COMPARISON OF BRAIN METABOLITE CHANGES IN MANGANESE-EXPOSED WELDERS AND SMELTERS

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Introduction: Excessive manganese (Mn) exposure is known to cause cognitive, psychiatric and motor deficits [1]. Mn overexposure occurs in different occupational settings, where the type and level of exposure may vary. Magnetic resonance imaging (MRI) and spectroscopy (MRS) can be used to evaluate brain Mn accumulation and to measure Mn-induced metabolite changes non-invasively. The aim of this study was to compare metabolite changes among different brain regions of welders and smelters following occupational Mn exposure.

Materials and Methods: Nine male Mn-exposed smelters (mean ± SD: age, 39.3 ± 7.0 years; duration of exposure, 20.4 ± 6.2 years; airborne Mn (as MnO_2), 0.40 ± 0.30 mg/m^3), 14 male Mn-exposed welders (mean ± SD: age, 34.4 ± 10.8 years; duration of exposure, 8.5 ± 4.4 years; mean airborne Mn (as MnO_2), 0.09 ± 0.14 mg/m^3) from two factories, and 23 age- and gender-matched controls with no history of Mn exposure (mean ± SD: age, 36.0 ± 10.7 years) were recruited in China.

MRI and MRS scans were performed on a 3T Philips Achieva whole-body clinical scanner (Philips Healthcare, Best, the Netherlands), equipped with an eight-channel head coil. In addition to imaging, short echo time (TE) ^{1}H spectra (PRESS localization; TR/TE=1500/30ms; CHESS water suppression) were acquired in each subject from four volumes of interest (VOIs): frontal cortex (8 ml), posterior cingulate cortex (PCC) (26.2 ml), hippocampus (3 ml), and a 22.5 ml voxel centered on the thalamus, but also containing portions of the globus pallidus, putamen, and other basal ganglia structures. For each of the VOIs, a reference spectrum was acquired without water suppression. These spectra were then used for phase and frequency correction of the corresponding water-suppressed spectra, and additionally as a concentration reference for water-scaled metabolite ratios. Shimming and other preparation phases were performed fully automatically, resulting in line widths of < 15 Hz for the unsuppressed water peak for all spectra.

MRS data processing and quantification were performed with LCModel [2]. All metabolite concentrations were scaled with respect to the unsuppressed water signal and expressed in institutional units. Only fitting results with LCModel %SD values < 20% were used for further statistical analysis. SPSS (PASW statistics 18) was used to perform the statistical analyses. The absolute metabolite concentrations were analyzed using general linear model (GLM) with groups as the independent variables adjusted for subjects' age and post-hoc pairwise tests. The significance levels for post-hoc tests were adjusted for multiple comparisons using the Bonferroni adjustment method. Statistical significance was evaluated at the p = 0.05 level.

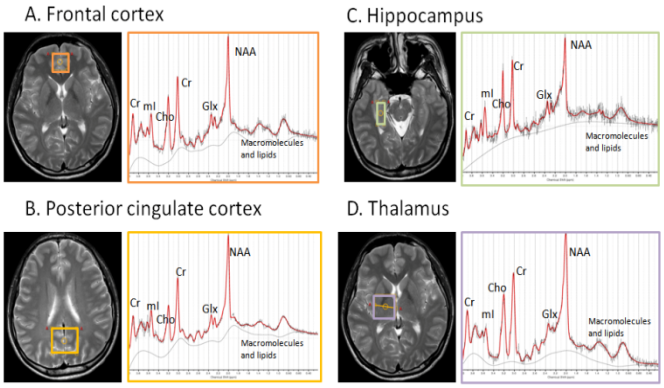

Figure 1: Volumes of interest (VOIs) for four brain regions and representative short-TE spectra with LCModel fitting for each region: A, frontal cortex; B, posterior cingulate cortex (PCC); C, hippocampus; D, thalamus.

Results: The welders, with lower airborne Mn exposure, showed significantly decreased creatine (Cr), glutamate (Glu), the sum of Glu and glutamine (Glx) in the frontal cortex ($p<0.05$, $p<0.01$ and $p<0.05$, respectively), significantly decreased myo-inositol (mI) and total N-acetyl-aspartate in the PCC ($p<0.01$ and $p<0.05$, respectively) and in the hippocampus (both $p<0.01$). No changes were found in the thalamus. On the other hand, the smelters, with higher airborne Mn exposure, showed no changes in the frontal cortex, decreased glycerophosphocholine and mI in the PCC (both $p<0.01$), decreased mI in the hippocampus ($p<0.01$) and increased Glu in the thalamus ($p<0.05$).

Discussion: These results suggest that Mn-induced brain metabolite changes may be regional in nature and more extensive in welders than in smelters. The frontal cortex seems to show a more profound change than the other brain areas tested in the welders. Further studies are needed to investigate the effects of exposure type and exposure duration on the mechanism of Mn neurotoxicity.

References: [1] Guilarte TR. Environ Health Perspect. 2010 Aug;118(8):1071-80; [2] Provencher SW. 1993. Magn Reson Med 30(6):672-679.

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