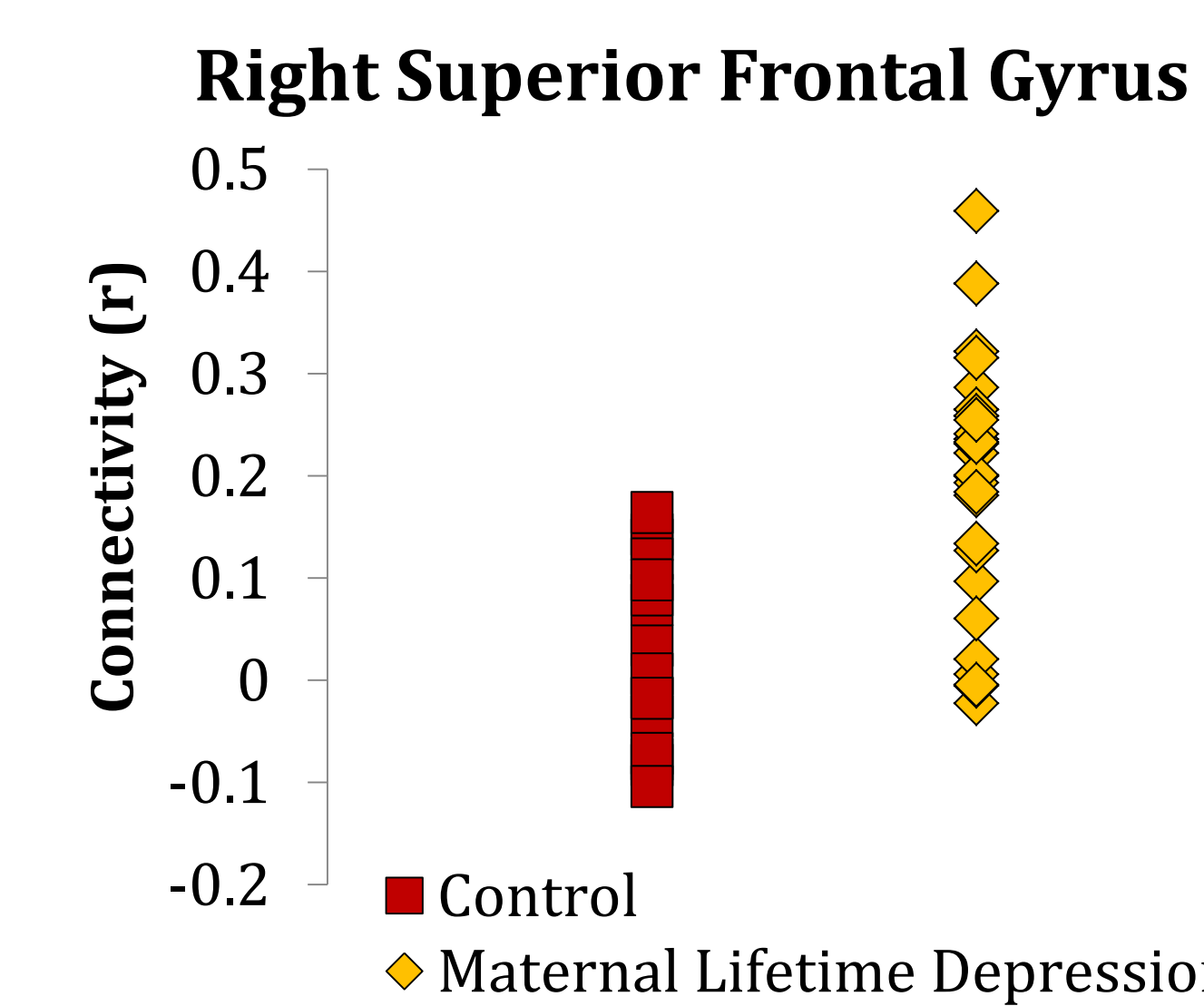
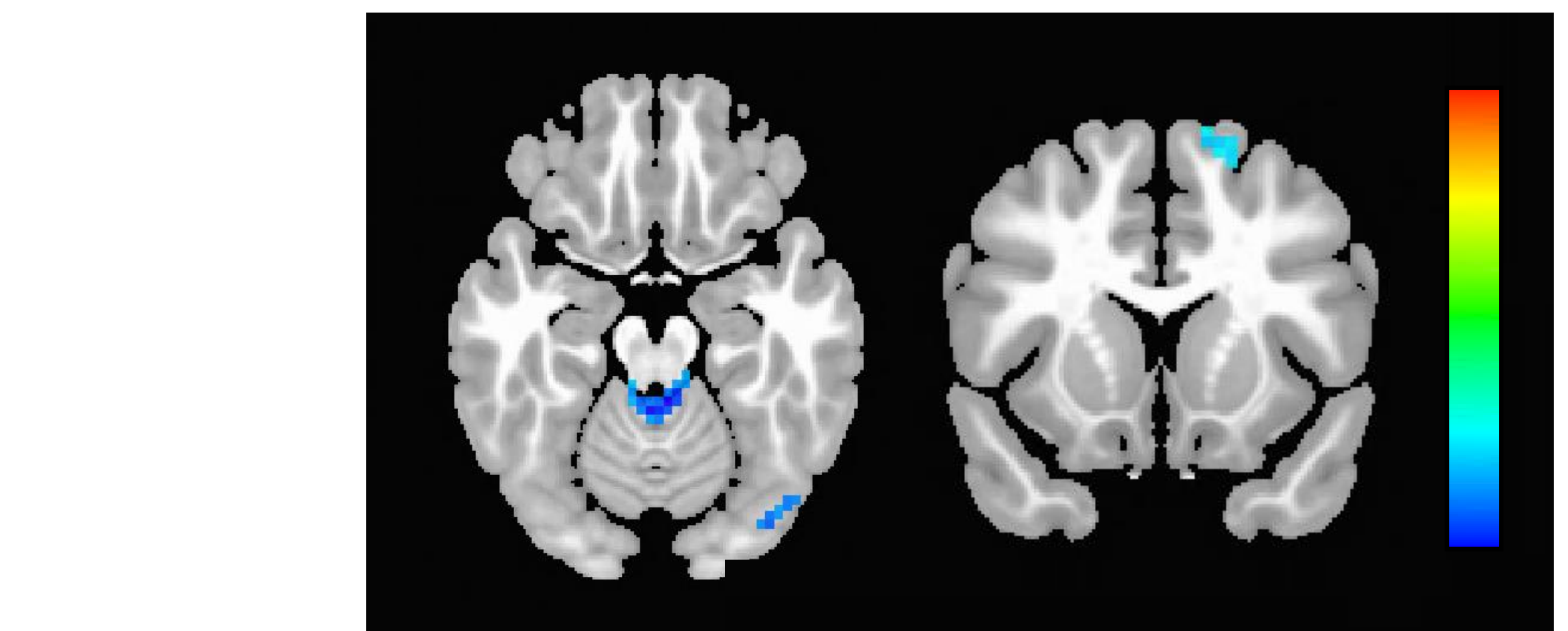
