



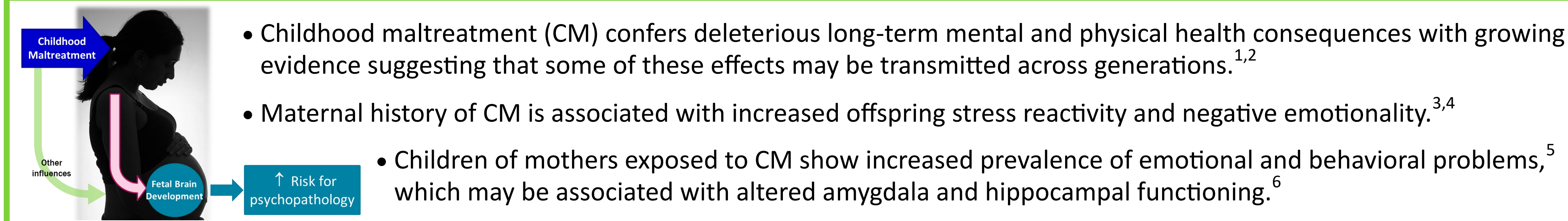
# A history of maternal childhood maltreatment is associated with neonatal amygdala and hippocampal resting state functional connectivity

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## Introduction—Maternal childhood maltreatment history may be a risk factor for offspring psychopathology



## Participants—65 mother-infant dyads at UC, Irvine

- Mothers completed the Childhood Trauma Questionnaire (CTQ)<sup>7</sup> midgestation; CTQ total score was log-transformed

### Exclusion criteria

- Mothers:** psychotropic medication, substance use, steroid use; high-risk pregnancy
- Infants:** congenital, genetic, neurologic disorders; pre-term birth (<34 weeks)

	Mean (SD) or N
Maternal age in 1 <sup>st</sup> trimester, Years	27.72 (5.40)
Maternal CTQ total score	36.62 (14.92)
Infant gestational age at birth, Weeks	38.95 (1.43)
Infant age at rsFC MRI scan, Days	24.15 (10.65)
Infant Sex: Male	35 (53.8%)

## Resting-state functional connectivity MRI acquired during infant natural sleep

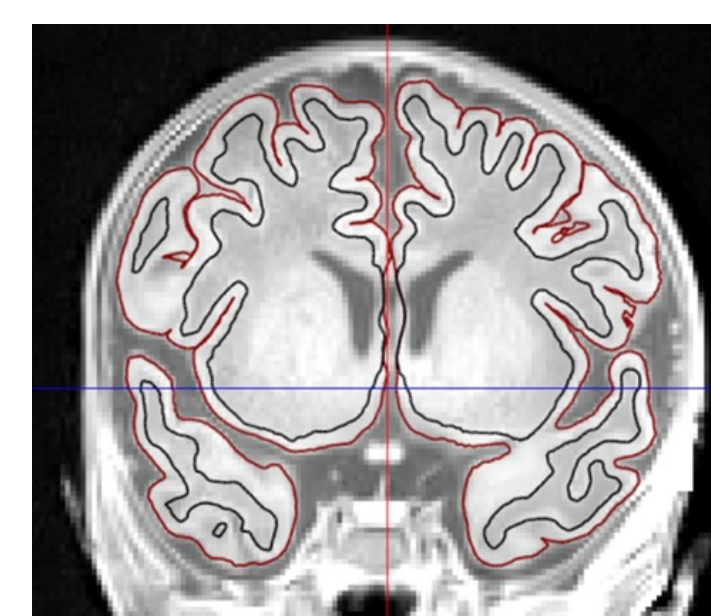
- Siemens 3T (TIM Trio)
- Volumes with framewise displacement >0.3 mm and functional scans with <4 minutes of data were excluded



T1	T2	rsFC
3D MP-RAGE	Turbo spin echo	Gradient-echo, EPT
TR/TE: 2400ms/3.16ms	TR/TE: 3200ms/255ms	TR/TE: 2000/30ms

## Amygdala and hippocampal connectivity to the cortex in association with maternal history of childhood maltreatment

- Cortical fMRI data processed through surface-based infant HCP-style pipeline
  - ANTs rician denoising, N4 bias field correction, and nonlinear warp used to improve masking/segmentation
  - Segmentations generated with ANTs JointLabel Fusion
- Left and right amygdala and hippocampus segmented using a multi-template based method combining T1 and T2 weighted high-resolution images with manual correction by Styner lab at UNC
- Individualized regions of interest (ROIs) transformed to atlas space and used as seeds for rsFC
- Each hemisphere's ROI blood oxygen-level dependent (BOLD) signal time series is correlated to each cortical vertices' times series
- Whole-brain greyordinate regression model performed using internal MPlus 8<sup>7</sup>
  - Predictor:** Log CTQ total score
  - Covariates:** Gestational age at birth and infant age at scan were included to account for neonatal brain maturity at the time of MRI scan acquisition; sex was included because of sex-specific differences in developmental trajectories and risk for psychopathology
  - Outcome:** Correlation vector between the amygdala or hippocampus timeseries and all cortical vertices' times series (left/right amygdala and hippocampus analyzed separately)
- Multiple comparison testing to identify significant regions using cluster-based detection
  - Cluster detection threshold of  $z=3.1$  ( $p=0.001$ ) to reduce false-positives in family-wise error based on Eklund et al.<sup>8</sup>



