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Research Report

Menstrual cycle variations in the BOLD-response to a number bisection task: Implications for research on sex differences

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ARTICLE INFO

Article history:
Accepted 24 August 2011
Available online 31 August 2011

Keywords:
Sex differences
Menstrual cycle
Number processing
Angular gyrus
Default mode network
Number bisection task

ABSTRACT

Numerical processing involves either number magnitude processing, which has been related to spatial abilities and relies on superior parietal regions, or arithmetic fact retrieval, which has been related to verbal abilities and involves the inferior parietal lobule. Since men score better in spatial and women in verbal tasks, we assume that women have advantages in fact retrieval, while men have benefits in number magnitude processing. According to findings on menstrual cycle variations in spatial and verbal abilities, fact retrieval should improve during the luteal phase and magnitude processing during the follicular phase. To dissociate sex- and menstrual cycle-dependent effects on fact retrieval and number magnitude processing, we applied a number bisection task in 15 men and 15 naturally cycling women. Multiplicative items (e.g. 12_15_18) are part of a multiplication series and can be solved by fact retrieval, while non-multiplicative items (e.g. 11_14_17) are not part of a multiplication series and require number magnitude processing. In men and women in their luteal phase, error rates were higher and deactivation of the medial prefrontal cortex and the bilateral inferior parietal lobules was stronger for non-multiplicative compared to multiplicative items (*positive multiplicativity effect*), while in the follicular phase women showed higher error rates and stronger deactivation in multiplicative compared to non-multiplicative items (*negative multiplicativity effect*). Thus, number magnitude processing improves, while arithmetic fact retrieval impairs during the follicular phase. While a female superiority in arithmetic fact retrieval could not be confirmed, we observed that sex differences are significantly modulated by menstrual cycle phase.

1. Introduction

Cognitive differences between men and women are debated since decades. Most researchers agree that, in general, women are superior in verbal tasks, whereas men are superior in spatial tasks (for reviews see Andreano and Cahill, 2009; Wallentin, 2009).

However in women, cognitive abilities, BOLD-response to cognitive tasks, and brain structure predictably vary with the menstrual cycle (e.g. Pletzer et al., 2010; Schoning et al., 2007).

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doi:10.1016/j.brainres.2011.08.058

In particular, spatial and verbal abilities and the associated brain activation patterns are cycle-dependent. Women score lower on mental rotation and other spatial tasks, when estrogen plasma levels are high, like in the late follicular (2–3 days pre-ovulation) and subsequent luteal phase compared to the menstrual and early follicular phase, when estrogen and progesterone plasma levels are low (Hampson, 1990; Hausmann et al., 2000; McCormick and Teillon, 2001; Schoning et al., 2007; Otero Dadín et al., 2009; but see Rosenberg and Park, 2002). These differences are accompanied by stronger parietal and frontal activation in response to spatial tasks during phases of high estrogen (Dietrich et al., 2001; Schoning et al., 2007; Weis et al., 2011). On the contrary, verbal abilities are increased during high estrogen phases compared to phases of low estrogen levels (Hampson, 1990; Rosenberg and Park, 2002; Otero Dadín et al., 2009; but see Mordecai et al., 2008). BOLD-response to verbal tasks is stronger in left and medial prefrontal regions when estrogen levels are high compared to phases of low estrogen (Fernández et al., 2003; Craig et al., 2008; Konrad et al., 2008; but see Gizewski et al., 2006). Recent studies on functional connectivity in spatial and verbal tasks reveal that these estrogen-related changes in brain activation may be attributable to changes in interhemispheric inhibition throughout the menstrual cycle (Weis et al., 2008, 2011). Interestingly, these differences in brain activity are present even in the absence of behavioral differences.

Consequently, the magnitude of sex differences in behavioral and neuronal correlates of spatial and verbal cognition depends on the menstrual cycle phase of women at the time of comparison. Shortly before ovulation and during the luteal phase, sex differences are most pronounced. During the menstrual phase, sex differences in cognitive tasks may even vanish (e.g. Dietrich et al., 2001; McCormick and Teillon, 2001). Thus, neglecting menstrual cycle phase when comparing cognitive abilities between the sexes may lead to an over- or underestimation of sex-dependent effects.

