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Sex and menstrual cycle phase at encoding influence emotional memory for gist and detail

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ABSTRACT

Sex influences on emotional memory have received increasing interest over the past decade. However, only a subset of this previous work explored the influence of sex on memory for central information (gist) and peripheral detail in emotional versus neutral contexts. Here we examined the influence of sex and menstrual cycle phase at encoding on memory for either an emotional or neutral story, specifically with respect to the retention of gist and peripheral detail. Healthy naturally cycling women and men viewed a brief, narrated, three-phase story containing neutral or emotionally arousing elements. One week later, participants received a surprise free recall test for story elements. The results indicate that naturally cycling women in the luteal (high hormone) phase of the menstrual cycle at encoding show enhanced memory for peripheral details, but not gist, when in the emotional compared with neutral stories ($p < .05$). In contrast, naturally cycling women in the follicular (low hormone) phase of the menstrual cycle at encoding did not show enhanced memory for gist or peripheral details in the emotional compared with neutral stories. Men show enhanced memory for gist, but not peripheral details, in the emotional versus neutral stories ($p < .05$). In addition, these sex influences on memory cannot be attributed to differences in attention or arousal; luteal women, follicular women, and men performed similarly on measures of attention (fixation time percentage) and arousal (pupil diameter changes) during the most arousing phase of the emotional story. These findings suggest that sex and menstrual cycle phase at encoding influence long term memory for different types of emotional information.

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1. Introduction

It is well established that emotionally arousing events tend to be better remembered than neutral events (Bradley, Greenwald, Perry, & Lang, 1992; Cahill & McGaugh, 1995; Cahill & McGaugh, 1998; McGaugh, 2000). Substantial evidence since the 1970s from both animal and human subject literature indicates that adrenal hormones (i.e. catecholamines and glucocorticoids) released during or after emotionally arousing events strongly influence the consolidation of long term memories (McGaugh & Roozendaal, 2002). These adrenal hormones interact to enhance memory consolidation for emotional experiences via actions involving the amygdala, a brain region believed to be critical for the modulation of memory consolidation (McGaugh, Cahill, & Roozendaal, 1996; Roozendaal, Cahill, & McGaugh, 1996b; Roozendaal, McEwen, & Chattarji, 2009).

Research also suggests that emotional memory is influenced by sex hormones, particularly ovarian hormones (e.g., Andreano, Arjomandi, & Cahill, 2008). Previous research examined whether sex differences in emotional memory could be influenced by menstrual cycle-related changes in sex hormone levels. Some studies have explored how sex and stress hormones interact to influence memory performance (Andreano et al., 2008), whereas other recent studies suggested that progesterone levels can influence emotional memory, even in the absence of a post-training stressor. Ertman, Andreano, and Cahill (2011) examined whether naturally cycling women in hormonally distinct phases of the menstrual cycle differentially recalled emotional images one week after encoding. Enhanced recall of emotional images was only observed in women in the luteal (high hormone) phase of the menstrual cycle; furthermore, regression analyses revealed a positive correlation between memory and progesterone levels at encoding (Ertman et al., 2011).

Human imaging studies have provided additional evidence that sex hormones influence memory. van Wingen et al. (2008) demonstrated that high levels of synthetic progesterone increased amygdala responses to emotional images relative to neutral images. These findings were further supported by a study examining the influence of sex hormones on amygdala and hippocampal activity, in which women in the mid-luteal phase exhibited an enhanced response to emotional images in the hippocampus and amygdala as

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compared to women in the early follicular phase (Andreano & Cahill, 2010). These findings suggest that sex hormones modulate the responsiveness of a key node in the brain's emotional memory circuitry – the amygdala.

Additional imaging studies have explored sex influences on the amygdala during emotionally arousing tasks, irrespective of sex and stress hormone levels. For example, several studies have reported a sex-related hemispheric lateralization of amygdala activity in relation to long-term emotional memory (e.g., Andreano & Cahill, 2009). Cahill et al. (2001) found that activity of the right hemisphere amygdala in men viewing emotional stimuli was significantly correlated with long-term recall of the stimuli; there was no relationship with the left hemisphere amygdala. However, activity in the left hemisphere, but not the right, amygdala in women viewing emotional stimuli was significantly related to long-term recall. This relationship was replicated in different paradigms investigating sex influences on emotional memory (Cahill, Uncapher, Kilpatrick, Alkire, & Turner, 2004; Canli, Desmond, Zhao, & Gabrieli, 2002; Mackiewicsz, Sarinopoulos, Cleven, & Nitschke, 2006). A subsequent study by Kilpatrick, Zald, Pardo, and Cahill (2006) demonstrated that a sex-related hemispheric lateralization of amygdala function exists even when men and women are resting, a finding strongly confirmed by Savic and Lindstrom (2008).

