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Sustained attention is favored by progesterone during early luteal phase and visuo-spatial memory by estrogens during ovulatory phase in young women

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Summary Studies examining the influence of the menstrual cycle on cognitive function have been highly contradictory. The maintenance of attention is key to successful information processing, however how it co-vary with other cognitive functions and mood in function of phases of the menstrual cycle is not well know. Therefore, neuropsychological performance of nine healthy women with regular menstrual cycles was assessed during ovulation (OVU), early luteal (EL), late luteal (LL) and menstrual (MEN) phases. Neuropsychological test scores of sustained attention, executive functions, manual coordination, visuo-spatial memory, verbal fluency, spatial ability, anxiety and depression were obtained and submitted to a principal components analysis (PCA).

Five eigenvectors that accounted the 68.31% of the total variance were identified. Performance of the sustained attention was grouped in an independent eigenvector (component 1), and the scores on verbal fluency and visuo-spatial memory were grouped together in an eigenvector (component 5), which explained 17.69% and 12.03% of the total variance, respectively. The component 1 ($p < 0.034$) and the component 5 ($p < 0.003$) showed significant variations during the menstrual cycle. Sustained attention showed an increase in the EL phase, when the progesterone is high. Visuo-spatial memory was increased, while that verbal fluency was decreased during the OVU phase, when the estrogens levels are high. These results indicate that sustained attention is favored by early luteal phase progesterone and do not covaried with any other neuropsychological variables studied. The influence of the estrogens on visuo-spatial memory was corroborated, and covaried inversely with verbal fluency.

1. Introduction

Fluctuation of the ovarian hormones might influence some aspects of the cognitive functions in women (Richardson, 1992; McEwen et al., 2002). Cognition refers to the human information processing, and includes functions such as

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attention, memory, learning, language processing, problem solving, abstract reasoning, planning, inference, and visual processes (Kolb and Whishaw, 1990). Changes in scores on neuropsychological tasks have been used to assess possible influence of ovarian hormone secretion during different menstrual cycle phases. This approach has demonstrated that some impairment in cognitive performance is a characteristic feature of the premenstrual period. Performance on motor coordination and verbal fluency show improvement during the periovulatory or early luteal (EL) phases, when estrogen and progesterone levels are high, but performance on spatial skills tasks is worse. During menstruation, when estrogen and progesterone levels are low, performance on spatial skills tasks improve and verbal and manual skills decline (Broverman et al., 1981; Hampson, 1990; Phillips and Silverman, 1997; Hausmann et al., 2000). Cyclic variations in the verbal memory and spatial memory (Phillips and Sherwin, 1992; Postma et al., 1999) have also been reported, with better performance during periods in which estrogen is high. Performance on frontal lobe tasks is better in the early luteal phase, when the progesterone level is high (Solís-Ortiz et al., 2004a), and high levels of estradiol and progesterone in the midluteal phase increase the attentional blink (Hollander et al., 2005). However, with the exception of abilities associated with gender differences (Hampson and Kimura, 1992), contradictory results have been reported for the other domains of cognitive function tested. Some of these problems may be related to methodological inconsistencies which are common in the majority of these studies (Sommer, 1992; Epting and Overman, 1998; Sherwin, 2003). The inconsistencies have been attributed in part to an inadequate capacity on the part of the research designs used, lack of control for anxiety and depressive symptoms that can negatively impact scores on neuropsychological tests, and the tests employed to assess cognition that inappropriately have been used may be insensitive to the possible influence of the menstrual cycle upon cognitive performance (Richardson, 1992; Sherwin, 2003).

Several studies made in human and animal models have suggested that ovarian steroids have diverse effects on brain function, in particular the hippocampus and prefrontal cortex (McEwen and Woolley, 1994; McEwen et al., 1997; Berman et al., 1997), brain regions involve in memory processes. Cognitive data from human using neuropsychological tests that measure prefrontal functions, have showed that young women performed better on frontal lobe task in the early luteal phase of menstrual cycle (Solís-Ortiz et al., 2004a). The performance on Trailmaking Test, Trail B was better during the follicular phase than during the luteal phase of the menstrual cycle (Kennan et al., 1992). Estrogen therapy administrated to perimenopausal or postmenopausal women selectively reduced errors of perseveration in the California Verbal Learning Test, a test that examines executive functions, mediated by the frontal cortex (Kennan et al., 2001; Joffe et al., 2006).

Behavioral data from rodents using tasks that involve hippocampal and prefrontal cortex functions have showed that estrogens and progestins enhance spatial learning of intact rats during proestrus or estrus and in ovariectomized rats administered estrogens, progesterone, or estrogens and progesterone in the object placement task (Frye et al., 2007). Rats in proestrus performed better than diestrus or estrus in the object recognition task associated with increases in serum of estrogens and progestins (Walf et al., 2006). It was also found that estrogens levels in the hippocampus and 5α-pregnan-3α-ol-20-one in the hippocampus and cortex were positively correlated with the performance in the object recognition task (Walf et al., 2006). Moreover, estrogen administration to ovariectomized female rats and young or aged mice also enhanced performance in a water escape working memory task (O'Neal et al., 1996) and in T-maze task (Heikkinen et al., 2004), tasks that are also mediated by the prefrontal cortex.

Progestins have also important effects and on EEG activity in humans (Friess et al., 1997), as well as in rats (Corsi-Cabrera et al., 2000; Fernandez-Guasti et al., 2003) and may influence motivation, reward, conditioning and stress in rats (Frye, 2007). One study found that ovariectomized rats treated with progesterone, dihydroprogesterone and 5α-pregnan-3α-ol-20-one performed better in the Y-maze, inhibitory avoidance and object recognition tasks (Frye and Lacey, 2000).

Most studies have made a comparison between test scores and phases of the menstrual cycle as a method to evaluate the neuropsychological function and its possible relation to sex hormones during the different phases of the menstrual cycle in women. In some cases, this method has provided of relevant information but in other cases the findings reported are discrepant. An analysis of the structure and the interrelationships of neuropsychological variables may help to better understand the effect of the menstrual cycle on cognitive performance. PCA allows for grouping variables that co-vary together separating them from others that are orthogonally independent and they are not correlated; it is therefore a useful statistical method to reduce variables and to investigate relationships between the new variables (Flury and Reidwyl, 1988). Those variables that get gathered in the same eigenvector are reflecting some common influence, while they are independent from those gathered in a different eigenvector. PCA, therefore, can be used to investigate how neuropsychological variables are grouped depending of the menstrual cycle phases.

The aim of the present investigation was to explore, by means of PCA, which neuropsychological test scores vary together or separately in a function of the phases of the menstrual cycle. It was hypothesized that the neuropsychological test scores extracted by PCA as gathered in the same eigenvector would reflect a common influence and those which are independent gather in several eigenvectors and this could better explain the neuropsychological changes in young women during the different menstrual cycle phases. With this purpose, scores on neuropsychological tests measuring sustained attention, executive functions, manual coordination, visuo-spatial memory, verbal fluency and spatial ability obtained from four phases of the menstrual cycle were submitted to PCA. Because variations on mood are also characteristic of the menstrual cycle (Bäckström et al., 1983; Solís-Ortiz and Corsi-Cabrera, 2002), and can influence cognitive performance, scores of anxiety and depression were also obtained in four phases of the menstrual cycle and were included in the PCA.