Effects of Early Deprivation and BDNF Genotype on Brain Development in Post-Institutionalized Youth

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Introduction

Animal studies have documented physiological and behavioral effects of early deprivation. Studies of post-institutionalized (PI) children suggest that early deprivation is associated with mild to severe deficits in cognitive and socioemotional development, and changes in the limbic system and prefrontal cortex. By adolescence, the neurocognitive outcomes of PI children vary substantially. One mechanism contributing to individual variation following deprivation may be specific genetic variants that support resilience. A candidate gene variant is the val66met polymorphism of the brain-derived neurotrophic factor (BDNF) gene, which is associated with volumetric differences in limbic and prefrontal areas in adults.

The current study used structural MRI to investigate brain development in PI children. We hypothesized that longer exposure to institutionalization would be associated with increased amygdala volume but decreased hippocampal and prefrontal volumes, and that val/val-BDNF carriers may show differential effects of early deprivation.

Questions

- Do post-institutionalized (PI) adolescents show altered development of limbic and prefrontal structures?
- Does BDNF genotype modulate effects of early deprivation?

Methods

Participants: 12-14 year olds either adopted internationally from institutional care or raised with Minnesota biological family

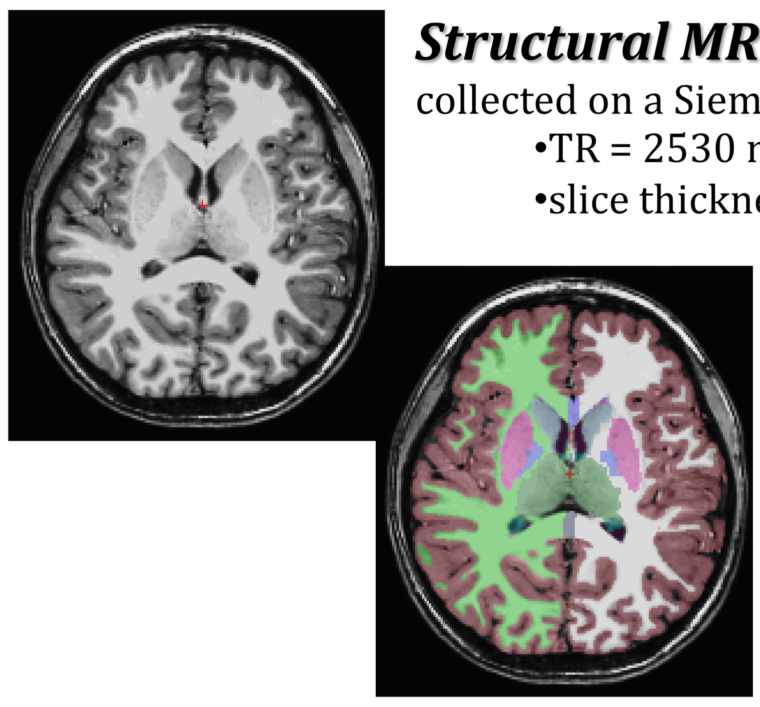
Non-Adopted
- n = 30 (17 male)
- no developmental, neurological, or psychiatric disorders

Early-Adopted
- n = 41 (11 male)
- adopted between age 4-12 months
- no FAS or developmental disorders

Late-Adopted
- n = 41 (13 male)
- adopted between age 13-78 months
- no FAS or developmental disorders

PI children were adopted from Asia (52.5%), Europe (36.6%), Pacific Islands (2.4%), and South America (8.5%) and had been living with their adoptive families for an average of 11.8 years

