# Early Life Stress, Physical Growth, and Structural Brain Development in Internationally Adopted Adolescents

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## Introduction

**How does early life stress impact relationships between physical growth, pubertal timing, and prefrontal cortex development at adolescence?**

**Animal studies have documented neuroanatomical and behavioral effects of early life deprivation.** Studies of children adopted from institutional care (**post-institutionalized; PI children**) suggest that this discrete time period of early life adversity is associated with long-term:

- differences in *cognitive and socioemotional development* (Gunnar et al., 2000)
- changes in the volume of the brain's *limbic system* (Mehta et al., 2009; Tottenham et al., 2010)
- alterations in gray and white matter development of the brain's *prefrontal cortex* (Eluvathingal et al., 2006; Behen et al., 2009; Govindan et al., 2010; Hodel et al., in prep)

**Poor growth in currently institutionalized children has long been recognized.**

- PI children show catch-up growth following adoption, although growth rate may fall off at adolescence resulting in PI children reaching shorter final height in comparison to their non-adopted peers (e.g. Parent et al., 2003; van IJzendoorn & Juffer, 2006)

**Variations in early life experiences alter pubertal timing and development.**

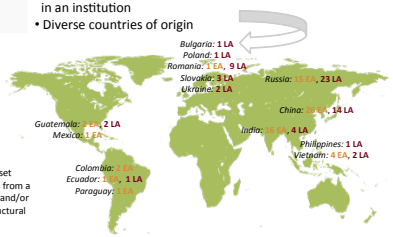
- PI children are at risk for earlier puberty (e.g. van IJzendoorn & Juffer, 2006), especially PI children with increased growth stunting at adoption followed by rapid catch-up growth (Johnson, 2002)

**This study characterizes the lasting impacts of early life stress on the intersection of physical growth, pubertal development, and prefrontal cortex volume in youth adopted internationally from orphanage care.**

## Participants

12-14 year old children either adopted internationally from institutional care or raised in Minnesota with their biological family

| Non-Adopted Control Children | Early Adopted (PI-EA) | Late Adopted (PI-LA) |
|---|---|---|
| N = 112 *(65 females)* | N = 69 *(52 females)* | N = 63 *(35 females)* |
| Not adopted | Adopted before 12 months | Adopted between 13-72 months |
| • No developmental, neurological, or psychiatric disorders | • No FAS or developmental disorders<br>• At least 50% of pre-adoptive care spent in an institution<br>• Diverse countries of origin | |




**Demographics:** Both PI and control children lived primarily in two-parent families, with most households having at least one parent who had completed college or a graduate level degree. Unlike PI children, control children were predominantly Caucasian.

**Excluded Participants:** The final data set described above includes participants from a larger project who provided pubertal and/or growth measures and segmented structural MRI data of acceptable quality.

## Methods

**Early Growth Measures in PI Children:**

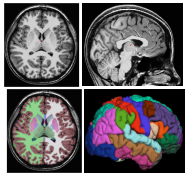
- *Z-scored height, weight, head circumference, and weight for height for age* from medical records of first post-adoption visit (WHO, 2006)

**Adolescent Growth Measures:**

- *Z-scored height and weight for age* from laboratory visit measurements (CDC, 2000)

**Puberty Measure:** Petersen Self-Rating Scale for Pubertal Development (Petersen et al., 1988)

- *Self-report measure* completed by the adolescent, assessing growth in height, growth of body hair, changes in skin, changes in voice and growth of facial hair (males), and breast development (females) along a 4 point Likert-scale and presence of menstruation (females)
- Reflects changes in adrenal, gonadal, and growth hormones
- Used to create both *continuous and categorical measures of pubertal development*



**Structural MRI Scan:** T1-weighted 3D MPRAGE anatomical series acquired on a Siemens 3T Trio Scanner

- TR = 2530 ms, TE = 3.56 ms, FOV = 256 mm, flip angle = 7 degrees
- 1 mm iso-voxel, 240 sagittal slices

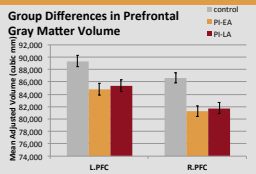
**MRI Analyses**: Freesurfer Image Analysis Suite was used to obtain automated, volumetric segmentation data

- Segmentation quality was hand-checked
- Analyses included age and sex as covariates

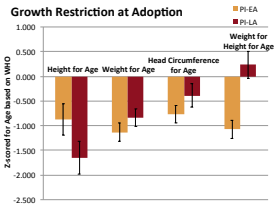
## Previous Results

Both earlier- and later-adopted PI children have reduced prefrontal cortex gray matter volume in comparison to non-adopted controls, even after adjusting for head size (Hodel et al., in prep).

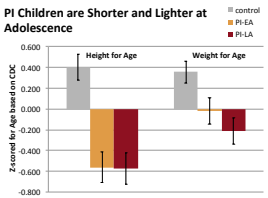
**Are prefrontal volume differences in PI adolescents related to broad alterations in physical growth?**




## Results: Growth Following Early Life Stress

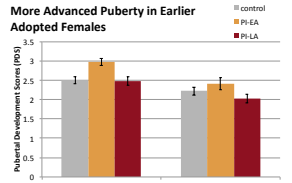



PI children showed evidence of growth restriction at adoption. Longer institutionalization predicted greater height stunting at adoption ($p=.25$, $p<.02$).



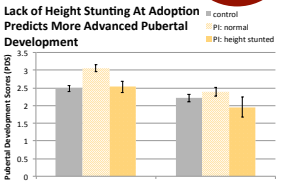

PI youth were shorter and lighter at adolescence than non-adopted peers. Height, weight, and head circumference at adoption predicted height and weight at adolescence (driven by later-adoptees).

## Results: Growth & Pubertal Development




Earlier-adopted children reported more advanced puberty than later-adopted children and non-adopted controls.

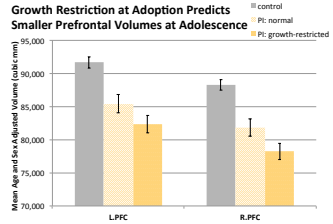
Younger age at adoption predicted more advanced pubertal development in PI youth ($p=-.37$, $p<.01$).




Height stunting at adoption predicted pubertal status ($p=.28$, $p<.01$); PI children with less height stunting at adoption reported more advanced puberty than height-stunted PI children and non-adopted controls.

Wasting (low weight for height at adoption) predicted more advanced pubertal status ($p=-.36$, $p<.01$).

## Results: Growth & Prefrontal Development




PI children who fell 1.5 *SD* below the z-scored mean for height, weight, or head circumference for age at adoption had reduced prefrontal volume versus PI children without growth restriction and non-adopted controls, even after controlling for measures of current body size.

## Conclusion

**Growth measures at adoption in post-institutionalized children provide a marker of developmental risk across intertwined biological systems.**

**Growth restriction at adoption is related to both pubertal timing and prefrontal cortex volume during early adolescence.**

- Both earlier and later adopted PI children showed evidence of growth restriction at adoption and remained shorter than their non-adopted peers at adolescence.
- More advanced pubertal development was reported by earlier-adopted children and by children who were less height-stunted at adoption (driven by earlier-adopted females).
- PI children who were more growth restricted at adoption showed the greatest decreases in prefrontal cortex volume at adolescence.

**A better understanding of catch-up growth, ethnicity effects, and longitudinal change will help explain how early life stress, growth, pubertal timing, and brain development interact, and how these factors may relate to the heightened risk of behavioral and emotional problems in PI adolescents.**

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