# Functional Measures of Prefrontal Regulation in Adolescents Experiencing Early Deprivation

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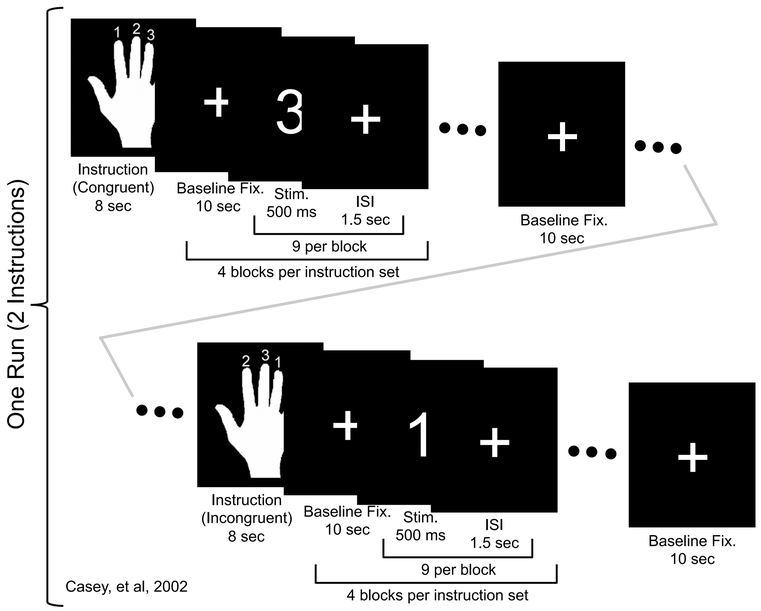
## Introduction

Children reared in orphanages experience deprivation as a result of inadequate physical care, and/or lack of cognitive and socio-emotional stimulation. Some domains improve following adoption; however, cognitive and emotional problems often persist. Previous studies have suggested altered structure and connectivity in this population. Few studies have addressed functional development of prefrontal regulatory systems. **The current study examined behavioral and neuroimaging measures of prefrontal function in post-institutionalized (PI) youth, emphasizing the effects of duration of deprivation.** Forty-eight PI youth (12-14 yrs.) and 24 non-adopted (NA) controls performed a cognitive conflict task involving motor relearning during fMRI scanning. PI youth were either early-adopted (EA; N=24) or late-adopted (LA; N=24).

## Behavioral Task




Task

Manual response, cognitive conflict task
Visual stimulus (1, 2, or 3) presented for 500 msec.
Each numerical stimulus is mapped to a specific finger response.
Participant must respond with corresponding button press.

Stimulus-Response Mappings

Number-to-finger mapping difficulty was manipulated.

- Congruent: Index-Middle-Ring : 1-2-3
- Incongruent: Index-Middle-Ring : 2-3-1 or 3-1-2

Stimulus-response mappings changed during the course of each scan, requiring participants to relearn response contingencies.

Runs

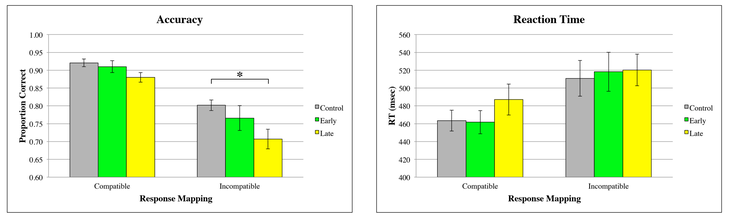
4 runs, each with one set of Congruent and one set of Incongruent response contingencies (sets contained 4 blocks of the same type).
Block order was pseudo-randomized within and across runs.
Participants responded using their dominant hand.

## Participants

| Group (F/M) | Age Test [SD] | Age Adopt [SD;range] | Time In Inst. [SD] |
|---|---|---|---|
| Non-Adopted (16/8) | 13y4m [6.4m] | --- | --- |
| Early-Adopted (13/11) | 13y2m [7.2m] | 8.0m [2.3m; 4-12m] | 7.3m [2.1m] |
| Late-Adopted (13/11) | 12y10m [6.5m] | 24.4m [10.5m; 13-51m] | 21.0m [8.4m] |

- PI youth were adopted from non-US orphanages into MN families (16 S.E. Asia; 28 Europe; 4 S. America)
- PI youth were institutionalized at 0 to 22 months of age for a minimum of 4 months and at least 50% of their pre-adoptive life (M=2.1m; SD=4.7m)
- Normal or corrected-to-normal vision
- No evidence of FAS or neurological disease

## Behavioral Performance




PI youth were less accurate and slower to respond than typically-developing controls, suggesting the task was more effortful for PI youth. All participants had accuracy greater than 70% for Congruent trials.

