15%), neutral-Go (35%), and neutral-Nogo (15%). In angry-Go and -Nogo, the angry face of a child was presented with a Go and Nogo cue, respectively. In the trial of neutral-Go and -Nogo, the neutral face of a child was presented with a Go and Nogo cue, respectively. Two letters (M and W) were used as the Go and Nogo cues. The cues were located between the eyes on the faces of the children. The participants were asked to respond as quickly as possible with their index finger to the picture with the Go-cue but to withhold a response to the picture with the Nogo-cue. A block including 240 trials was carried out four times.

During the task, task performance (response time and accuracy). The electroencephalogram was also measured by a 64-channel EEG measuring system (64-channel HydroCel GSN, Net Amps 200 64-channel EEG Amplifier, and Net Station, ver. 4.1.2; Electrical Geodesics Inc., USA) with a hardware filter (0.01 to 200 Hz). The data were sampled at 500Hz. In an offline analysis, the sensitivity (d-prime) was estimated following the signal detection theory (Macmillan, Creelman, & Creelman, 2004) as an index of task performance. In addition, two event-related potentials (Nogo-N2 and Nogo-P3) were calculated from the electroencephalogram at the frontal area (electrodes located near the Fz and FCz) during correct-Nogo trials. Nogo-N2 and Nogo-P3 were defined as the negative peak potential between 200 and 300 ms and the positive peak potential between 350 and 550 ms after the Nogo-cue presentations, respectively.

Statistical analysis

A two-way analysis of variance (ANOVA) was performed with menstrual cycles (follicular and luteal phases) and facial expression of distractors (angry and neutral) as factors influencing the d-prime, Nogo-N2 amplitude, Nogo-N2 latency, Nogo-P3 amplitude, and Nogo-P3 latency. Degrees of freedom were corrected with the Greenhouse-Geisser method and the Bonferroni-Holm method was used to adjust the P-value during post hoc tests.

When the interaction between the menstrual cycles and facial expression of distractors was significant, a correlation analysis was performed to investigate the associations of oxytocin and prolactin levels with the distractive effects on inhibitory processes. For both angry and neutral conditions, Pearson's correlation coefficients were calculated for the change rate of the maternal hormone levels (oxytocin and prolactin) from the follicular to luteal phases and the indexes of behavioral inhibition from the follicular to luteal phases. A comparison between the correlations for angry and neutral conditions was made by the Fisher r-to-z transformation. Non-correlation tests were also performed. All significance levels for statistical tests were set to 5%.

Results

Table 1 shows the mean and SD of d-prime, Nogo-N2 amplitude, Nogo-N2 latency, Nogo-P3 amplitude, and Nogo-P3 latency in the follicular and luteal phases. For Nogo-N2 latency, the ANOVA showed a significant interaction between menstrual cycles (follicular and luteal phases) and facial expression of distractors (angry and neutral) ($F(1,15)=5.41$, $p=0.034$) (Table 2). Post hoc tests showed that Nogo-N2 latency was delayed by the angry faces only in the luteal phase. Correlation analysis showed that the change rate of Nogo-N2 latency from the follicular to luteal phases was positively correlated with the change rate of prolactin levels ($r=0.64$, $p=0.007$) only in the angry condition ($t(13)=2.25$, $p=0.042$). The prolongation rate of Nogo-N2 latency from follicular to luteal phases was significantly associated with the increasing rate of prolactin levels from follicular to luteal phases only for the angry distractor condition.

Regarding the d-prime, Nogo-P3 amplitude, and Nogo-P3 latency, there were significant main effects of the facial expression of distractors (d-prime; $F(1,15)=29.4$, $p<0.0001$, Nogo-P3 amplitudes; $F(1,15)=10.38$, $p=0.005$, Nogo-P3 latency; $F(1,15)=5.76$, $p=0.029$) (Table 2). Post hoc tests showed that the d-prime for angry faces was lower than for neutral faces. This suggests that task performance was decreased by angry faces compared with neutral faces. Post hoc tests also showed that Nogo-P3 amplitude for angry was smaller than for neutral, and Nogo-P3 latency for angry was longer than for neutral. This means inhibitory processes reflected by Nogo-P3 were diminished and prolonged in the angry condition compared with the neutral condition. The summary of the ANOVA is shown in Table 2.