## Citations

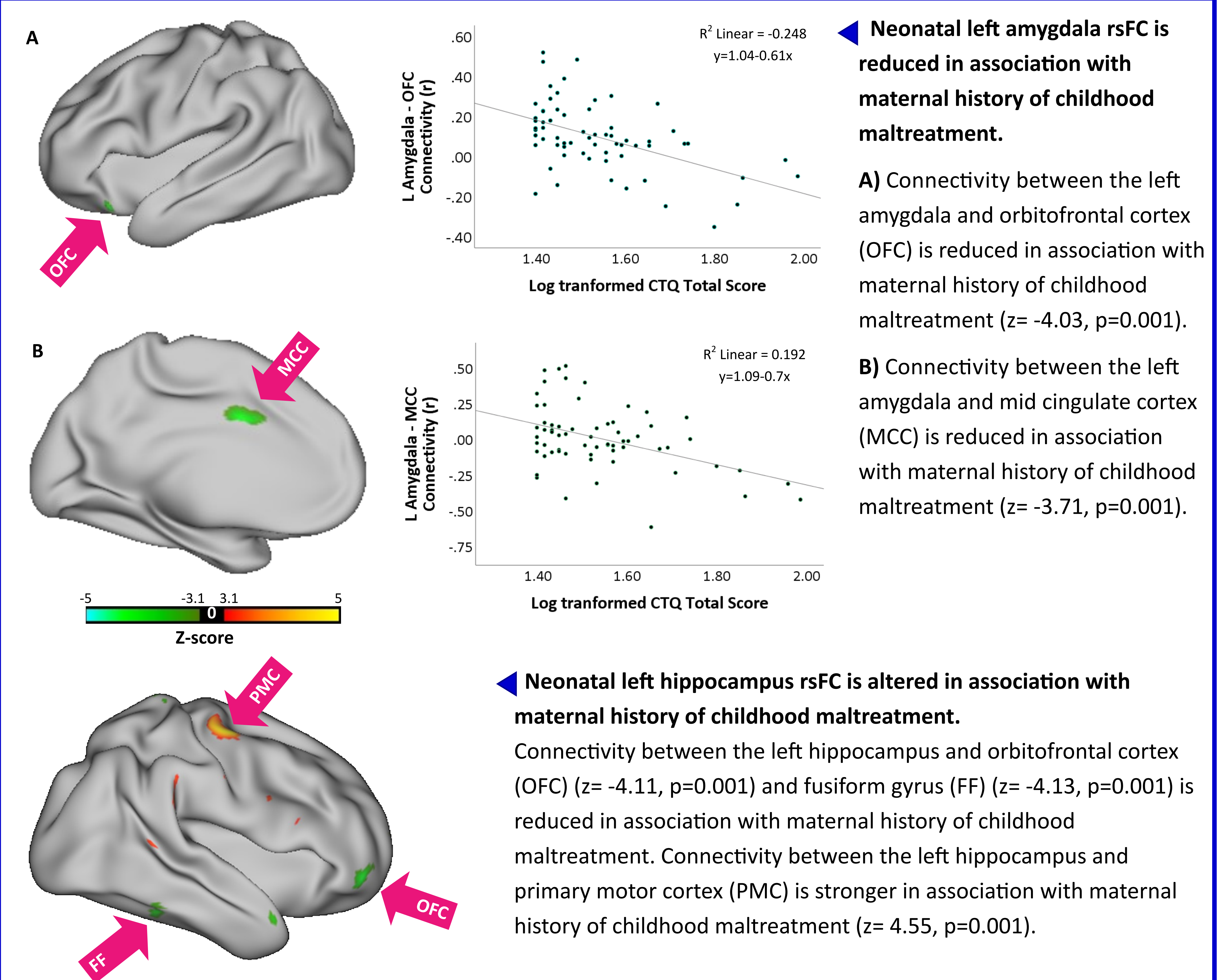
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## Results—Maternal history of childhood maltreatment is associated with alterations in offspring left amygdala and left hippocampus connectivity



## Discussion

- Maternal CM history is associated with reduced offspring amygdala OFC and MCC connectivity and may relate to increased prevalence of affective disorders in children of CM-exposed mothers.
  - The OFC is involved in impulse control, decision-making, learning and reinforcement, control of reward and punishment-related behavior, and modulation of physiological changes associated with emotion<sup>9</sup>; suppression of amygdala to OFC connectivity is thought to relate to anger and recklessness in PTSD.<sup>10</sup>
  - The MCC is involved in social decision-making<sup>11</sup> and emotional awareness.<sup>12</sup> MCC disease vulnerabilities include depression and PTSD<sup>13</sup> with one study suggesting that alterations to the MCC may represent familial risk for PTSD.<sup>14</sup>
  - Alterations in amygdala to OFC and cingulate cortex connectivity have been demonstrated in adult studies of PTSD.<sup>15</sup>
- Maternal CM history is associated with reduced hippocampus OFC and FF connectivity and stronger hippocampus PMC connectivity.
  - The primary motor cortex is involved in voluntary movement.<sup>16</sup> Increased motor cortex activation has been reported in PTSD and is thought to be related to autonomic stress response regulation.<sup>17,18</sup>
  - The fusiform gyrus is involved in object, facial, and pattern recognition.<sup>19</sup> Alterations in hippocampal to fusiform gyrus connectivity have been shown following childhood maltreatment.<sup>20</sup> There is evidence of alterations in limbic to sensory processing and integration regions following pre- and postnatal exposures.<sup>21</sup>
- Since alterations in amygdala and hippocampal connectivity can be observed shortly after birth, this effect may originate during the child's intrauterine period of life.
- Future work aims at identifying environmental and maternal biologic mediators that might underlie the intergenerational transmission of maternal childhood stress.