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The effect of sex and menstrual phase on memory formation during a nap

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ABSTRACT

Memory formation can be influenced by sleep and sex hormones in both men and women, and by the menstrual cycle in women. Though many studies have shown that sleep benefits the consolidation of memories, it is not clear whether this effect differs between men and women in general or according to menstrual phase in women. The present study investigated the effect of sex and menstrual cycle on memory consolidation of face-name associations (FNA) following a daytime nap. Recognition memory was tested using a face-name paired associates task with a polysomnographic nap between morning and evening testing. Seventeen healthy women (age: 20.75 (1.98) years) were studied at two time points of their menstrual cycles, defined from self-report and separated by 2 weeks (perimenses: −5 days to +6 days from the start of menses, and non-perimenses: outside of the perimenses phase), and compared with eighteen healthy men (age: 22.01 (2.91) years). Regardless of menstrual phase, women had better pre-nap performance than men. Further, menstrual phase affected post-nap memory consolidation, with women showing greater forgetting in their perimenses phase compared with their non-perimenses phase and men. Interestingly, post-nap performance correlated with electrophysiological events during sleep (slow oscillations, spindles, and temporal coupling between the two), however, these correlations differed according to menstrual phase and sex. Men's performance improvement was associated with the temporal coupling of spindles and slow oscillations (i.e., spindle/SO coincidence) as well as spindles. Women, however, showed an association with slow oscillations during non-perimenses, whereas when they were in their perimenses phase of their cycle, women appeared to show an association only with sleep spindle events for consolidation. These findings add to the growing literature demonstrating sex and menstrual phase effects on memory formation during sleep.

1. Introduction

Men and women differ across a range of laboratory tested cognitive domains including memory, visual and acoustic perception, navigation, and audition (Astur, Ortiz, & Sutherland, 1998; Canli, Desmond, Zhao, & Gabrieli, 2002; Giret, Menardy, & Del Negro, 2015; Lewin, Wolgers, & Herlitz, 2001; McDevitt, Rokem, Silver, & Mednick, 2014; Murai, Saito, Masuda, & Itoh, 1998; reviewed in Cahill, 2006). For example, memory performance that relies on the hippocampus, such as word and picture recall and recognition, story recall and name recognition, is better in women than men (reviewed in Herlitz, Airaksinen, & Nordström, 1999). In contrast, men outperform women on visual-spatial tasks and certain mathematical abilities (Halpern, 1992; Lewin et al., 2001). Furthermore, women and men use different strategies in tasks that involve mental rotation, (e.g. spatial navigation), where men rely more on Euclidean directions, while women focus on memory for landmarks (Dabbs, Chang, Strong, & Milun, 1998; Lawton, 1996). Although complete mechanistic explanations of these sex-based differences have not been identified, prior work suggests that sex hormones play an important role (Brinton, 2009; Mizuno & Giese, 2010).

In women, sex hormones fluctuate across a monthly cycle (Rousseau, 1998). Along with several other hormones (Baker & Driver, 2007), estrogen and progesterone cycle through two main phases across a typical 28-day menstrual cycle in women (Fig. 1A). The first half of the cycle (i.e., follicular phase; days 1–14) begins with menses (day 1–6) with low levels of estrogen and progesterone, followed by a rise in estrogen that peaks on days 12–14, just before ovulation. The second part of the cycle (i.e., luteal phase; days 15–28) is characterized by an increase in progesterone and estrogen, as they are released from the corpus luteum. If there is no implantation, hormone levels decline

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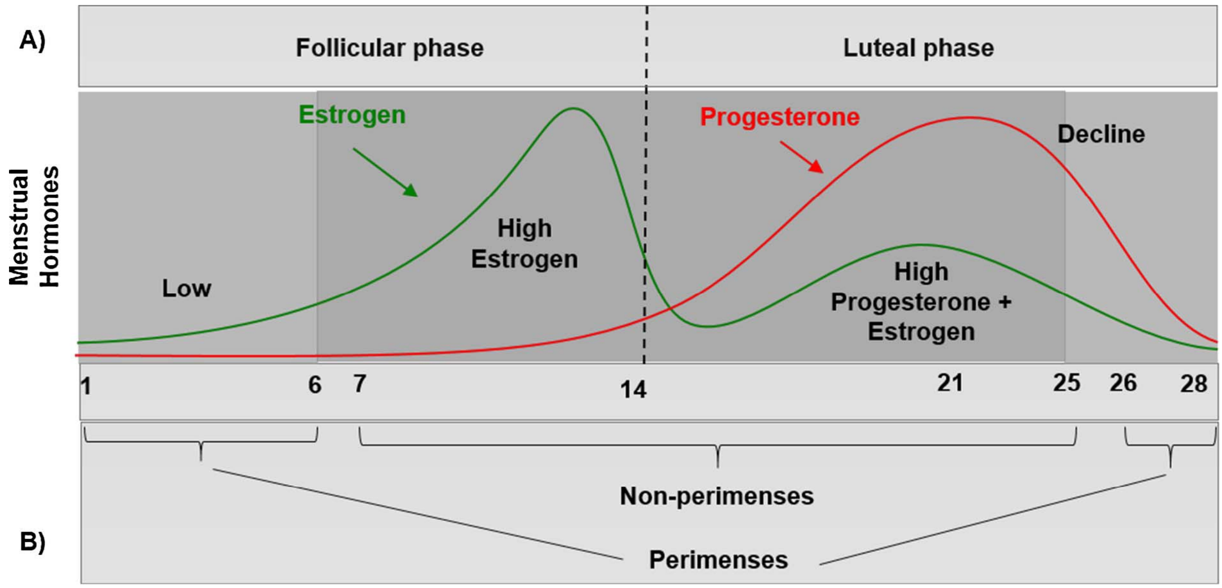

Fig. 1. The panel demonstrates fluctuations in hormones across the menstrual cycle. (A) Shows the follicular and luteal phases and (B) shows categorization in the current study defined from self-report.

during the last week of the luteal phase and menstruation occurs.