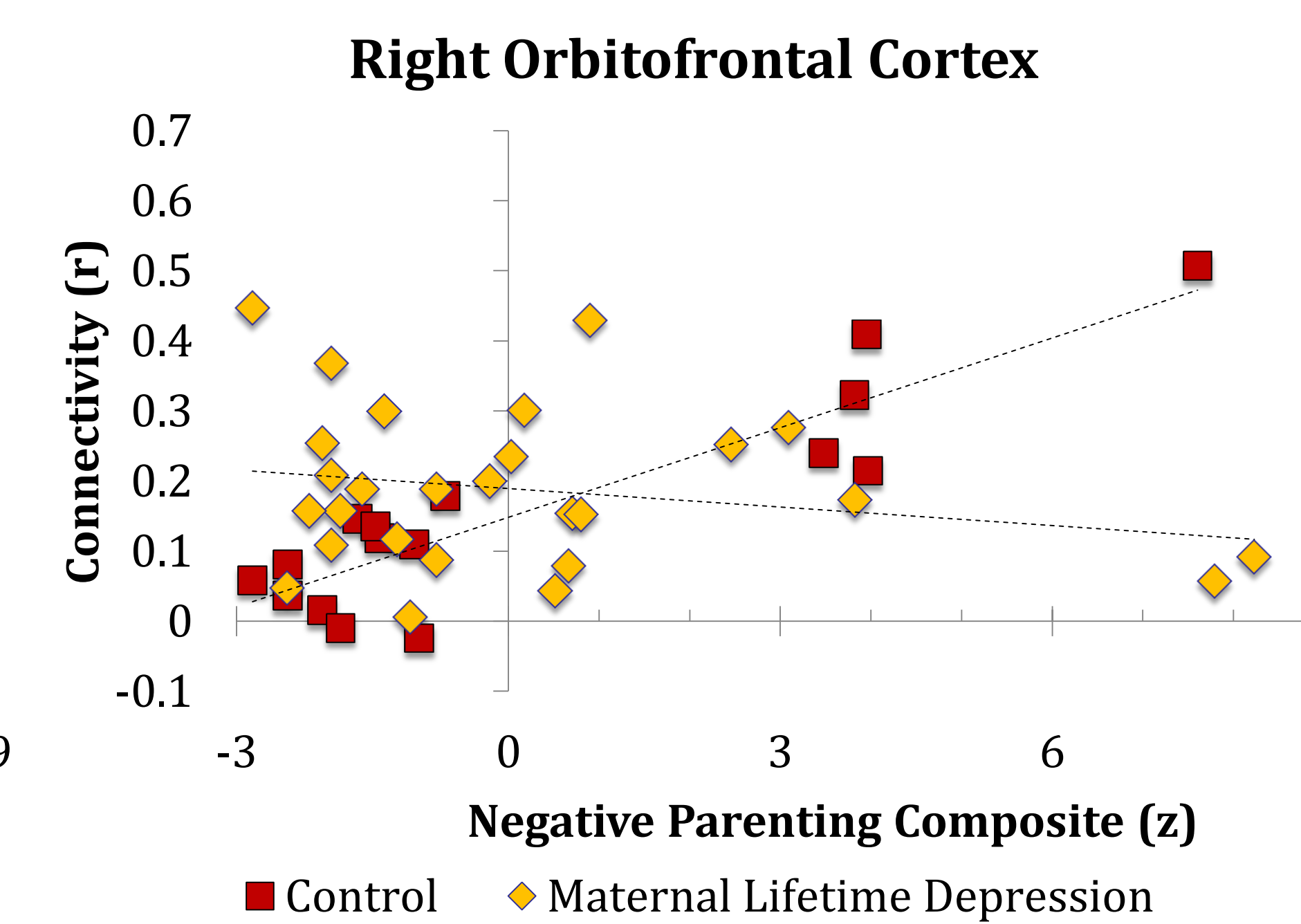
