



Language lateralization and cognitive control across the menstrual cycle assessed with a dichotic-listening paradigm

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Summary Lateralization has been shown to vary across the menstrual cycle, however, the underlying mechanisms are not fully understood, and results are inconsistent. Additionally, it has been suggested that estradiol enhances cognitive control. By modulating attention in a consonant-vowel dichotic listening test, the current study aims to investigate the effects of cycle-related changes on language lateralization (non-forced condition), as well as the effects of estradiol-modulated cognitive control (forced left condition) on the ear advantage. Fifteen women and fifteen men tested three times on the dichotic listening test, women once in menstrual, follicular, and luteal phase (verified by hormone assays). Whereas the results from the non-forced and forced-right condition remained stable, results from the forced left condition changed across the cycle, where women in the follicular phase compared to both menstrual and luteal phases showed a stronger left ear advantage, i.e. better cognitive control performance. The increase in performance from menstrual to follicular phase correlated negatively with increase in estradiol levels, indicating a shift from a stimulus-driven right ear advantage (indicating a left hemispheric asymmetry for language) when estradiol levels were low toward a cognitively controlled left ear advantage when estradiol levels were high. This finding strongly suggests an active role of estradiol on cognitive control. The study further suggests that the degree of cognitive control demands of a given task is important to consider when investigating lateralization across the menstrual cycle.

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1. Introduction

Fluctuating levels of gonadal steroid hormones across the menstrual cycle have been suggested to induce a modulating effect on neuronal activity. Behavioral studies in normally cycling women addressing the effect of gonadal steroid hormones on brain functions fall in either of two categories: Studies examining the hormonal effect on cognitive functioning per se, or on the underlying functional cerebral organization of these cognitive functions, e.g. lateralization. Positive effects of gonadal steroid hormones on cognition were mainly found in research that focused on postmenopausal women and hormone therapy which involves estrogen either alone or in combination with gestagen. Although contradictions exist, some of these studies report a performance enhancing effect of hormone therapy on tasks assessing verbal memory (Wolf and Kirschbaum, 2002), working memory (Keenan et al., 2001), cognitive inhibition (Marinho et al., 2008; Wolf and Kirschbaum, 2002) and other executive functions (Keenan et al., 2001). Further, an influence of estrogen on working memory in normally cycling women has been shown to be especially strong when high level of cognitive control is required (Jacobs and D'Esposito, 2011). In line with this, Keenan et al. (2001) suggested that the observed effect of estrogen on cognition is caused by its influence in particular on the prefrontal cortex (PFC) and that this can account for the menstrual cycle effects in various types of tasks.

One basic organization principal of the human cortex is the hemispheric asymmetry or lateralization of cognitive functions, hereby defined as the differential involvement of the left and right hemisphere when performing a certain cognitive task. A widely accepted example of lateralization is the processing of language in the left hemisphere. Gonadal steroid hormones have been suggested to influence this lateralization with respect to both its overall organization, primarily studied with testosterone (Geschwind and Galaburda, 1985), and its activation effect, especially by ovarian hormones. It has been suggested that in particular estradiol and progesterone are influencing the degree of lateralization, with a reduced lateralization in cycle phases with high levels of estradiol and/or progesterone, i.e. the follicular and luteal phase, as compared to the menstrual phase where level of both estradiol and progesterone is low (Hausmann, 2005; Hausmann et al., 2002; Hausmann and Güntürkün, 2000; Sanders and Wenmoth, 1998). However, the results across studies are inconsistent, and some in fact report reversed results, with less pronounced lateralization in the menstrual phase (Cowell et al., 2011; Hampson, 1990a,b; Sanders and Wenmoth, 1998; Wadnerkar et al., 2008), or even that no cycle effect was revealed (Compton et al., 2004). However, most of the studies reporting a reduced lateralization in the menstrual phase are studies on consonant-vowel dichotic listening (Cowell et al., 2011; Sanders and Wenmoth, 1998; Wadnerkar et al., 2008), while the majority of studies reporting reduced lateralization in high hormonal phases have used visual half field tasks (Hausmann, 2005; Hausmann and Güntürkün, 2000). Likewise, one study suggested the task modality to interact with lateralization across the cycle. Thus, left hemispheric language lateralization, investigated using dichotic listening with speech sounds (e.g. /pee/, /bee/), was reduced in the menstrual compared to luteal phase, while for music dichotic listening, right

hemispheric lateralization was reduced in the luteal phase compared to menstrual phase (Sanders and Wenmoth, 1998). Also, dichotic listening and visual half field tasks often differ in another important aspect: While the above referred dichotic listening studies measure a perceptual preference, visual half field studies typically measure differences in performance by accuracy and response times. Additional explanations for the inconsistency can be found in methodological differences across studies. First, studies differ in the selection of cycle phases as well as the methods to estimate cycle phases (e.g. day count, hormone essays, etc.). Second, studies that did use hormone assays have taken different diagnostic fluids (i.e., blood or saliva) which can largely affect the levels of biologically active steroid hormones, and thus the correlation between hormone levels and degree in lateralization.

Dichotic listening is a classical paradigm for investigating language lateralization in the auditory domain (Bryden, 1988; Kimura, 1961a,b). The Bergen version of the dichotic listening paradigm (Hugdahl, 1995; Hugdahl and Andersson, 1986) entails the presentation of two meaningless consonant-vowel syllables (e.g., /ba/, /pa/) which are administered simultaneously, one to the left and one to the right ear. The stimuli are presented with three different instructions: the non-forced (NF) condition where the participant is instructed to report the sound heard most clearly, and the forced right (FR) and forced left (FL) conditions, where the participant is asked to selectively attend to and report from the respective ears. A right-ear advantage is usually obtained in the NF condition, reflecting a left hemispheric dominance for speech perception (Kimura, 1967; Pollmann et al., 2002), since the majority of neuronal fibers from the right ear are terminating in the left temporal lobe. Further, the FR condition typically demonstrates an enhanced right-ear advantage while the FL demonstrates – in healthy and young adult participants – a reduction of the right-ear advantage or even a reverse to a left-ear advantage (Hugdahl et al., 2009). Studies that have used the dichotic listening paradigm and found less pronounced lateralization in the menstrual phase compared to the luteal phase, have applied only the NF condition (Cowell et al., 2011; Sanders and Wenmoth, 1998), or have averaged the respective right ear scores and left ear scores from all three conditions (Wadnerkar et al., 2008). However, the recent years of dichotic listening research suggest that the three conditions are qualitatively different from each other, reflecting different cognitive processes. Whereas the NF condition targets pure language lateralization, the FR condition is thought to require selective attention and the FL condition, additionally, cognitive control processes (Hugdahl, 2003; Hugdahl et al., 2009; Løberg et al., 1999; Oie and Hugdahl, 2008). In these studies, cognitive control is defined as the ability to override a stimulus-driven response in the favor of an instruction-driven one (i.e., top-down process), while selective attention is defined as directing attention toward a preferred stimulus (i.e., bottom-up process). In the FR condition, the participant is instructed to report syllables from the ear which also without attention instruction is preferably reported in the NF condition, thus being supported by the bottom-up effect. In contrast, in the FL condition the participant is asked to report the task specific non-dominant stimulus and inhibit the dominant one. This requires executive or cognitive control

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