

# Altered working memory process in welders using N-back fMRI

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## Introduction

Welding caused frequent unprotected exposure to toxic metal fumes, and fine particulate [1]. One of the toxic metals that have received considerable attention in welding is manganese. While manganese is an essential metal and normally present in the brain in trace quantities, excessive exposure to manganese is known to cause manganism. With high T1 signal intensity in basal ganglia especially in globus pallidus, manganism resembles Parkinson's disease, with neuropsychiatric symptoms such as learning and recall deficits, impaired speech, mood and emotional disturbance, and working memory deficit in addition to significant motor dysfunction [2]. In this study, we employed a verbal variant of the 2-back working memory task and seek to compare the working memory neural network of welders with controls using functional magnetic resonance imaging to evaluate a subclinical dysfunction of working memory network.

## Subjects and methods

Twenty three males aged more than 40 years, who were fulltime current welder with more than 5 years welding experience in factories were recruited to present study. Twenty three age- and gender-matched, non welding production workers from the same workplace, who were not exposed to other hazardous material such as paint, were recruited as control group in the present study. All subjects were right handed according to the Edinburgh handedness scale. After detailed explanation of the study design and potential risks, all subjects gave written informed consent. All study protocols were approved by the local Internal Review Board (IRB). We analyzed airborne Mn levels using a graphite furnace atomic absorption spectrophotometer. Each blood sample was also analyzed for complete blood counts, hemoglobin and hematocrit levels, as well as liver function.

Functional magnetic resonance imaging was employed to assess cortical activities during the performance of a 2-back working memory paradigm using Korean alphabet as mnemonic content. BOLD functional images were acquired using a 3.0T GE HD scanner (EPI, TR=4000ms, TE=40ms, matrix=64x64, Thickness=3.0mm, FOV=192mm, 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 v. 7.2 and SPM2. 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 welder group 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

There were no significant differences between two groups in terms of smoking, alcohol use, education level, liver, and hemoglobin level. Therefore, the Mn accumulation in the welders was not due to liver dysfunction or iron-deficient anemia, both of which are important causes of Mn accumulation in the brain [3]. Mean blood Mn concentration (1.55  $\mu\text{g/dL}$ ) was significantly higher in the welders than that (1.15  $\mu\text{g/dL}$ ) in the control group. Mean and standard deviation values of workplace air concentrations of Mn were 0.14 and 0.08  $\text{mg/m}^3$ , respectively.

Compared to control subjects, the behavioral data showed that welders were not significantly different at the 2-back task for response accuracy ( $P=0.78$ ) (Fig1). That is, welders had a normal behavioral performance. Our within group analysis revealed that control and welder subjects showed bilateral activation of the lateral prefrontal cortex, anterior cingulate cortex and parietal cortex (Fig2 a, b). However, welders demonstrated more widespread brain activation patterns compared to control subjects. To examine whether there were any regions within the working memory network that showed group differences, we conducted two-sample *t*-tests. For control subjects, relative to the welders, no voxels reached statistical significance. When welders were compared to control subjects, welders show greater activation of the left ventrolateral prefrontal cortex, premotor and medial prefrontal cortex (Fig2 c). From our result that welder exhibited hyperactivity within the working memory neural network while performing the n-back task, it is strongly suggested that welder might need greater cognitive control and maintenance of information in order to process information as efficiently as control subjects. This study provides first evidence that welder need greater activation within the same neural network to maintain a similar level of performance as controls during a working memory task. In conclusion, the current study suggests that welders may recruit more brain resources than controls during cognitive control to compensate an impaired cognitive capacity.

## References

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## Results Data

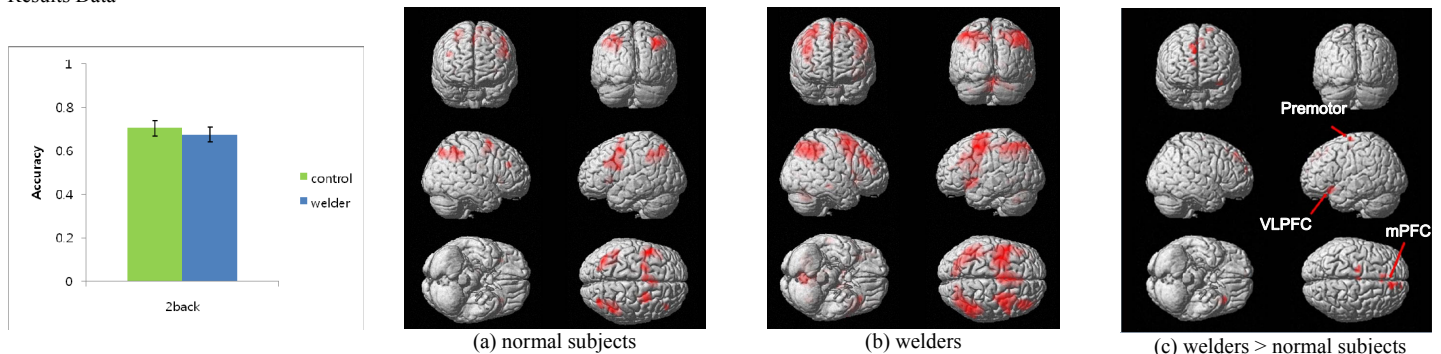


Fig 1. The accuracy of n-back performance. Welders were not significantly different at the 2-back task for response accuracy ( $P=0.78$ )

Fig 2. Brain activations during the 2-back memory task in normal subjects (a) and welders (b). Statistical parametric maps of brain regions of (a) and (b) (one-sample *t*-test for each group of 23 subjects) showing significant activation at a statistical threshold of  $P < 0.05$ (corrected). Statistical parametric maps of brain regions of (c) (two-sample *t*-test) showing significantly more activation in welders compared to normal subjects ( $P < 0.05$ , FDR corrected).