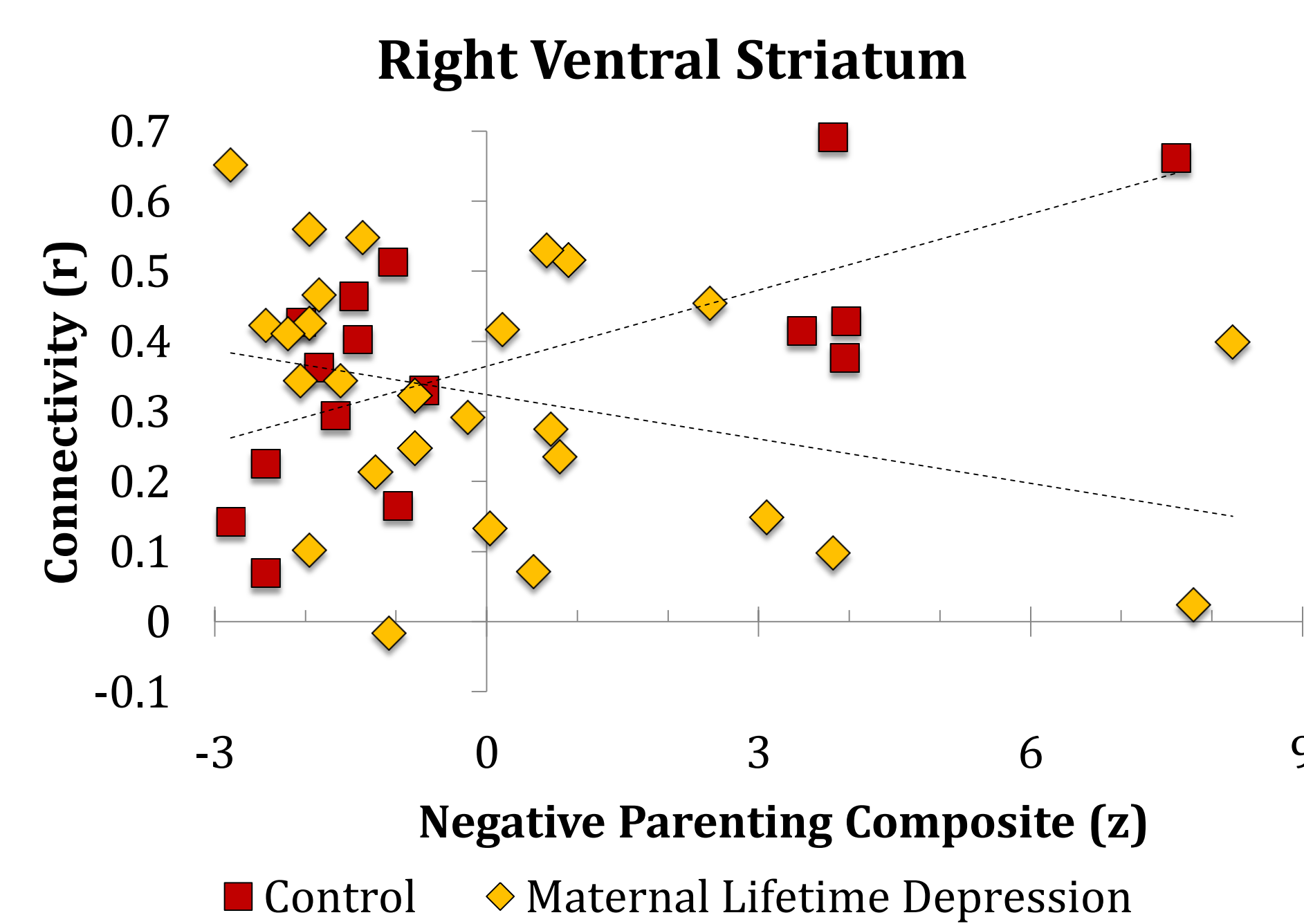
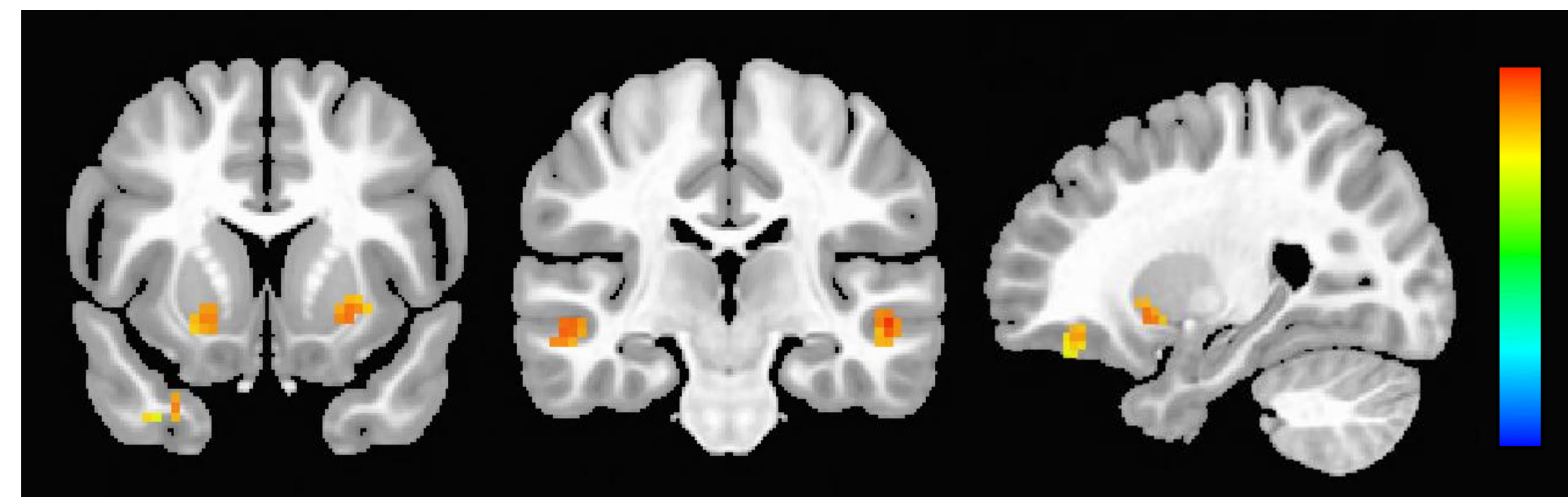