Table 1. The mean and SD of d-prime, Nogo-N2 amplitude, Nogo-N2 latency, Nogo-P3 amplitude, and Nogo-P3latency in the follicular and luteal phases

Mean (SD)	follicular phases		luteal phases	
	angry	neutral	angry	neutral
d-prime	1.09(0.45)	1.27(0.54)	1.13(0.46)	1.29(0.46)
Nogo-N2 amplitude (μV)	-4.37(1.68)	-4.22(1.88)	-4.48(2.15)	-4.41(2.10)
Nogo-N2 latency (ms)	235.6(15.5)	236.2(16.5)	239.7(26.5)	232.6(20.6)
Nogo-P3 amplitude (μV)	2.05(1.78)	2.30(1.79)	1.74(2.17)	1.98(2.17)
Nogo-P3 latency (ms)	467.8(28.79)	458.6(31.82)	479.4(29.67)	467.5(28.88)

Table 2. Statistical results of ANOVA for d-prime, Nogo-N2 amplitude, Nogo-N2 latency, Nogo-P3 amplitude, and Nogo-P3 latency in the follicular and luteal phases

F-value	menstrual cycles	facial expression of distractors	menstrual cycles × facial expression of distractors
d-prime	0.13	**29.4*****	0.15
Nogo-N2 amplitude (μV)	0.24	0.78	0.24
Nogo-N2 latency (ms)	0.005	4.38	**5.41***
Nogo-P3 amplitude (μV)	1.16	**10.38****	0.008
Nogo-P3 latency (ms)	2.12	**5.76***	0.188

*p<0.05, **p<0.01, ***p<0.001

Discussions

The aim of this study was to investigate the fluctuations of the distractive effects of children's facial expressions on behavioral inhibition with menstrual cycles. The associations of oxytocin and prolactin concentrations with fluctuations of behavioral inhibition were also tested. The experiment was conducted at two points of the

menstrual cycle (follicular and luteal phases). The distractive effects of children's facial expressions on behavioral inhibition were evaluated by task performance (d-prime) and event-related potentials (Nogo-N2 and Nogo-P3). A significant interaction between menstrual cycle and facial expression of the distractor were observed only for Nogo-N2 latency. Furthermore, Nogo-N2 latency was delayed in the angry condition compared with the neutral condition only in the luteal phase. This fluctuation of Nogo-N2 latency was associated with the variation of prolactin concentration with menstrual cycles. The distractive effects of angry faces were observed for the performance (d-prime) and inhibitory processes reflected by Nogo-P3; however, there are no significant effects of the menstrual cycles.

Our results suggest that the fluctuations of the facial distraction on behavioral inhibition appear in a part of the inhibitory processes, which can be observed as prolonged Nogo-N2 latency. It is thought that Nogo-N2 reflects inhibitory processes preceding motor control processes called premotor levels (Falkenstein, Hoormann, & Hohnsbein, 1999; Nieuwenhuis, Yeung, van den Wildenberg, & Ridderinkhof, 2003; Smith, Johnstone, & Barry, 2008). Prolongation of Nogo-N2 is thought to reflect the delay of the inhibitory processes in the premotor levels. Thus, our findings indicate that the inhibitory processes in the promoter levels are delayed by children's angry faces compared with children's neutral faces only in the luteal phases. The results also show the associations between the fluctuations of the prolactin concentrations and Nogo-N2 latency for angry faces. This suggests that fluctuations of the inhibitory processes in the promoter levels may be associated with the variation of serum prolactin concentrations within menstrual cycles. A previous study indicates the possibility that prolactin has effects on psychological processing related to others' faces (Zebrowitz et al., 2018). Such effects of prolactin may cause the delay of inhibitory processes via rising of the priority of processes related to a child's angry face.

In contrast, the effects of menstrual cycles were not confirmed for performance (d-prime) and the inhibitory processes reflected by Nogo-P3. The results suggest that menstrual cycles have effects on a part of the facial distraction on behavioral inhibition. The results also suggest that there may be a complex structure modulating the distractive effects of children's angry faces on behavioral inhibition. The structure possibly consists of at least two processes. One may be a process related to the delay of the premotor inhibitory processes, affected by both children's angry faces and menstrual cycles especially in the luteal phases. This process may be associated with the concentration of prolactin. Another is possibly a process that has emotional effects on motor control processes regardless of the menstrual cycle. The process may be reflected by d-prime and Nogo-P3.

Conclusions

In conclusion, our findings suggest that the distractive effects of children's angry faces on prolonged behavioral inhibition in the premotor levels may fluctuate in natural menstrual cycles, and it is enhanced in the luteal phases. This may be associated with the fluctuations of the prolactin concentration within menstrual cycles. The findings also suggest that menstrual cycles have effects on facial processes (Derntl et al., 2008; Osório et al., 2018; Pearson & Lewis, 2005) and a part of the behavioral inhibitory processes related to facial processing.

There are some limitations of this study and the need for further studies. First, serum oxytocin and prolactin were used in this study. It was suggested that peripheral plasma oxytocin affects central oxytocinergic brain activity (Ebstein, Knafo, Mankuta, Chew, & Lai, 2012) and peripheral prolactin is considered the major effector within the brain (Torner, 2016). However, serum oxytocin and prolactin associations with facial processes in the brain could not be directly confirmed. Second, experiments were conducted at only two points of the menstrual cycle. By measuring at more points of the menstrual cycle, it may be possible to capture more details of the fluctuations.

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