Childhood Obesity is Associated with Lower Grey Matter Volume in Children

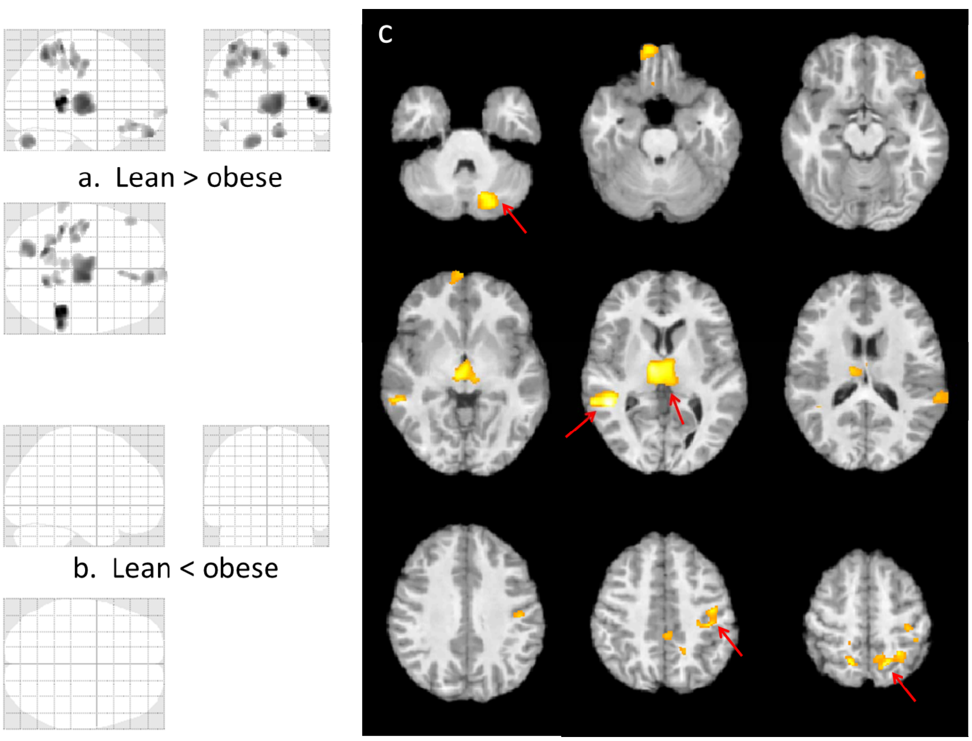
Xiawei Ou[1,2], Aline Andres[3,4], R.T. Pivik[3,4], Mario Cleves[3,4], and Thomas Badger[3,4]

[1]*Arkansas Children's Hospital Research Institute, Arkansas Children's Nutrition Center, Little Rock, AR, United States,* [2]*Radiology and Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, United States,* [3]*Arkansas Children's Nutrition Center, Little Rock, AR, United States,* [4]*University of Arkansas for Medical Sciences, AR, United States*

INTRODUCTION: Childhood obesity has become one of the most prominent pediatric health concerns in the US, with the prevalence dramatically increased during the past 30 years. Recent studies have shown that obesity may be associated with changes in brain structure and function. For example, grey matter atrophy was observed in adults with morbid obesity. However, the effects of childhood obesity on brain development in otherwise healthy children are less clear. The aim of our study was to evaluate grey matter development in healthy school-age children who are either normal weight or obese. We used voxel-based morphometry (VBM) which provides a sensitive and objective comparison of regional grey matter volume between groups.

METHODS: Healthy normal weight (N=12, BMI-for-age <75th percentile) or obese (N=12, BMI-for-age >95th percentile) children (age 8-10 years) were recruited for this IRB approved study. Inclusion criteria were: parental report of full-term gestation, birth weight between 5th – 95th percentiles, and mostly breastfeeding during the first 6 months of life; overall healthy; and right hand dominance. Exclusion criteria were: maternal diabetes; maternal alcohol, tobacco, or drug use during pregnancy; For the child, chronic sleep disorder; history of psychological or psychiatric diagnoses; history of neurological impairment or injury; surgical implant or other foreign object in the body; dental work which may cause artifacts in MRI, and claustrophobia. All participants underwent an MRI examination of the brain performed on a 1.5 Tesla Philips Achieva MRI system with a standard 8-channel SENSE head coil and a sagittal T1-weighted 3D turbo field echo sequence with 7.4 ms TR, 3.5 ms TE, 8º flip angle, no slice gap, 1 mm x 1 mm x 1 mm acquisition voxel size, and 256 x 232 x 150 matrix size. The T1-weighted images were exported to a workstation with MATLAB software for VBM analysis. VBM8 toolbox included in SPM8 was used. A pediatric T1 template (age ~9 years) and customized tissue probability maps were created based on the NIH data by the Template-O-Matic toolbox. The T1 images were then segmented into grey matter, white matter, and CSF by VBM8. Default parameters for Gaussians per class, bias regularization and cutoff FWHM, warping regularization, sample distance were used. High-dimensional DARTEL was used for spatial normalization. A spatial adaptive non-local means denoising filter and the default random field weighting and partitions cleaning in VBM8 were applied. Non-linear modulated normalized grey matter images corrected for individual brain size were generated and smoothed using a Guassian kernel of FWHM 8 mm in each direction. The smoothed grey matter images were used for the subsequent voxel-wise statistical comparison of regional grey matter volume between groups. P<0.001 uncorrected in two sample t-test with a cluster size threshold of 100 voxels was used to illustrate overall differences, and p<0.05 (FWE corrected at the cluster level) was used to determine regions with significantly different regional grey matter volume. Age at MRI was included as a covariate in the VBM analysis since the brain continues to grow in 8-10 year old children. Gender was also included as a covariate.

RESULTS:



VBM analysis of regional grey matter volume showed that at p<0.001 and cluster size >100 voxels, normal weight children had multiple regions in the brain with higher grey matter volume (**Figure a**), while there were no regions with lower grey matter volume (**Figure b**). The VBM results were overlaid on T1 weighted images normalized to the customized pediatric template (**Figure c**), and the clusters (yellow/orange) with higher regional grey matter volume in normal weight versus obese children are located in: left cerebellum, right gyrus rectus, left lateral orbital gyrus, right frontomarginal gyrus, left/right thalami, right middle temporal gyrus, left superior temporal gyrus, left pre/postcentral gyri, precuneus, and left/right superior parietal gyri. After family wise error (FWE) correction to control for multiple comparisons, five clusters still showed significantly higher (p<0.05, corrected) regional grey matter volume in normal weight versus obese children (**Figure c,** red arrows), including the right middle temporal gyrus, the left/right thalami, the left superior parietal lobule, the left pre/postcentral gyri, and the left cerebellum.

CONCLUSIONS: Our results showed that obese (otherwise healthy) children had significantly lower regional grey matter volume in widespread brain regions compared to normal weight children, and suggest that obesity-linked body composition changes include the brain as well as other tissues.

ACKNOWLEDGEMENTS: This study was supported by the Marion B. Lyon New Scientist Development Award at the Arkansas Children's Hospital Research Institute and by the Arkansas Children's Nutrition Center funded by the U.S. Department of Agriculture-ARS-CRIS 6251-51000-005-00D.