Introduction

Interaction Between Parenting and Maternal Depression

Main Effect of Maternal Lifetime Depression

- Offspring of depressed mothers are at increased risk for emotional and behavioral disorders and social impairment.
- Negative parenting styles have been proposed as one mechanism of transmission of risk.
 - Depressed mothers display higher levels of hostility and intrusiveness than non-depressed mothers (Lovejoy et al., 2000).
 - These parenting styles associated with maternal depression may impact children's neural and behavioral development.
- The hippocampus, a medial temporal lobe structure, has been shown to be particularly sensitive to the early parenting environment.
 - For example, rat pups of low licking-grooming mothers demonstrate changes in hippocampal structure and function. Similar structural changes have been documented in humans experiencing extreme levels of negative parenting (e.g., abuse, neglect) (Belsky & de Haan, 2011; Champagne et al., 2008; Liu et al., 2000; Luby et al., 2012; Rao et al., 2010).
- Moreover, adults with depression show changes in hippocampal morphology, suggesting the hippocampus plays a role in the pathophysiology of the disorder.
- The relation between maternal depression and early parenting on the development of offspring's hippocampal networks may elucidate mechanisms that contribute to increased risk for negative outcomes in children of depressed mothers.



Region	k	x	y	z	t
Cerebellum	45	4	-41	-20	-4.15
Right Superior Frontal Gyrus	22	13	16	67	-3.68
Inferior Occipital Gyrus	20	37	-83	-20	-3.23

