Gender and Hormone Levels Influence Cortical Activation during Synonym Generation. An fMRI Study across Menstrual Cycle and Sex at 3 T.

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Introduction

As known from data from animal experiments, steroid hormones have an effect on brain function (1). Newer investigations with humans have shown that the level of sexual hormones and the menstrual cycle might be important factors for the activation of cortical networks (2,3). The aim of this study is to examine systematically possible gender differences and menstrual cycle effects using a difficult synonym generation task, during which behavioral gender differences had recently been reported (4).
There are just a few previous studies that have addressed gender differences in verbal fluency and other language tasks (5-8), and results remain inconsistent.

Materials and Methods

30 healthy right-handed volunteers were examined with fMRI at 3 T (Gyroscan Intera 3.0T, Philips, NL). Women were examined twice – once during menstruation and once during the mid-luteal phase of their cycle, in randomized order. Menstrual phase was determined based on anamnesis and measured serum level of sexual hormones at the day of the fMRI examination. After analysis of sexual hormone level 12 women whose menstrual cycle phase was confirmed based on hormone levels and 12 men (age, 23-54) were included in the final analysis.
Synonyms had to be generated silently for visually presented German adjectives. During each of the four synonym generation conditions, 10 words were presented with an MR compatible projection system on a screen at the rear of the scanner ("Presentation" software, Neurobehavioral Systems, Albany, CA, USA; beamer system, Covilex, Magdeburg, GER) during fMRI scans. Each word was shown for 2 s and followed by a 13 s time window for continuous generation of synonymous words. 30 s blocks of active synonym generation alternated with 30 s rest periods, a black screen with fixation cross. For the second examination of women an equivalent version of the activation paradigm was used with different stimulus material.
In addition to T1w anatomical data, functional data were acquired with a multi slice single shot EPI sequence covering the whole head (36 slices with isotropic voxels of 3.6 mm, TR = 3 s, TE = 50 ms). Data analysis was performed using SPM2 (Wellcome Dept. Cogn. Neurol, London, UK). After fMRI scanning the subjects' synonym generation ability was tested outside the scanner with subjects speaking aloud.

Results

As an initial step, with-in group statistical inferences were assessed for generating synonyms vs. baseline. The synonym-generation task activated highly significantly a network comprising predominantly the left dorsolateral and inferior frontal cortex, and the occipital cortex ($p<.001$). Contrasts between groups demonstrate that the activation of the lateral frontal area was less pronounced for women during menstruation than for men, whereas women during midluteal phase showed a pattern more similar to men. As an example the contrast in Brodmann area 46 is given in Fig. 1. However, activation differences were not accompanied by performance differences.

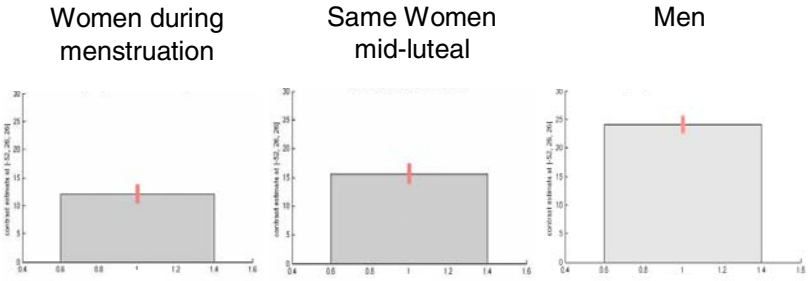

Fig. 1: Contrast estimate and 90% CI of Brodmann Area 46

Discussion

The data demonstrate that the activation of cortical networks by generation of synonyms depends significantly on sex and menstrual cycle. Sexual hormone levels of estradiol and progesterone, which fluctuate during the menstrual cycle, may modulate the cortex or neurovascular coupling. Our results are in accordance with the few previous investigations on the influence of the menstrual cycle, which also show an increased activation in mid-luteal phase (2,3). As a consequence, the effect of these factors should be taken into account in future studies with fMRI.

References

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