

# Occupational Solvent Exposure and Working Memory Function

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## INTRODUCTION

In this report we used Blood Oxygen Level Dependent (BOLD) functional Magnetic Resonance Imaging (fMRI) to investigate the functional deficits of subjects with long-term occupational solvent exposure. Subjects underwent fMRI while performing a Sternberg task and N-back working memory task. We used an exploratory voxel-wise and a region of interest (ROI) analysis to test the hypothesis that the occupationally exposed subjects show hypo-activation in regions associated with working memory when compared to a carefully matched control group.

## METHODS

**Imaging.** All imaging was performed on a 1.5T Allegra MRI scanner (Siemens, Erlangen, Germany). Functional MRI BOLD images were acquired with a gradient echo-planar using the following protocol: 32 axial slices, 3mm skip 1mm, TR=2.5s, TE=30 ms, flip angle=90°, FOV=21 cm, matrix size=64x64. fMRI data was analyzed using SPM2 (Wellcome Department of Cognitive Neurology, London). Images were motion corrected, smoothed (6mm<sup>3</sup>) and coregistered to a matching T2 weighted image and then normalized to the standard MNI template. A version of the Sternberg memory task was used in a block designed fMRI. Activation was quantified as the difference between the maintenance phase of the Sternberg task and the inter-trial rest period of the block design. Imaging data were analyzed for patient specific N-back related activation by contrasting the fixation and task performance periods in a block design.

**Subjects.** A total of 39 controls (carpenters, painters and glazers) and 46 solvent exposed subjects (painters) with > 10 years of exposure to organic solvent mixtures but who were otherwise healthy, were recruited from a larger study evaluating the cognitive and sensory effects of chronic solvent exposure. Data from 30 controls and 29 exposed subjects were analyzed for the Sternberg task, and data from 29 controls and 34 exposed subjects were analyzed for the N-back task.

**RESULTS.** Voxel-wise t-tests were used to explore differences in activation related to the fMRI tasks. As hypothesized, subjects that were exposed to organic solvents showed decreased activation in the dorsolateral prefrontal cortex (DLPFC) and also some regions of the cingulate gyrus. Specifically, the exposed subjects showed decreased activation during the Sternberg task in the left DLPFC, and dorsal regions of the cingulate gyrus and supplementary motor areas of the frontal cortex (Figure 1). Figure 1 shows the group activation map in red of all subjects that performed the Sternberg task overlaid on a brain in the standard MNI space. Positive and negative t-values that met statistical criteria ( $p < 0.01$ ; cluster size > 16) were overlaid in green and blue, respectively; thus, areas of green indicate lower activation in exposed patients while blue indicates higher activation. The activation map and color scheme in Figure 2 is the same as Figure 1 and shows the results from the N-back working memory task. During this task, decreased activation of the exposed subjects was seen bilaterally in the DLPFC and a region of the anterior cingulate. The voxel-wise comparisons between the BOLD activations of exposed and non-exposed subjects did not reveal any significant increased activity in the exposed sample (no blue) so we are not able to conclude the use of a compensatory diffuse regions of activation in solvent exposed subjects.

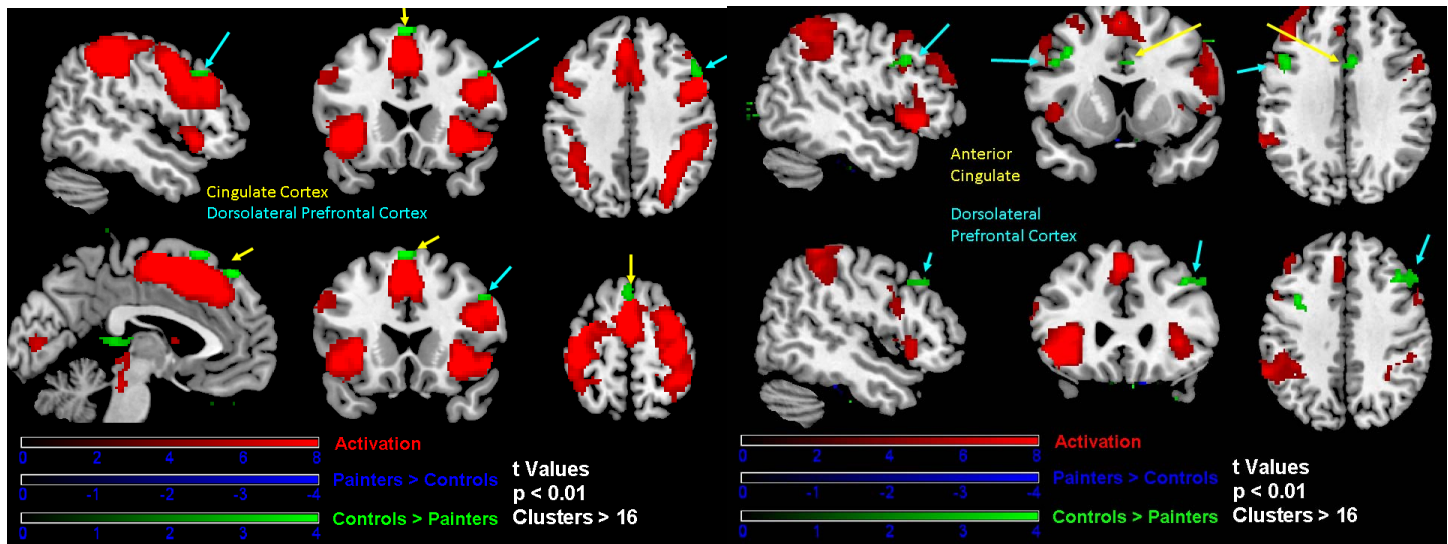


Figure 1. t-test of 30 Control, 36 exposed subjects performing a Sternberg task

Figure 2. t-test of 29 control, 33 exposed subjects performing an N-back task

We further investigated the effects of solvent exposure by extracting BOLD activations from regions of interest (ROIs) and testing for dose-effect relationships. Spherical volumes of 3mm radii were extracted from the most activated region of each cluster by each task. The amount of activation from each region was entered into Statistica for further analysis. Partial correlation coefficients were computed for solvent exposure and regional activation while controlling for the confounding factors of verbal IQ, lead exposure, lifetime alcohol, marijuana and cocaine use. The Sternberg activations did not reveal significant correlations between solvent exposure and activation when the potential confounds were included in the analysis. The N-back activations, however, showed negative correlations between activation and solvent exposure. The finding is consistent with t-test results that showed a decrease in activation related to solvent exposure.

## DISCUSSION

As hypothesized, prolonged occupational solvent exposure is related to a decreased activation in regions associated with working memory. The two pronged approach, the Sternberg and N-back tasks, revealed similar deficits. The consistency as well as the results of the ROI analysis bolsters confidence in the results of the exploratory analysis. Additionally, the lack of clusters with increased activation support a hypothesis that solvent exposure is related to hypo-activation of brain structures involved in working memory.

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