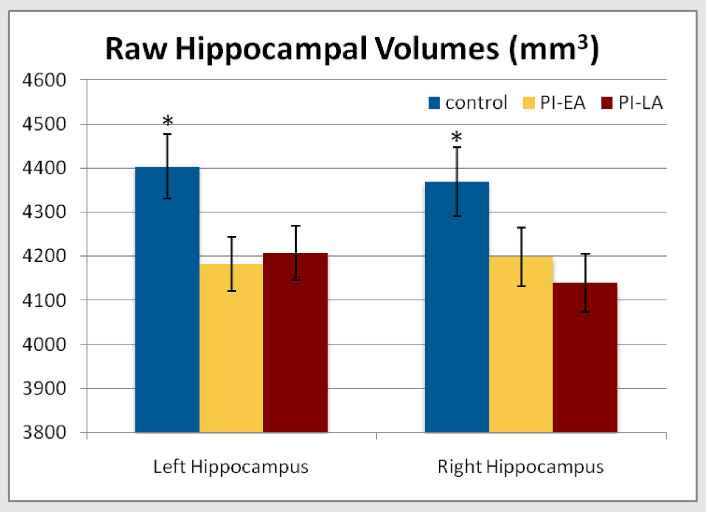
BDNF Genotyping: PI children were selected to participate based on home salivary DNA samples which were genotyped for the val66met polymorphism of the BDNF gene
- n = 41 val/val-BDNF genotype (16 early-adopted)
- n = 41 any met-BDNF genotype (23 early-adopted)



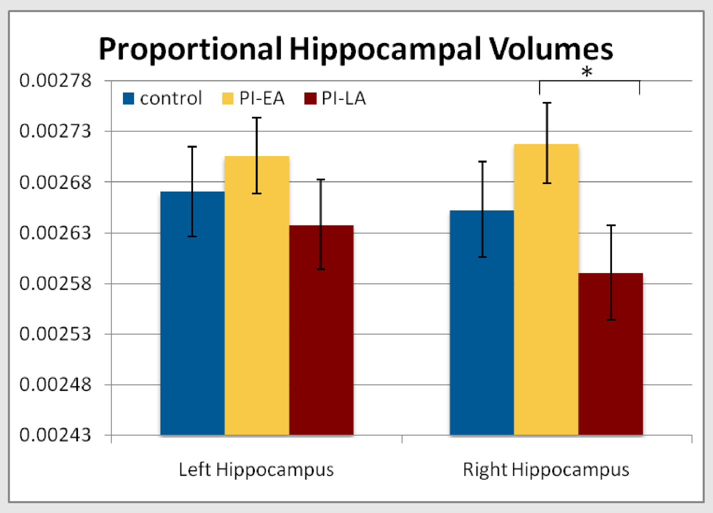
Structural MRI Scan: T1-weighted anatomical 3-D MPRAGE images collected on a Siemens 3T Trio scanner
- TR = 2530 ms, TE = 3.65 ms, FOV = 256 mm, flip angle = 7º
- slice thickness = 1mm, 240 sagittal slices

MRI Analyses: Freesurfer was used to obtain automated, volumetric segmentation data of subcortical and cortical structures
- analyses used raw volumetric data and volumetric measurements corrected proportionally for intracranial volume
- analyses included age and gender as covariates

Results: Hippocampal Volume



- non-adopted children had larger bilateral uncorrected hippocampal volumes



- **early-adopted children had larger proportional right hippocampal volumes than late-adopted children**

- BDNF genotype and the interaction between BNDF genotype and duration of institutional care did not predict hippocampal volumes

Acknowledgments

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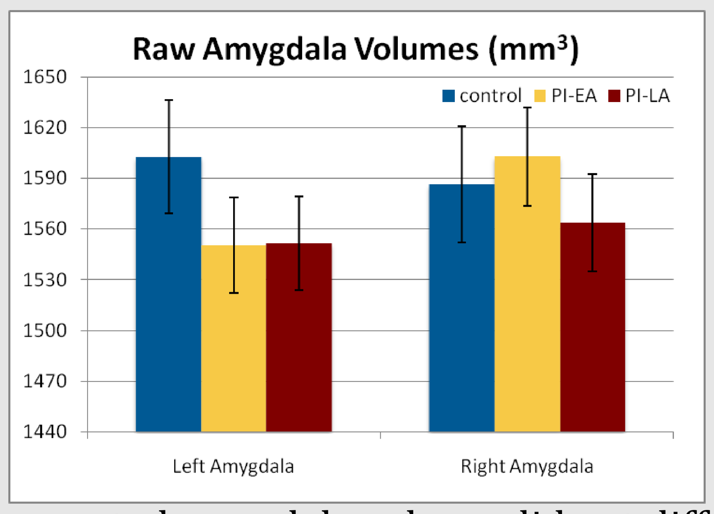
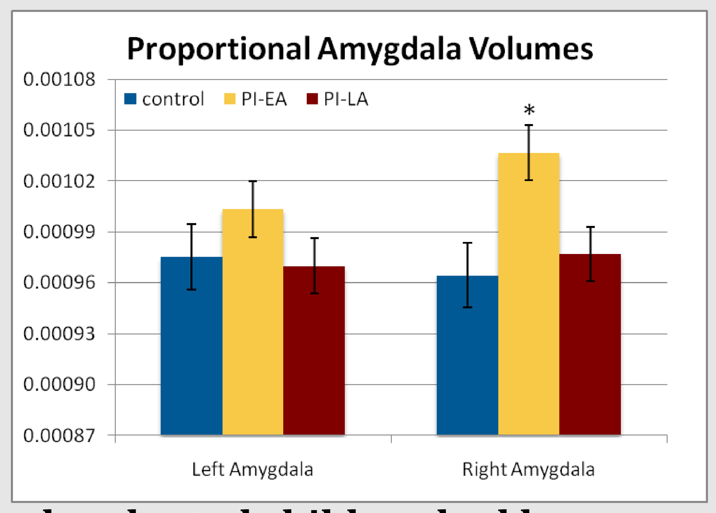
International Adoption Project I.A.P