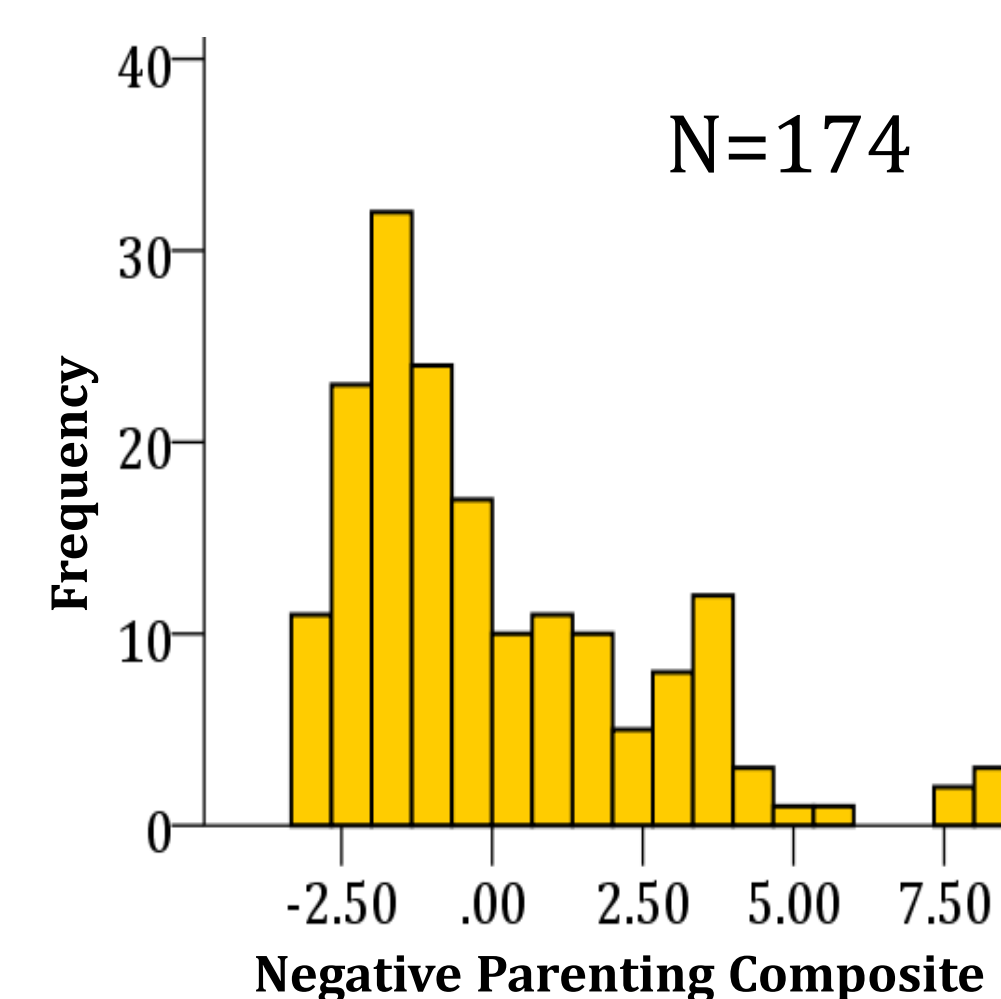
Offspring of mothers with a lifetime history of depression demonstrated greater hippocampal connectivity in cerebellum, SFG, and Inferior Occipital Gyrus than their non-depressed counterparts.

The present investigation sought to test the interaction between negative parenting and maternal lifetime depression on hippocampal connectivity, with follow-up analyses assessing the main effects of negative parenting and maternal lifetime depression.

Methods – Wave 1

Participants

- 174 children (85 male) aged 3-5 years ($M = 49.72 \pm 9.73$ months) participated in the first wave.
- Children were recruited based on their mother's lifetime history of depressive disorder (major depressive disorder (MDD) or Dysthymia), assessed using the SCID
 - No maternal lifetime depressive disorder ($n=83$)
 - Maternal lifetime depressive disorder ($n=83$)



Observational Parenting Assessment

- Children and their parents worked together to complete six tasks (e.g., Book readings, Maze, Blocks) modified from the Teaching Tasks Battery (Egeland et al., 1995)
- Each episode was coded on a 5-point scale
 - Maternal Intrusiveness, Maternal Hostility, and Maternal Support (reverse-scored) were combined across episodes and converted to z-scores for a composite measure of Negative Parenting

Region	k	x	y	z	t
Right Cerebellum	280	-2	-80	-38	4.52
Right Middle Temporal Gyrus	50	52	-26	-5	3.97
Right Orbitofrontal Gyrus	28	25	37	-14	4.14
Right Ventral Striatum	26	25	10	-8	3.2
Left Temporal Pole	23	-29	13	-35	3.76
Left Ventral Striatum	23	-20	13	-8	3.54
Medial Prefrontal Cortex	23	-2	40	52	2.98
Left Middle Temporal Gyrus	22	-53	-20	-5	3.57

Early negative parenting and maternal lifetime depression interacted to predict offspring's hippocampal connectivity. In offspring of mothers with no depression history, higher levels of early negative parenting predicted *increased* connectivity whereas in the offspring of mothers with a history of depression, greater early negative parenting was associated with *decreased* connectivity in a number of regions throughout the cortex.

- Negative Parenting behaviors demonstrated regionally-specific associations with hippocampal connectivity, resulting in increased or decreased connectivity.
- Offspring of mothers with a lifetime history of depression demonstrated greater hippocampal connectivity than their non-depressed counterparts in regions of the cerebellum and SFG.
- Our results provide evidence that parenting behavior interacts with maternal depression status, resulting in different patterns of hippocampal connectivity for the offspring of depressed and non-depressed mothers.
 - Offspring of non-depressed mothers show increased hippocampal connectivity with the right OFC and right ventral striatum in response to negative parenting whereas offspring of depressed mothers demonstrate decreased connectivity.
- These results provide valuable insights into the neural mechanisms that put offspring of depressed parents at increased risk for psychopathology.
 - The Fusiform Gyrus, a region implicated in face processing showed greater hippocampal connectivity with increased negative parenting, suggesting individuals with more negative parenting may have better memory for faces, which may make them more perceptive to changes in facial expressions.
 - Similarly, decreased connectivity with the medial prefrontal cortex may predict deficits in inhibition and emotion regulation.
 - Different connectivity profiles in the OFC and Ventral Striatum between offspring of depressed and non-depressed mothers may have important implications for emotion and reward processing, behaviors which have been implicated in the etiology of depressive disorders.
 - The different direction of effects may suggest a mediating effect of genetics, through increased risk or resilience.
- Future investigations should directly investigate the behavioral implications for the observed changes in connectivity