These fluctuations in sex hormones may influence cognitive performance across a woman's cycle. Studies have shown cognitive differences between women in the early follicular phase when hormones are low (i.e., menses) compared with other phases of the menstrual cycle (Hampson, 1990a,b; Maki, Rich, & Rosenbaum, 2002). For example, one study found that spatial abilities were increased in women during the early follicular phase, whereas fine motor skills and verbal fluency were enhanced during the mid-luteal phase (Hampson, 1990a,b). Similarly, another study reported enhanced articulatory and fine motor skills, but poorer spatial ability, during the late follicular phase (days 13–15, high estrogen) compared to the early follicular phase (days 3–5, low estrogen and progesterone) (Hampson, 1990a,b). These findings suggest that female cognition may be dynamically modulated by sex hormone levels. Although sex hormones could directly impact cognitive processing, it is also possible that hormones interact with other brain functions that mediate the relation between sex hormones and cognition, especially the interaction between sleep and memory consolidation (Genzel et al., 2012).

In addition to sex and sex hormones, sleep and sleep-related neural activity influence cognitive performance. Studies have shown that sleep supports transforming new experiences into long-term memories (i.e., consolidation) (Diekelmann & Born, 2010). For declarative memory, i.e., explicit memory for events and facts, consolidation is demonstrated by decreased forgetting of information after a period of sleep, compared to an equivalent amount of time awake (Mednick, Cai, Shuman, Anagnostaras, & Wixted, 2011). Furthermore, several pieces of evidence converge to suggest that improved memory retention is directly related to specific events during sleep including sleep spindles (bursts of fast, 12–15 Hz thalamic activity) and slow oscillations (SO, high voltage up and down states < 1 Hz that reflect periods of neuronal spiking and neuronal silence, respectively). Specifically, in rats hippocampal ripples were found to occur in temporal proximity to cortical sleep spindles, suggesting an information transfer between the hippocampus and neocortex, which is supposed to underlie the consolidation of declarative memories during sleep (Girardeau, Benchenane, Wiener, Buzsáki, & Zugaro, 2009; Ji & Wilson, 2007; Maingret, Girardeau, Todorova, Goutierre, & Zugaro, 2016). In particular, spindles and SOs have independent features that correlate with improvements in declarative memory formation (Clemens, Fabo, & Halasz, 2005; Gais, Mölle, Helms, & Born, 2002; Mednick et al., 2013; Oyanedel et al., 2014; Schabus et al., 2004). Interestingly, experimentally increasing spindles (Mednick et al., 2013) and SOs (Binder et al., 2014; Marshall, Helgadóttir, Mölle, & Born, 2006) improves declarative memory performance, suggesting a causal role for these sleep features for memory consolidation. Further, the coincidence or coupling of SOs and spindle events may be a key mechanism of memory consolidation during sleep (Mölle, Bergmann, Marshall, & Born, 2011; Staresina et al., 2015), with several studies suggesting spindles that occur during the SO up-state are optimal (Gais & Born, 2004; Mölle, Eschenko, Gais, Sara, & Born, 2009). In line with these studies, Niknazar, Krishnan, Bazhenov, and Mednick (2015) showed pharmacologically boosting the temporal consistency of SO/spindle events during Stage 2 sleep benefitted verbal memory. Together, these findings suggest that declarative memory consolidation benefits from coupling of neural oscillations associated with thalamically-generated spindles and cortically-generated SOs. However, few studies have considered sex or menstrual phase effects on sleep-related memory consolidation.

McDevitt et al. (2014) examined the effect of sleep on a non-declarative, visual learning task in men and women. Although no baseline differences were found, post-sleep performance revealed differences between men and women, with men showing learning that was highly specific to the trained visual target, whereas learning in women transferred to an untrained target condition. Genzel et al. (2012, 2015) investigated the interaction between sex hormone levels and sleep-related memory consolidation in women and found that, women in their mid-luteal phase (i.e. third week of the cycle) and men performed better compared to women during menses, on a declarative and procedural motor memory task after a nap. Estrogen correlated with declarative and progesterone correlated with motor performance improvement (Genzel et al., 2012). In addition, sleep spindles were related to memory enhancement, but only for women during their luteal phase and men, suggesting that sex hormones and phase in menstrual cycle in women may moderate the relation between sleep features and sleep-dependent memory consolidation.

The present study aimed to investigate further the influence of sex and menstrual phase on sleep-related memory consolidation using a nap paradigm, and considered possible links between memory performance and SOs and spindle dynamics. Women were tested at two time points in their menstrual cycles, two weeks apart. One visit occurred in the perimenses phase, based on self-report (between 5 days before and 6 days after menses onset) and the other visit occurred outside of this