Institute of Child Development I.C.D.

Results: Amygdala Volume



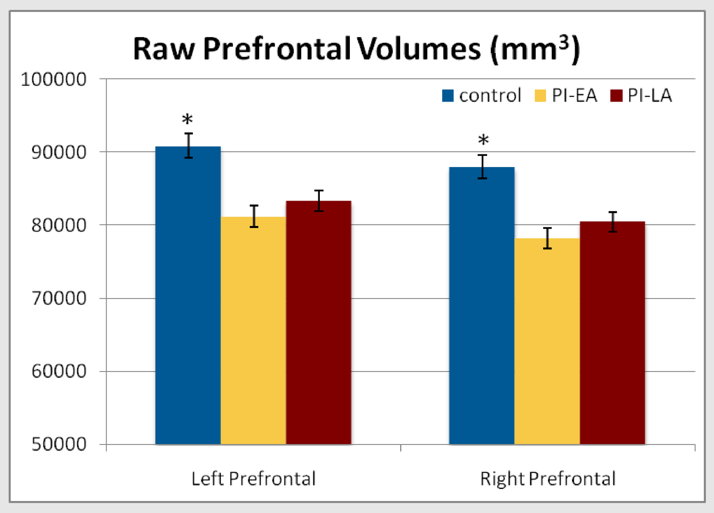
- uncorrected amygdala volume did not differ between control and PI children



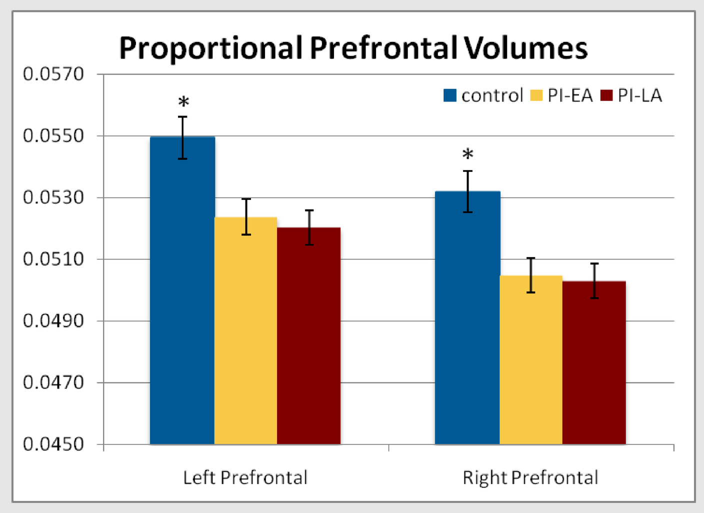
- **early-adopted children had larger proportional right amygdala volumes than control and late-adopted children**

- BDNF genotype and the interaction between BNDF genotype and duration of institutional care did not predict amygdala volumes

Results: Prefrontal Cortex Volume



- PI children had smaller whole brain volumes than non-adopted children, including smaller uncorrected volumes in prefrontal, temporal, and parietal lobes

