Data Supplement for Barch et al., Effect of Hippocampal and Amygdala Connectivity on the Relationship Between Preschool Poverty and School-Age Depression. Am J Psychiatry (doi: 10.1176/appi.ajp.2015.15081014)

## **Supplemental Materials**

## Participants

Participants were 105 children (54 females) from a larger sample enrolled in the 12-year longitudinal Preschool Depression Study (N=305 at baseline, between ages 3 and 6). Children were invited to participate in the scanning portion of the study if they were psychiatrically healthy or if they had experienced a history of clinical depression or anxiety. Children with only a history of disruptive disorders were not invited to participate in the scanning portion of the study. A total of 169 of the original Preschool Depression Study children were invited to scan, along with an additional 41 new healthy children (who did not have preschool income or depression data, and thus were not included in the current study). Sixteen of the remaining children did not have income-to-needs information available (primary due to the absence of family size information. Twelve children completed part of the scan session, but did not complete either resting-state scan. Thirty-six children did not have scan data that passed our very stringent movement correction procedures and criteria, outlined below. In addition, 102 of the 105 children in the final sample had two resting-state runs.

## **Functional Connectivity Data Processing**

Resting-state functional connectivity processing occurred in three stages using in-house software. First, nuisance variables were regressed from the BOLD data (average signal from the ventricles, white matter, and whole brain as defined by FreeSurfer segmentation as well as 6 head realignment parameters and their derivatives [24 parameters from Volterra series

expansion]), a temporal band-pass filter was applied (0.009 Hz < f < 0.08 Hz), and spatial smoothing was applied (6 mm full width at half maximum). Average global signal and its derivate were regressed out of the BOLD data, which has been shown to reduce motion and signal artifacts (1–4).

Next, frames with excess head motion artifact were censored based on frame-wise displacement (FD) as previously described by Power et al. (3). FD is a sum of the absolute values of the six linear and rotational head displacement values from the realignment parameters estimated in step 4 of the above preprocessing (the three rotational values are converted to millimeters as displacement on the surface of a sphere of radius 50 mm). Volumes with FD >0.2 were censored from all subsequent analyses. Furthermore, any scan runs with less than 40 frames remaining after censoring and participants with less than 110 total frames remaining across all available runs were excluded from further analyses. Finally, the initial rs-fcMRI processing (nuisance regressors, band-pass filtering, smoothing) was reapplied to the raw data (output of the initial preprocessing) interpolating over the frames censored in the previous stage (3).

## Is the Relationship Between Income-to-Needs Ratio and Amygdala/Hippocampal Connectivity Accounted for by Amygdala/Hippocampal Volume?

As noted, numerous studies have found that poverty predicts hippocampal and amygdala volume, including our own previous work on the hippocampus. Partial correlations controlling for sex and age at scan indicated that income-to-needs again predicts both left (r = .20, p = .029) and right (r = .26, p = .006) hippocampal volume and both left (r = .25, p = .007) and right (r = .17, p = .047) amygdala volume. However, partial correlations controlling for age and sex reveal only a single significant relationship between either left or right hippocampal volume and left hippocampus to posterior cingulate connectivity; r = .21, p = .023). There were two significant

correlations with right amygdala volume, and two significant correlations with left amygdala volume: 1) left amygdala to left middle temporal gyrus; r = .23, p = .015); and 2) right amygdala to left paracentral; r = .20, p = .029). However, none of these correlations between volume and connectivity survived Bonferroni correction, and none were significant with the connectivity measures that related to depression severity. Thus, the influence of income-to-needs on amygdala and hippocampal connectivity is at least partially independent of the effect of income-to-needs on amygdala and hippocampal volume.

#### Specificity to Negative as Compared to Anxious Mood or Life Events

Given that some previous studies have also linked amygdala connectivity to anxiety, we also examined whether income-to-needs or amygdala/hippocampal connectivity predicted anxiety or externalizing psychopathology at the time of scan. Income-to-needs was not significantly correlated with anxiety severity (r = -.04, p = .35), but was correlated with externalizing psychopathology (r = -.22, p = -.22). There was only one significant correlation with anxiety with connectivity, specifically with left amygdala to left putamen (r = .21, p = .017), but this relationship did not survive Bonferroni correction. There were two significant correlations between externalizing psychopathology and connectivity, left hippocampus to superior frontal cortex (r = .21, p = .03) and left amygdala to right precuneus (r = .22, p = .02), but neither of these correlations survived Bonferroni correction.

# Do Either Caregiving or Life Stress Mediate the Relationship of Poverty to Brain Connectivity?

*Stressful life events:* Both the PAPA and CAPA also reliably capture experiences of stressful and traumatic life events (5, 6). The sum number of instances of life events between baseline and time of scan were used for the current analysis.

Parental caregiving: At the second assessment wave (ages 4-7 years), parent-child

dyads were observed interacting during the "waiting task," a structured task designed to elicit mild dyadic stress (7). This laboratory task requires the child to wait for 8 min before opening a brightly wrapped gift within arm's reach. Children are told that they can open the gift once their caregiver completes questionnaires. Raters blind to the child's mental health status, trained to reliability, coded the interaction for caregivers' use of both supportive (e.g., praising the child for waiting) and nonsupportive (e.g., threats about negative consequences) strategies. This task has acceptable psychometric properties and is a well-validated and widely used parenting measure (7-9).

To examine whether supportive or hostile caregiving or stressful/traumatic life events mediated the influence of poverty on amygdala or hippocampal connectivity, we examined Pearson's product moment correlations (SPSS Statistics v21 (IBM Corp., Armonk, N.Y.) between activity in each of the regions identified in the income-to-needs regression and maternal caregiving and life events. When a correlation was obtained, we tested for mediation using bias-corrected 95% confidence intervals using bootstrapping with n = 10,000 resamples via the PROCESS procedure for SPSS (10, 11).

There were no correlations with supportive parenting. Two regions showed significant correlations with nonsupportive parenting, with a positive correlation between left hippocampal to fusiform connectivity (i.e., more nonsupportive parenting associated with less negative connectivity) and a negative correlation between left hippocampal to posterior cingulate connectivity (i.e., more nonsupportive parenting, less of the normative positive connectivity). Greater stressful life events were positively correlated with connectivity between left amygdala and right superior frontal gyrus (i.e., greater stressful events, less of the normative negative connectivity). However, neither nonsupportive parenting nor life stress were significant mediators of the relationship between poverty and amygdala/hippocampal connectivity (all 95% bootstrap confidence intervals included 0).

## Supplemental References

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