**Accuracy**: Responses to Incongruent mappings were less accurate than responses to Congruent mappings ($F(1,69)=107.1$, $p<.001$), and accuracy was lower as a function of duration of institutionalization ($F(2,69)=3.7$, $p<.05$). Accuracy for Incongruent trials was significantly lower for Late-adopted PI youth than for Controls (Tukey, $p<.05$).

**Reaction time**: Congruent mappings produced faster reaction times than Incongruent mappings ($F(1,69)=43.4$, $p<.001$). No significant differences in reaction time were observed between groups for Congruent or Incongruent response mappings (all $p>.05$). Z-score normalized reaction times produced equivalent findings.

## Neuroimaging Methods

Magnet: Siemens 3T Tim Trio with 12-channel phased-array head coil
Structural: MPRAGE, 1.0 mm isovoxel, 50% gap
Fieldmap and Functional: EPI, 34 interleaved axial slices, 3.125 x 3.125 x 3.0 mm voxels, 33% gap
Data processing (FSL)

- B0 unwarping
- Motion and slice-time correction
- High-pass filtering and spatial smoothing (6mm FWHM)
- Co-registration with structural volume
- Transformation into 2 mm MNI space
- Block design with fixation as baseline
- Focused on group differences in Incongruent > Congruent

Areas of significant activation were identified using a whole-brain voxel-wise analysis at $p<.005$ with a minimum contiguous volume criterion of 390 $mm^3$ (equivalent to 10 functional voxels, including the gap).

## Neuroimaging Results

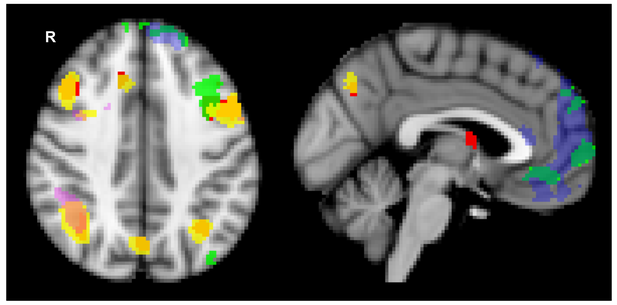
**Task effect: Incongruent > Congruent**

Non-adopted, Early-adopted, and Late-adopted youth all activated a similar brain network, suggesting that differences in behavior are not due to differential network recruitment among groups. LA youth showed the greatest area of extent, followed by EA youth, and NA controls. Activation included bilateral insula, lateral frontal pole, inferior and middle frontal gyri, paracingulate gyrus, superior frontal gyrus, supramarginal gyrus, superior parietal lobule, lateral occipital cortex, and precuneus.

**Group differences in task effect: Incongruent > Congruent**

Summary

- Any institutionalization: Left DLPFC
- EA youth only: Medial prefrontal cortex
- LA youth only: Right DLPFC and Right posterior parietal cortex




PI > Ctrl (Red / Orange underlay)
- Bilateral dorsolateral prefrontal cortex (DLPFC)
- Right anterior cingulate cortex
- Bilateral posterior parietal cortex
- Precuneus
- Left thalamus

LA > Ctrl (Yellow overlay)
- Co-active with PI > Ctrl, except in left thalamus

EA > Ctrl (Green overlay)
- Co-active with LA > Ctrl in L DLPFC
- Left DLPFC activation extends rostrally and dorsally
- Bilateral frontal pole

LA > EA (Pink overlay)
- Partially co-active with LA > Ctrl in right DLPFC
- Co-active with PI > Ctrl and LA > Ctrl in right posterior parietal cortex

EA > LA (Blue overlay)
- Anterior and inferior frontal pole
- Left middle temporal gyrus
- Left hippocampus

## Conclusions

- Behavioral and functional imaging results support the hypothesis that early deprivation is associated with long-term alterations in the development of prefrontal circuitry, and that developmental outcomes vary with individual differences in early experience.
- PI children showed increased activity in DLPFC compared to non-adopted controls, suggesting that factors associated with even brief periods of early deprivation may have long-term impacts on prefrontal function.
- Prefrontal cortex and other regions showed additional effects of duration of deprivation. Recruitment of additional regions in EA youth may reflect compensatory activity, given this group's normative task performance. The function of additional activity in LA youth is unclear.
- Future work will investigate whether activity in these regions predicts behavioral performance for the different groups.

Casey, B. J., Thomas, K. M., Davidson, M. C., Kunz, K., & Franzen, P. L. (2002). Dissociating striatal and hippocampal function developmentally with a stimulus-response compatibility task. *Journal of Neuroscience,* 22, 8647-8652.

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