Voxel-based morphometric analysis of brain in welders with chronic manganese exposure

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Introduction

As for the presence of subclinical functional brain abnormalities in Mn-exposed welders, advanced magnetic resonance imaging (MRI) techniques, i.e., functional MRI and diffusion tensor imaging, as well as magnetic resonance spectroscopy have revealed a cerebral involvement in the pathoanatomy of Mn neurotoxicity in Mn-exposed welders. However, to date, no previous study has investigated the changes in brain volume in welders with chronic Mn exposure. Furthermore, it is important question whether the neurobehavioral dysfunctions, which are often found in Mn-exposed welders, are associated with structural brain abnormalities in Mn-exposed welders. Recent studies using voxel-based morphometry (VBM) demonstrated that VBM, voxel-wise comparisons of gray and white matter at a whole-brain level, has been useful in characterizing subtle changes in brain structure in a variety of diseases associated with neurological and psychiatric dysfunction. The purpose of the present study was to evaluate the relation between structural abnormality in brain and subclinical dysfunction in welders with chronic exposure to Mn. VBM was used (i) to assess the difference in gray and white matter volume between welders and healthy age-matched control subjects and (ii) to investigate the relation between the decreased brain volume and decline in performance on neurobehavioral tests.

Subjects and methods

Our study population included 40 males aged 40 years and older who were full-time welders with more than 5 years of experience working in factories. The control group consisted of 26 age- and gender-matched, non-welding production workers from the same workplaces who were not exposed to paint or other hazardous materials. All participants were right-handed according to the Edinburgh handedness scale. All participants provided written informed consent after receiving a detailed explanation of the study design and potential risks. The study protocol and scoring procedures were approved by the institutional review board(IRB). Neurobehavioral tests included the digit symbol test, the digit span test, the Korean Auditory Verbal Learning Test (K-AVLT), the Korean Complex Figure Test (K-CFT), the Verbal Fluency test, the Stroop test, the grooved pegboard test, and the finger tapping test. The MRI examinations were performed with 3.0 Tesla whole body scanner (Signa Exite HD, GE, USA) with a 8 channel head coil. 3D fast spoiled gradient echo T1-weighted image was obtained (FSPGR 3D, repetition time 7.8 ms, echo time 3.0 ms, flip angle 20°, slice thickness 1.3mm, no gap, 256x256 matrix size and 24cm field of view). Image processing and statistical analyses were performed using MATLAB v. R2009a (The Math works Inc., Natick, MA, USA) and SPM8 (SPM;Wellcome Department of Imaging Neuroscience, London, UK; http://www.fil.ion.ucl.ac.uk). Volumetry analyzed using T1WI and VBM8 toolbox underlying SPM8 (http://dbm.neuro.uni-jena.de). The SPSS (v14) software was used for all statistical analyses.

Results and Discussion

Significant regional volume reductions were observed in welders with chronic Mn exposure compared to healthy controls (FDR corrected $p < 0.05$, cluster size of 64) in the cerebellar gray (C1) and white matter (C2), globus pallidus (Fig. 1). No areas of significantly decreased brain volume were observed in healthy control subjects compared with welders with chronic Mn exposure. Table 1 lists the results of multiple regression analysis of neurobehavioral performance using volumetric indices as predictors. Welders showed decreased various cognitive and motor functions (e.g., verbal/visual, short-term/long-term, working memory, and fine motor functions) compared with healthy controls. In addition, attention and executive functions were lower in welders than in controls. Our results are consistent with previous reports [1-3]. After controlling for age, educational level, smoking, and alcohol consumption, all of volumetric indicies such as C1, C2, and GP were significantly associated with fine motor functions. Thus decreased brain volume suggested impaired fine motor functions. In addition, frontal lobe function such as KCF (inhibition) and the Stroop error index were associated with cerebellar volume. In conclusion, the present research showed significant correlations between several neurobehavioral deficits and volumetric indices.

References

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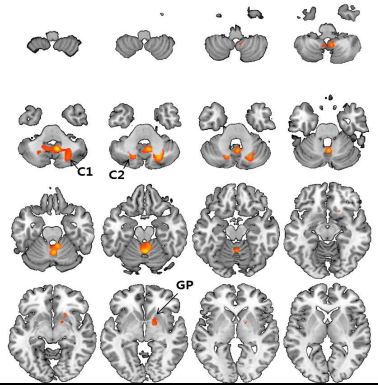

Fig 1. Brain regions (C1, C2 and GP), in which welders showed reduced brain volume compared to age-matched health control subjects (p<0.05, FDR corrected)

	C1		Model		C2		Model		GP		Model	
	beta	p-value	R^2	p-value	beta	p-value	R^2	p-value	beta	p-value	R^2	p-value
K-CFT (copy)	-1.644	0.854	0.146	0.084	2.545	0.833	0.146	0.083	10.258	0.573	0.150	0.075
K-CFT (immediate recall)	-0.400	0.983	0.121	0.162	3.187	0.902	0.121	0.161	42.993	0.270	0.138	0.103
K-CFT (delayed recall)	2.614	0.888	0.123	0.151	8.864	0.723	0.125	0.146	17.959	0.635	0.126	0.140
K-CFT (inhibition)	-18.033	**<0.001**	0.363	**<0.001**	-18.354	**0.001**	0.236	**0.006**	-23.362	**0.004**	0.186	**0.027**
Stroop Color	6.041	0.681	0.037	0.807	4.051	0.838	0.035	0.827	-8.670	0.772	0.035	0.820
Stroop Word	-22.366	0.229	0.111	0.202	-35.423	0.156	0.120	0.165	-34.825	0.360	0.102	0.249
Stroop Color/Word	-26.632	0.234	0.092	0.311	-37.408	0.214	0.094	0.299	-50.318	0.271	0.089	0.333
Stroop error index	-9.798	**0.018**	0.182	**0.030**	-15.241	**0.006**	0.209	**0.013**	-9.209	0.284	0.119	0.170
Pegboard (dominant hand)	-86.412	**<0.001**	0.339	**<0.001**	-94.128	**0.004**	0.283	**0.001**	-133.852	**0.007**	0.270	**0.002**
Pegboard (non-dominant hand)	-94.120	**0.027**	0.278	**0.001**	-143.533	**0.012**	0.295	**0.001**	-171.897	**0.049**	0.265	**0.002**

Bold values mean statistical significance ($p < 0.05$).

Table 1. Multiple regression for neurobehavioral tests with change percent of volumetry after control of age,educational level, smoking status, and drinking status.