Several studies expanded upon this sex-related hemisphere laterality of amygdala function to examine sex influences on emotional information processing. There is evidence for a hemispheric specialization in the processing of global (gist) versus local (detail) information from an event; the right hemisphere is associated with the processing of gist whereas the left hemisphere is associated with detail processing (Fink, Marshall, Halligan, & Dolan, 1999; Fink et al., 1996). Cahill and van Stegeren (2003) integrated these hemispheric laterality findings to test the hypothesis that a β-adrenergic blocker, by presumably impairing the amygdala's modulatory effects on memory, should impair memory for gist of an emotionally arousing story in men (by impairing right amygdala/hemisphere functions) but memory for details of the same story in women (by impairing left amygdala/hemisphere functions). Results from the study supported the hypothesis.

Potential sex influences on memory for central information (gist) and detail from an emotional event have been explored in several studies (Cahill, Gorski, Belcher, & Huynh, 2004; Cahill & van Stegeren, 2003; Seidlitz & Diener, 1998). Recently, we reported that women taking hormonal contraception had enhanced memory for the gist, but not for the details, of an emotional story, whereas naturally cycling women had enhanced memory for the details, but not gist (Nielsen, Ertman, Lakhani, & Cahill, 2011). These findings suggest that sex hormones influence the retention of gist versus detail from an emotional event. To date, however, potential effects of menstrual cycle at encoding on retention of gist and detail remain unexamined.

The present study investigated memory for gist and detail of an emotional story in naturally cycling women as well as in men, specifically focusing on the influence of menstrual-cycle related sex hormone fluctuations at encoding. Women on hormonal contraception were not included in this study since the focus was on the relationship between emotional memory for gist and detail and endogenous sex hormones.

Based on our previous study (Nielsen et al., 2011), we predicted that naturally cycling women in the *high sex hormone*, or luteal, phase of the menstrual cycle would exhibit enhanced memory for the total details of an emotional story as well as details from the most emotional phase, "phase 2;" more specifically, based on previous work with sex hormones and emotional memory, we predicted that higher levels of progesterone would relate to enhanced retention of detail memory. We also hypothesized that both women in the follicular, or *low sex hormone*, phase of the menstrual cycle and men would not show enhanced memory for emotional story details (Cahill & van Stegeren, 2003; Nielsen et al., 2011).

2. Materials and methods

2.1. Participants

Eighty-nine naturally cycling (NC) female and 43 male undergraduate students from the University of California, Irvine between the ages of 18–33 participated in this study, which was approved by the university's Institutional Review Board. The subjects received course credit for their participation in the study. Participants were asked to refrain from alcohol, caffeine, and cardiovascular exercise for 24 h prior to each experimental session to control for outside influences that could affect baseline stress hormone levels. To avoid contamination of salivary samples, participants were asked to fast 1 h prior to each experimental session as well as refrain from brushing teeth within the hour before their appointment.

Of the participants, 20 naturally cycling women were excluded due to irregular menstrual cycles (i.e. inconsistent menstruation patterns, 13), failure to return for the second experimental session (5), progesterone levels three standard deviations above the mean (1), or nursing (1). Ten naturally cycling women were also excluded for having progesterone and 17β-estradiol levels well outside of the expected hormone ranges (6 Luteal, 4 Follicular). Four men were excluded based on their failure to return for the second experimental session (2), having neutral recall scores more than three standard deviations above the mean (1), or taking more than three prescription medications (1). Of the participants included in the final analyses, six participants reported using one or two prescription medications (3 men, 1 follicular woman, 2 luteal women). The final analyses included data from 59 NC women and 39 men. The NC women were further divided into a "follicular" group (1–14 days from the start of menstruation) or a "luteal" group (15–30 days from the start of menstruation) (Azziz et al., 1999; De Bondt et al., 2013; Franklin et al., 2008; Sakaki & Mather, 2012). We used a forward day count from the first day of menstruation to determine menstrual cycle position, and all women included in these analyses had progesterone and 17β-estradiol levels within the expected hormone ranges (Salimetrics, State College, PA). Of the NC women, 28 women were in the follicular phase of the menstrual cycle, and 31 women reported being in the luteal phase at the time of encoding.

2.2. Procedures

All experimental sessions were conducted between the hours of 12:00 and 18:00 to control for the effects of circadian rhythm on salivary alpha amylase and cortisol levels. During the first experimental session, participants filled out a screening questionnaire and three cognitive assessments including the BEM Sex Roles Inventory (BEM; Bem, 1981), the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988), and the Mehrabian test (Mehrabian, 1994). The BEM was implemented to assess masculine and feminine influences/traits within each individual participant, whereas the PANAS was given to measure the participants' affect at the time of testing. The Mehrabian was implemented to assess levels of trait anxiety (Mehrabian, 1994). These questionnaires were implemented to standardize the activities between each participant's arrival and their baseline sample; scores from these questionnaires were not analyzed with respect to memory.

Fifteen minutes after their arrival, participants provided a 1-mL saliva sample using the "passive drool" collection method. Following the baseline saliva sample, participants underwent a 5-pt.