Sex differences in brain activation during a working memory task in adult patients with ADHD

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Introduction

Attention-deficit/hyperactivity disorder (ADHD) in adulthood is a serious and frequent psychiatric disorder with a strong neurobiological background (Bachmann et al. 2016).

Task-based fMRI, using a variety of sensory and cognitive paradigms, has demonstrated hypoactivation of a fronto-parietal network and hyperactivation of visual, dorsal attention and default mode networks (Cortese et al. 2012). Most participants in these neuroimaging studies were men and thus it remains unclear if changes in brain activation found in men with ADHD also apply to women with ADHD.

Objective

To study potential sex differences in neural function, we acquired **fMRI during a one-back working memory task** in women and men with ADHD.

Materials and Methods

Patients

Brain imaging data from **31 women** (42 ± 11 years) and **24 men** (37 ± 12 years) with adult ADHD were analyzed. The diagnosis of ADHD was established by expert psychiatrists and validated using observer-rating and self-rating scales. The study was approved by the local ethics committee.

Task

To probe working memory function, patients performed a **one-back letter task during fMRI**. With button presses of their left and right hand, patients had to indicate if the presented letter was a target (preceding letter was the same) or non-target (preceding letter was different). Patients performed 2 runs of 300 stimuli (89 target, 211 non-target; interstimulus interval: 1 s) each.

Magnetic resonance imaging

T1-weighted anatomical and T2*-weighted functional images were acquired on a Siemens Magnetom Trio at 3 T. For BOLD fMRI, gradient-echo echoplanar imaging was performed (TR: 2250 ms, TE: 30 ms, voxel size: 3x3x3 mm^3, 36 slices).

FMRI data analysis was carried out using **FSL** (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/). Pre-processing included motion correction, non-brain removal, spatial smoothing (5 mm) and highpass temporal filtering. A linear model was then fitted to the fMRI data. Six events were modeled as regressors of interest: correct and incorrect responses as well as omissions for target and non-target stimuli. Individual age was added as regressor of no interest in the group analysis.

Results

Behavioral performance during the fMRI experiment was not significantly different between women and men. Women identified 61% ± 14% of target trials correctly, men 60% ± 16% (p = 0.83). Reaction time in target-correct trials was 573 ± 73 ms in women and 546 ± 73 ms in men (p = 0.2).

Brain activation associated with target-correct trials was significantly stronger in men compared to women in following areas: **bilateral posterior cingulate gyrus, left superior parietal lobule, right frontal pole and right lentiform nucleus.** Brain areas with significantly stronger activation in women compared to men were not found.

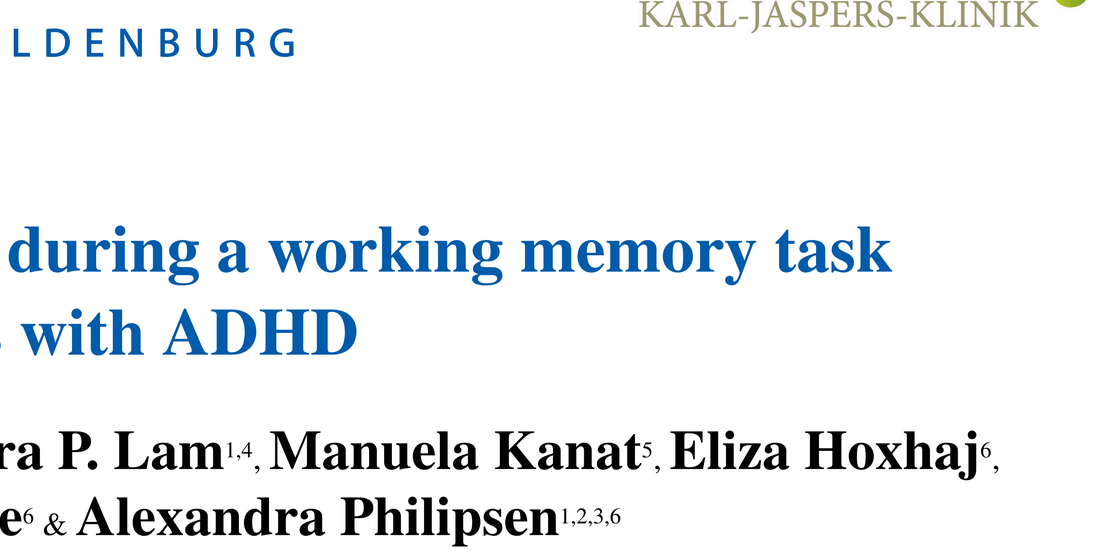

Figure 1: Brain activation during a one-back letter task, men > women.
Brain regions color-coded in red and yellow show stronger activation in men than in women. Z-statistic images are overlaid onto the mean structural T1-weighted image of the participants. The upper two rows show axial images of the brain in radiological convention (the right hemisphere is on the left). The last row shows sagittal images of the right (images 1-3) and left hemisphere (image 4).
LN: lentiform nucleus. P: putamen. FP: frontal pole. PCG: posterior cingulate gyrus. SPL: superior parietal lobule.

Conclusions

We performed a comparison of brain activation during a working memory task between men and women with ADHD. While the accuracy of responses and the latency of correct responses was not significantly different between the sexes, men showed several clusters of increased neural activation relative to women.

The largest cluster contained the **bilateral posterior cingulate gyrus**, a key component of the default mode network (Greicius et al. 2003). Activation of the posterior cingulate gyrus during the one-back task may suggest a dysfunction of the default mode network in men with ADHD. In addition, men had greater brain activation in **frontal and striatal regions** that, while subserving many different functions, are an important part of the circuits generating executive functions. Our results imply that men recruit larger neural resources than women to achieve similar behavioral performance during the one-back task.

In summary, our study adds to the small corpus of literature on sex differences in adult ADHD (Valera et al. 2010) and provides evidence that cognitive functions may be represented differently in men and women with ADHD.

References

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