Sex-dependent differences in mathematical achievement tests and their interpretation have fuelled intense discussions on differences in mathematical capacities between the sexes. Whereas some authors describe a male superiority in mathematical tasks (Benbow, 1988; Casey et al., 1995; Geary, 1996; Rosselli et al., 2009; Sappington and Topolski, 2005), others do not observe sex differences or state that they may be restricted to complex tasks (Hyde, 2005; Hyde et al., 1990; Raymond and Benbow, 1986; Spelke, 2005). General mathematical achievement tests include multiplications, divisions, additions, subtractions, and small text examples. Accordingly, some items may require fact retrieval from a mental multiplication table, other items may require magnitude processing on a mental number line, and others abstract reasoning. In the number processing literature the distinction of a nonverbal quantity system, subserving magnitude processing, and a language-mediated memory system, subserving the retrieval of arithmetic facts, is widely accepted (Dehaene et al., 1999; Dehaene et al., 2003). The lack of distinction between fact retrieval (= verbal) and magnitude (= spatial) processing strategies on the one hand and ignoring the menstrual cycle phase on the other hand may have contributed to the inconsistent reports on sex differences in mathematical performance (Benbow, 1988; Casey et al., 1995; Geary, 1996; Hyde, 2005; Hyde et al., 1990; Raymond and Benbow, 1986; Rosselli et al., 2009; Sappington and Topolski, 2005; Spelke, 2005).

Although numerical abilities are important in everyday life and may be a predictor in academic career, menstrual cycle modulation of number processing has so far rarely been investigated. If number magnitude processing relates to spatial processing (Hubbard et al., 2005) and the retrieval of arithmetic facts to verbal processing (Dehaene et al., 2003), number magnitude processing should be improved during the follicular phase and impaired during the luteal phase, while arithmetic fact retrieval should be impaired during the follicular phase and improved during the luteal phase.

Neurocognitive studies confirm that different arithmetic tasks, like multiplication or subtraction, involve different brain areas to a different degree. Brain lesions and neuroimaging studies reveal that number magnitude and spatial processing are represented in similar parietal circuits overlapping around the intraparietal sulcus (IPS) bilaterally (see Hubbard et al., 2005 for a review). The left angular gyrus (AG), a part of the default mode network (DMN; Raichle et al., 2001; Laird et al., 2009), has been ascribed a key role in arithmetic fact retrieval (Dehaene et al., 2003). Tasks requiring magnitude processing (e.g. subtraction, untrained problems) lead to stronger activation of the IPS, but stronger deactivation of the AG and connected regions of the DMN, like the medial prefrontal cortex (mPFC), compared to tasks that can be solved via fact retrieval (e.g. multiplication, trained problems) (Chochon et al., 1999; Lee, 2000; Grabner et al., 2009; Delazer et al., 2003, 2004; Ischebeck et al., 2006, 2007; see Dehaene et al., 2003 for a review).

A recent neuroimaging study demonstrated that, despite the lack of performance differences, men show a stronger BOLD-response compared to women in the right IPS, AG, lingual and parahippocampal gyri during mental calculation contrasted to an identification task (Keller and Menon, 2009). Thereby the AG was activated in men but deactivated in women. In this study, the authors did not distinguish between different operations and processing strategies. They used three operand equations (e.g. $6+3-2=7$), involving single-digit addition, which is likely solved by fact retrieval, and subtraction, which relies on number magnitude processing. Furthermore, they did not control for the menstrual cycle phase of women.

To address the question, whether number processing is cycle dependent and whether number magnitudes and arithmetic facts are differentially affected, we chose a number bisection task (Nuerk et al., 2002), which combines number magnitude processing and verbal number processing. Participants have to decide, whether the middle of three numbers is the correct mean of the outer two numbers. If the three numbers are part of a multiplication series (multiplicative items; e.g. 12_15_18) the task can be solved on the basis of fact retrieval (= verbal number processing) from a mental multiplication table. If the three numbers are not part of a multiplication series (non-multiplicative items; e.g. 11_14_17), participants have to rely on magnitude processing along a mental number line. Therefore, if the use of arithmetic fact retrieval for multiplicative items coincides with an advantage in either fact retrieval or magnitude processing, we expect a significant multiplicativity effect (non-multiplicative–multiplicative