

Working memory impairment in occupational lead exposure subjects associated with altered frontoparietal memory network

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Introduction

Lead is a potent environmental neurotoxicant that causes widespread effects on brain function and occupational lead exposure remain a major public health problem [1,2]. Previous study revealed that occupational lead exposure was associated with impaired performance on neurobehavioral tests comprising verbal and visual memory, attention, and motor function [3]. However, no investigations have directly examined neural processing during performance of working memory in occupational lead exposure, except for a research about early childhood lead exposure [4]. In the current study, using fMRI, we investigated the possible differences in neural correlates related to working memory between lead exposure subjects and age-matched healthy subjects.

Subjects and methods

A total of 65 female subjects (31 lead exposure subjects and 34 healthy controls) were enrolled in this study. We recruited retired former lead female workers who had worked in plants producing lead batteries. Control subjects were manual workers who were not exposed to lead, solvents in the same factories. All participants agreed to participate in our fMRI study and provided written informed consent. The protocol used for this study was approved by the Institutional Review Board of university hospital. Functional magnetic resonance imaging was employed to assess cortical activities during the performance of 0-back and 2-back working memory paradigm using Korean alphabet as mnemonic content. In the 0-back condition, participants were asked to remember a target letter that was presented at the beginning of each trial block. In the 2-back condition, they were asked to respond when a letter matched one that had been presented two letters before the present letter. BOLD functional images were acquired using a 3.0T GE HD scanner (EPI, TR=3000ms, TE=40ms, matrix=64x64, Thickness=4.0mm, FOV=220mm, no gap). Anatomical images were acquired using 3D-FSPGR sequence (TR=7.8ms, TE=3ms, matrix=256x256, no gap). Image processing and statistical analyses were carried out using MATLAB and SPM8. In fMRI data within-group analysis, contrast images from the analysis of individual subjects were analyzed by one-sample *t*-test, thereby generating a random-effects model, allowing inference to the general population. The SPM{t}s were thresholded at $P < 0.05$, false discovery rate (FDR) corrected for multiple comparisons across the whole brain. To make direct comparisons of brain activations between control and lead exposure subjects during 2-back memory task, contrast images for the main effects were assessed using a two-sample *t*-test. SPM{t}s were thresholded at $P < 0.05$, FDR corrected for multiple comparisons across the whole brain.

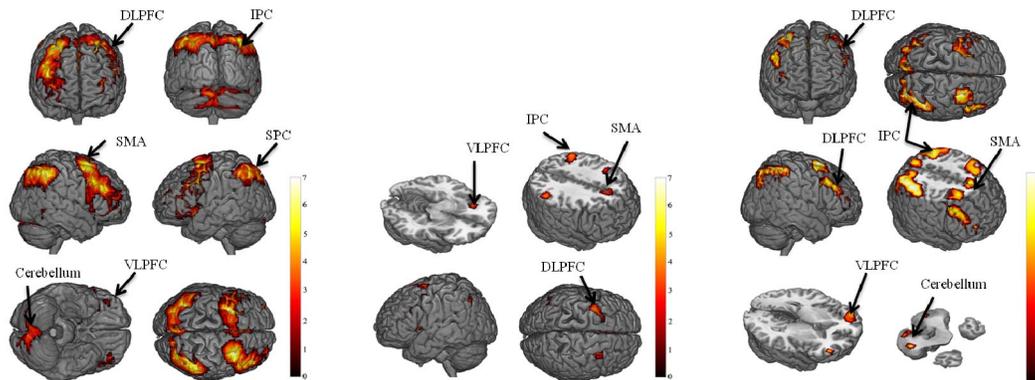
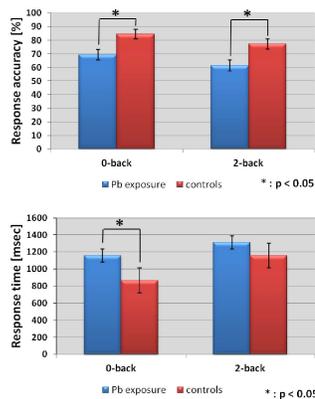
Results and Discussion

We found that healthy subjects showed better performance in terms of accuracy and reaction times during the task (Fig. 1). Differences in task accuracy and response time between the two groups were statistically significant ($p < 0.05$, Student's *t*-test) except for 2-back reaction time ($p = 0.4$, Student's *t*-test). In between-group analyses, lead exposure subjects showed reduced activation in the dorsolateral, dorsomedial and ventrolateral prefrontal cortex, and inferior parietal cortex (Fig. 2). Our findings suggest that functional abnormalities in the frontoparietal working memory network might contribute to impairments in maintenance and manipulation of working memory in lead exposure subjects.

References

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Results Data



(a) healthy subjects

(b) Pb exposure subjects

(c) healthy subjects > Pb exposure

Fig 1. Mean n-back working memory task performance in the lead exposure group (blue) and in the control group (red).

Fig 2. Brain activations during the 2-back memory task in healthy subjects (a) and Pb exposure subjects (b). Statistical parametric maps of brain regions of (a) and (b) (one-sample *t*-test for each group) showing significant activation at a statistical threshold of $P < 0.05$ (FDR-corrected). Statistical parametric maps of brain regions of (c) (two-sample *t*-test) showing significantly reduced activation in Pb exposure subjects compared to healthy subjects ($P < 0.05$, FDR-corrected).