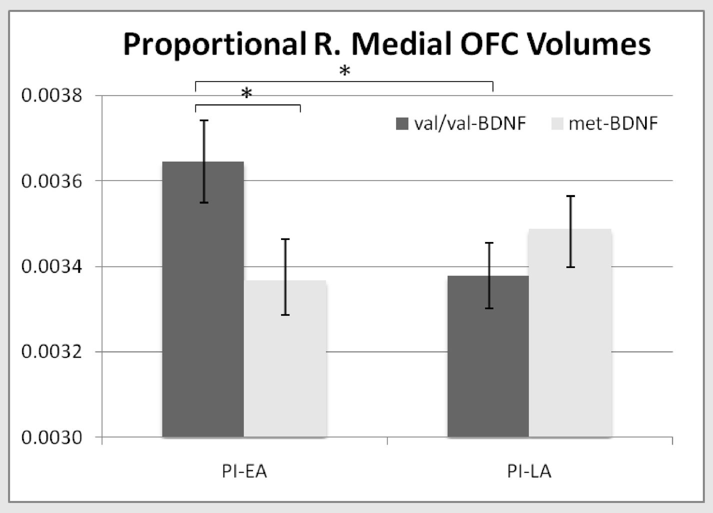


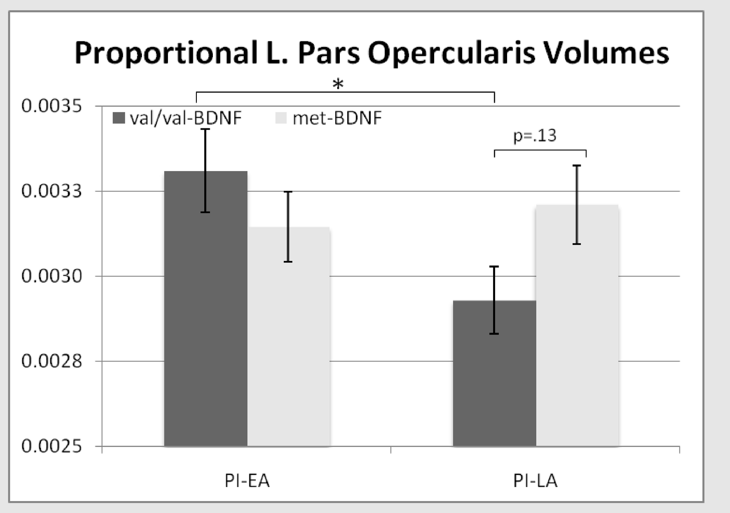
- **after correcting for whole brain volume, PI children had smaller proportional prefrontal volumes than non-adopted children** but group differences in other corrected lobe volumes were non-significant

Regional Prefrontal Volume: PI children had smaller proportional volumes than non-adopted children in the following regions, with no effect of duration of institutional care ($p<.05$):
- bilateral pars opercularis
- bilateral superior frontal gyrus
- left caudal middle frontal gyrus
- left lateral orbitofrontal cortex
- left pars orbitalis
- right rostral anterior cingulate
- right rostral middle frontal gyrus

BDNF Genotype: PI children with the val/val-BDNF genotype had larger proportional volumes than PI children with a met-BDNF allele in the following prefrontal regions ($p<.05$):
- left lateral orbitofrontal cortex
- left pars orbitalis

BDNF Genotype x Duration of Institutionalization:





- **early adoption and the val/val-BDNF genotype were associated with larger corrected right medial ofc volumes in PI children; similar trends were observed in corrected left pars opercularis volumes**

Discussion

Data suggest there are persisting effects of a discrete, early period of deprivation on morphological development of the hippocampus, amygdala, and prefrontal cortex
- increased hippocampal and amygdala volumes in early-adopted children may reflect selective sparing
- prefrontal volumes were reduced in both early- and late-adopted children, suggesting this region may be particularly vulnerable to deprivation

BDNF genotype may modulate effects of early deprivation in regions of prefrontal cortex

Future directions: As part of a large center grant, this project will continue to investigate genotype by environment interactions as a mechanism for explaining later developmental outcomes in PI children

Summary

By early adolescence, post-institutionalized (PI) children show altered patterns of structural brain development in limbic and prefrontal areas. Differences in duration of institutional care and BDNF genotype impact morphological brain development in PI children.