Environmental Lead Exposure Alters Brain Volume: Results of a VBM Analysis

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Purpose: The developing brain is particularly sensitive to environmental toxins. Ongoing research of a birth cohort recruited over twenty years ago has shown that cognitive, developmental and behavioral deficits correlate with measured blood lead levels. As these subjects enter adulthood, we investigated the influence of childhood lead exposure with alterations in brain structure assessed with voxel based morphometric (VBM) analyses of high-resolution magnetic resonance imaging (MRI).

Materials and Methods: One hundred fifty nine members of the lead study cohort, ages 20-23 years, completed an imaging protocol using a 1.5T MR scanner. An axial three-dimensional, inversion recovery prepped, fast spoiled gradient echo (3D IR FSPGR) was acquired for VBM analyses [TE=5.4 msec, TR=12.5 msec, TI=300 msec, FOV = 24 cm, 1.5-mm thick with contiguous slices]. All automated image processing was performed using Statistical Parameter Mapping software (SPM2 (*1*)). Blood lead levels were measured in this cohort every three months for the first five years of life and every six months from 5 - 6.5 years with a mean value determined for childhood. For the studied cohort, the mean blood lead levels ranged from 4.7 to 37 ug/dL. The SPM2 program for VBM allows segmentation of tissue classes (gray, white and CSF) and comparison of structural imaging volumes with continuous and/or categorical variables. Comparisons with mean childhood blood lead levels adjusted for possible confounding demographic variables (age, gender), cognitive performance measures (IQ), marijuana usage and birth histories (birth weight, and gestational age) were performed. A linear regression model was used to evaluate the correlation between brain volumes and mean lead levels adjusted for significant confounders.

Results: Gray matter (GM) reductions were observed in frontal, temporal, parietal and occipital lobes, the basal ganglia and the cerebellum for the lead cohort. Regional clusters ($p<0.001$, with a cluster threshold minimum of 200 voxels) demonstrate gray matter loss significantly correlates with increasing lead exposure.

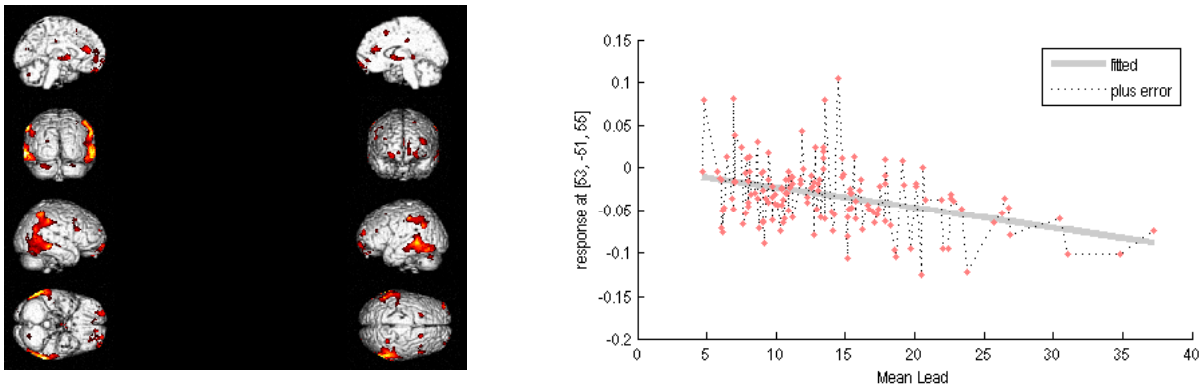

Figure 1. A) Regions with significant gray matter reductions are overlaid on a template brain rendering; B) Individual mean volumes within a parietal cortex cluster (MNI coordinate 53, -51, 55) plotted against mean childhood blood lead levels for subjects demonstrating the reduction in volume correlated with lead.

White matter (WM) reductions associated with mean childhood blood lead levels, while present, were not as diffuse as those in gray matter. The most significant WM volume loss associated with mean childhood blood lead levels is found in orbital frontal white matter.

Conclusions: VBM analyses of high-resolution MR images offers novel information about the regions altered by childhood lead exposure. Subjects exposed to significant levels of lead during childhood demonstrate reductions in total brain volume with regional gray and white matter deficits that correlate with mean childhood blood lead levels. In particular, frontal lobe gray and white matter reductions may explain deficits in cognitive and behavioral outcomes clinically observed in populations with significant lead exposure.

Reference: 1. J. Ashburner, K. J. Friston, *Neuroimage* **11**, 805 (Jun, 2000).