The Influence of Childhood Lead Exposure on Language Function in Young Adults: An FMRI Study

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Introduction

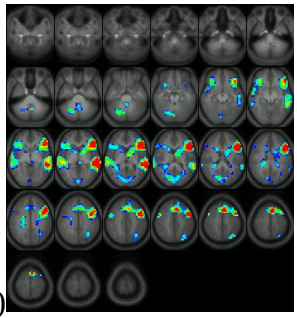
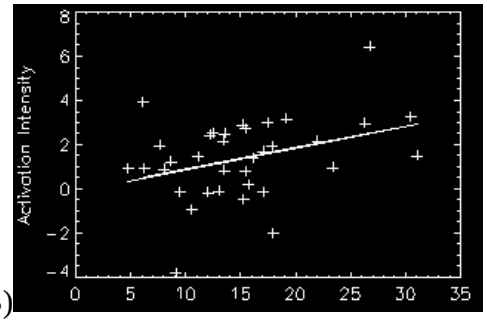
The neurotoxic effects of environmental lead exposure in children have been recognized for over a century, but the mechanism of lead's toxicity on the developing central nervous system remains poorly understood. New evidence suggests that levels of lead exposure currently deemed safe may be detrimental to children. Moreover, the existing evidence indicates that the adverse consequences of lead exposure persist into early adulthood. Ongoing research of a birth cohort recruited twenty years ago has shown that cognitive, developmental and behavioral deficits correlate with measured blood lead levels. 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. As these subjects enter adulthood, we investigated the influence of childhood lead exposure on language function with functional magnetic resonance imaging (fMRI) using a verb generation paradigm.

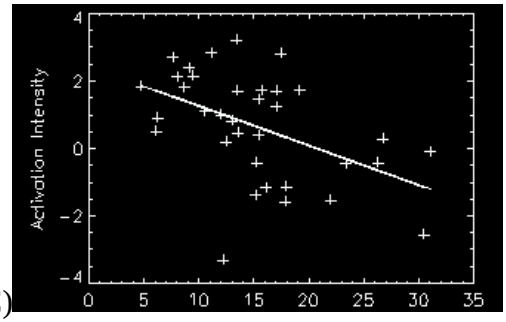
Methods

Thirty-five members of the lead study cohort, ages 20-23 years, performed an integrated verb generation/finger tapping paradigm while imaged in a Bruker 3T MR scanner using a T2*-weighted, gradient echo, Echo Planar Imaging (EPI) sequence (TR/TE = 3000/38 ms, FOV = 25.6 x 25.6 cm, matrix = 64 x 64, slice thickness = 5mm). Twenty-four slices were acquired at 110 time points during the alternating 30-s periods of control and activation for a 5.5 minute scan duration. In addition, a whole brain T1-weighted scan was acquired for anatomical co-registration. FMRI image processing was performed with custom software. For each subject, a Z-score map was determined by, on a pixel-by-pixel basis, calculating the t-value and converting to a Z-score. Individual Z-maps are combined to generate a composite Z-map. A linear regression model was used to evaluate the correlation between brain activation and mean childhood blood lead levels.

Results

A composite Z-map reveals the activation associated with the verb generation task (Figure A). The activation of the right inferior temporal gyrus, the contra-lateral area to the traditional Wernicke area, showed significant positive correlation with the mean childhood lead level ($R = 0.35$, $p < 0.04$) (Figure B). The activation of the left frontal area, e.g. traditional Broca area, showed a strong inverse correlation with the mean childhood lead level ($R = -0.47$, $p < 0.005$) (Figure C).

A)  B) 

C) 

Conclusions

Elevated childhood lead exposure strongly influences neural substrates of semantic language function demonstrated as a selective, deleterious effect on normal language areas with concomitant recruitment of contra-lateral regions, resulting in striking, exposure-dependent, reorganization of language function.