Discussion

Methods – Wave 2

Participants

- A total of 64 children have completed the Wave 2 Imaging session. Participants were excluded due to failure to complete the resting-state scan ($n=5$), motion exceeding 3mm (1 voxel) in any direction or rotation ($n=14$), or completing the scan with incorrect parameters ($n=2$). Data from 43 participants (23/53% female) aged 5-8 years ($M = 7.43 \pm 0.8$ years) were included in analyses.
 - No Maternal Lifetime Depressive Disorder ($n=16$)
 - Maternal Lifetime Depressive Disorder ($n=27$)

MR Data Collection

Functional and anatomical data were collected at the Maryland Neuroimaging Center using a 12-channel coil in a Siemen's 3T scanner. Participants watched a video of abstract patterns/shapes during a 6-minute acquisition of resting-state functional data.

Data Processing

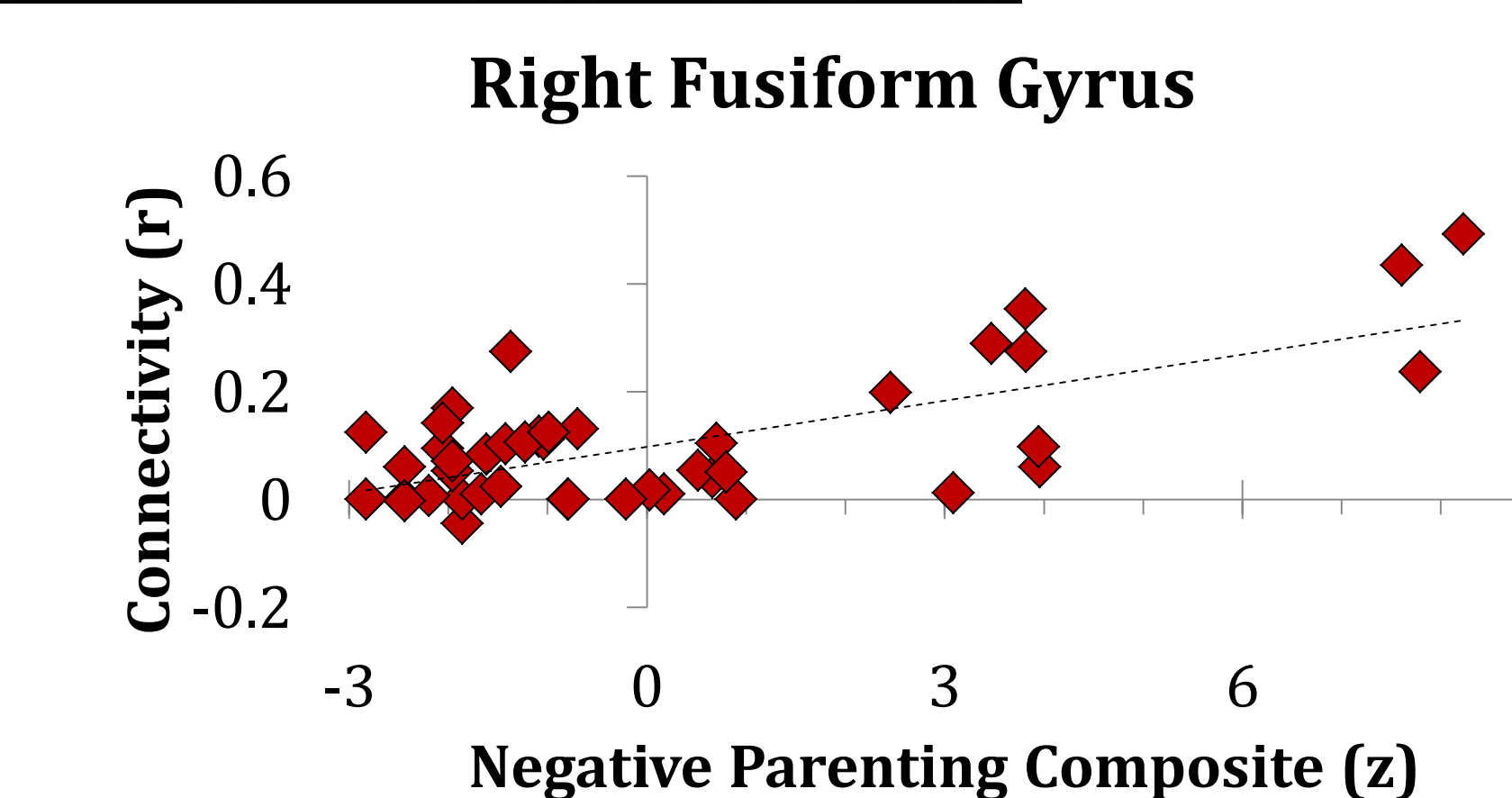
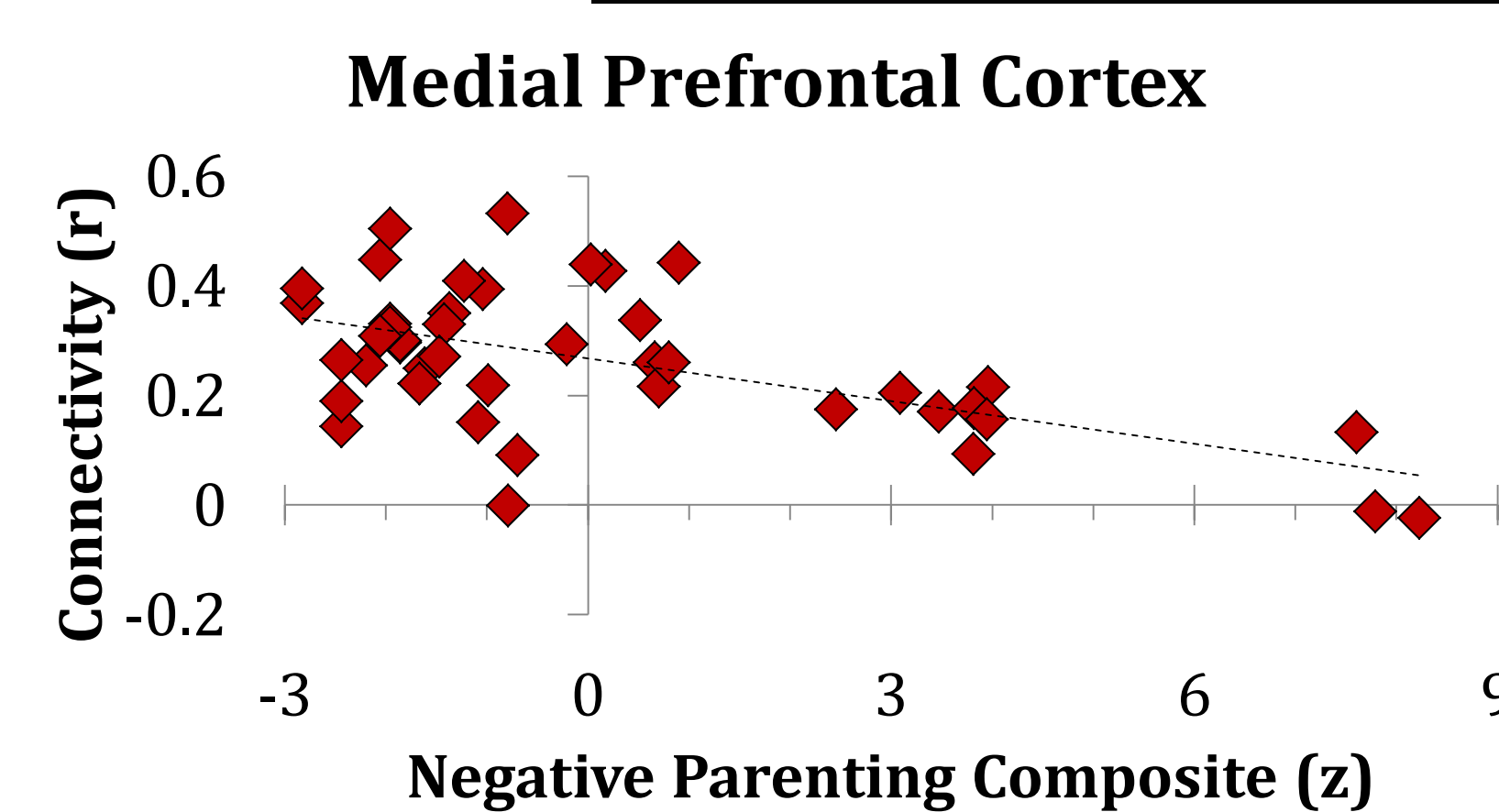
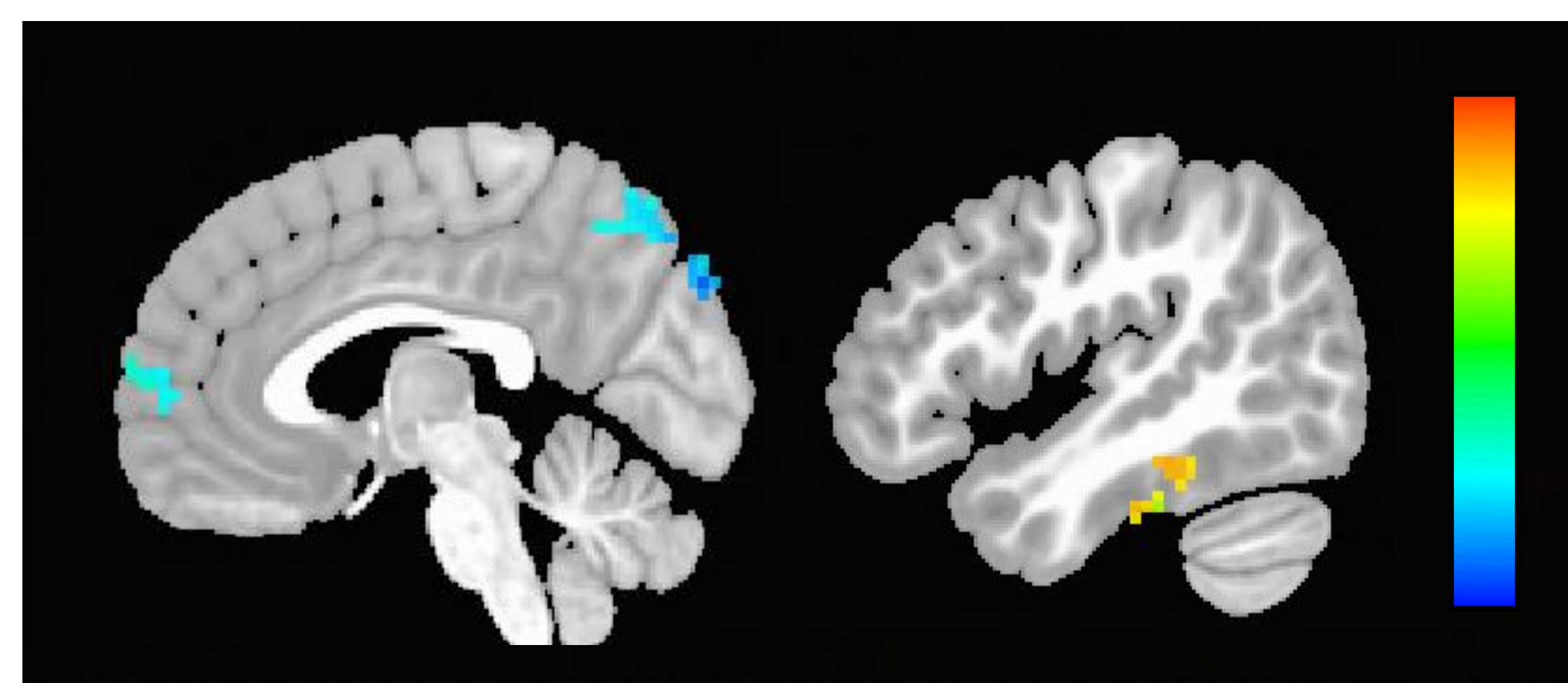
- All functional analyses were conducted using AFNI (Cox, 1996).
- BOLD signal from white matter and CSF masks and continuous motion regressors from 6 directions (roll, pitch, yaw, x, y, z) and their temporal derivatives were included as noise covariates.
- Data were band-pass filtered at $.009 < f < .08$.
- Framewise displacements > 1 mm were censored.

Analysis

Correlation coefficients were computed between bilateral hippocampal regions of interest and the whole brain using the Negative Parenting Composite and Maternal Depression status as covariates.

- Given the exploratory nature of the question and small sample size, results are thresholded at $p=.01$, uncorrected and limited to clusters > 20 voxels

Main Effect of Parenting



Region	k	x	y	z	t
Medial Prefrontal Cortex	54	-2	61	10	-3.46
Right Fusiform Gyrus	32	40	-23	-29	5.03
Left Precuneus	30	-5	-80	46	-3.06
Left Cuneus	29	-2	-89	34	-4.59
Left Posterior Hippocampus	27	-29	-38	1	3.04
Right Fusiform Gyrus	23	46	-35	-17	3.83

Early negative parenting demonstrated regionally-specific effects on hippocampal connectivity, with greater early negative parenting associated with decreased connectivity in some regions (e.g., medial prefrontal cortex), but increased connectivity in others (e.g., the right Fusiform Gyrus).

Note: There was no difference between Maternal Depression and Control subgroups on Parenting Composite scores ($p=.24$).

Acknowledgements

We would like to thank the families for participating in this study and members of CSEL, NCCL, and the MNC for assistance with subject recruitment and testing, particularly Marisa Tolep, Stephanie Merwin, Katherine Leppert, Heather Clark, Lauren Weiss, Alan Siegel, and Louis Marti. This research was supported by the University of Maryland (UMD) College of Behavioral and Social Sciences Dean's Research Initiative Award (LRD), the UMD Research and Scholars Award (LRD), the UMD MRI Dean's Research Initiative (LRD, TR), and the National Science Foundation (NSF) in partnership with the University of Maryland ADVANCE Program for Inclusive Excellence Award (LRD, TR).

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