**No Associations in Preregistered Study of Youth Depression and Functional
Connectivity of Fronto-parietal and Default Mode Networks**

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Abstract

Adolescence is characterized by vulnerability to the onset of major depressive disorder (MDD). The goal of this preregistered study was to assess neural correlates of depression symptoms in young adolescents, both cross-sectionally and longitudinally. The default mode network (DMN) is believed to support internal attention towards self-referential thoughts, while the fronto-parietal network (FPN) is theorized to support cognitive control and regulation of attention. As MDD diagnosis has been associated with heightened connectivity within DMN regions and diminished connectivity within FPN regions relative to healthy controls, our study builds upon group-difference analyses by using dimensional measures of depression severity. Our preregistered hypotheses were that within-DMN functional connectivity would be positively associated with concurrent depression severity, while within-FPN functional connectivity would be negatively associated with concurrent depression severity. Preregistered analyses also examined between DMN-FPN connectivity as an alternative predictor variable, and assessed the longitudinal associations between all three functional connectivity measures and change in depression severity over three subsequent waves. Multiple regression models tested cross-sectional analyses and hierarchical linear models tested longitudinal analyses. One hundred and twenty-four youth

completed a resting state functional MRI. Their depression severity was assessed at the time of the scan and at three follow-up sessions. None of the predictor variables were associated with concurrent or depression severity, nor with the slope of depression symptom trajectories in longitudinal analyses. These negative results add to extant cross-sectional studies, and may inform future investigations of brain correlates of depression psychopathology in youth.

Keywords: Adolescence; Depression; Longitudinal; Brain development; Resting state

MRI

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Major Depressive Disorder (MDD), characterized by a loss of interest and persistent low mood, is the leading cause of disability worldwide (World Health Organization, 2020) and contributes greatly to global disease burden (Murray et al., 2012). Around 2% of pre-pubertal children will receive a diagnosis of MDD, with that number rising to 7% or even 13% in adolescence (Perou et al., 2013; Bose et al., 2018). Youth depression predicts earlier recurrence and higher risk for other mood disorders (Kovacs, 1996), as well as a host of adverse socio-economic outcomes, including lower educational attainment (Clayborne et al., 2019), higher health-care utilization and increased work impairment (Keenan-Miller et al., 2007), and poorer mental health outcomes in adulthood (Fergusson & Woodward, 2002; D. Johnson et al., 2018). Most alarmingly, youth depression is a major risk factor for suicide (Kandel et al., 1991; Perou et al., 2013), the third leading cause of death for 5 to 14-year-olds (Kochanek et al., 2019). Therefore, youth depression is a serious health problem which requires extensive research efforts and immediate intervention.

Recent research initiatives, such as the Research Domain Criteria (RDoC), have

proposed that a mechanistic understanding of psychiatric disorders will lead to more accurate diagnoses and effective treatments (Insel et al., 2010). One proposed mechanism is that large-scale brain networks, when dysregulated, disrupt typical functioning and contribute to psychiatric disorders such as MDD (Menon, 2011). Resting-state functional connectivity MRI (rs-fcMRI), which measures correlations of spontaneous low-frequency fluctuation in blood oxygen level dependent (BOLD) signals among brain regions in subjects at rest (Biswal et al., 1995), allows neuroscientists to explore functional network structure of the brain (Bullmore & Sporns, 2009). It can be used to understand differences in network connectivity in clinical populations independent of any task paradigm, thereby avoiding confounders associated with task implementation (Fox & Greicius, 2010).

Previous rs-fcMRI studies have associated hyperconnectivity within the default mode network (DMN) regions with MDD diagnosis (Alexopoulos et al., 2012; Greicius et al., 2007; Jin et al., 2011; Kaiser et al., 2015; Rzepa & McCabe, 2018; Zhao et al., 2019; Zhu, Wang et al., 2012; Zhu, Zhu et al., 2017). Heightened within-DMN connectivity was also found among individuals with high familial risk for MDD (Posner et al., 2016; Shapero et al., 2019). The DMN, initially defined using rs-fcMRI (Greicius et al., 2003), is posited to

support a “task-negative mode” (Greicius et al., 2003; Raichle et al., 2001) and self-referential processes (Gusnard et al., 2001; Northoff et al., 2006; Sheline et al., 2009). Its key nodes include the medial prefrontal cortex (PFC), the precuneus, and the posterior cingulate cortex, all of which are believed to support self-related consciousness and mental representations (Cavanna & Trimble, 2006; Davey et al., 2016; Meyer & Lieberman, 2018; S. C. Johnson et al., 2002). The posterior cingulate cortex has been associated with optimizing the balance between externally- and internally-oriented attention (Shannon & Buckner, 2004; Singh & Fawcett, 2008). Rumination, a form of excessive, repetitive thinking about one’s feelings and problems without actively addressing these problems (Nolen-Hoeksema et al., 2008), is a maladaptive type of self-referential process. Rumination has been associated with increased negative affect (Mor & Winquist, 2002) and depressive symptoms (Sarin et al., 2005; Segerstrom, et al., 2000; Spasojević & Alloy, 2001). Therefore, it has been proposed that MDD patients exhibit hyperconnected DMN which underlies their excessive rumination (Alexopoulos et al., 2012; Berman et al., 2011), leaving insufficient attention and cognitive resources for external salient stimuli.

Hypoconnectivity within the frontoparietal network (FPN), which is believed to support top-down executive control (Dosenbach et al., 2007; Seely et al., 2007; Vincent et al., 2008), has also been associated with MDD diagnosis in several rs-fcMRI studies (Alexopoulos et al., 2012; Buchanan et al., 2014; Kaiser et al., 2015; W. Li et al., 2015; F. Pan et al., 2020; Wu et al., 2017). The network structure of the FPN was first defined using task fcMRI (Dosenbach et al., 2007). Key nodes of the FPN have been linked to major cognitive control processes which may be disrupted in depression. For instance, the intraparietal sulcus is believed to support top-down control of attention (Corbetta & Shulman, 2002), the lateral PFC has been associated with selecting responses most relevant to the goal while inhibiting irrelevant responses (Aron, Robbins, & Poldrack, 2004; Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Jiang & Kanwisher, 2003). Reduced within-FPN connectivity has been associated with greater cognitive impairments such as increased distractibility (Keller et al., 2019) and greater deficits in executive functions (Alexopoulos et al., 2012; F. Pan et al., 2020) in MDD patients. As MDD is characterized by moderate deficits across multiple cognitive domains (Millan et al., 2012; Rock et al., 2013; Zuckerman et al., 2018), within-FPN hypoconnectivity may contribute to cognitive dysfunctions in MDD (Cole et al., 2014).

Reduced connectivity between the FPN and DMN has also been highlighted by some previous rs-fcMRI studies in MDD patients (Kaiser et al., 2015) and in subclinical depression (Hwang et al., 2015) relative to healthy controls, and was associated with rumination (Connolly et al., 2013; Lydon-Staley et al., 2019) and other depressive symptoms (Hwang et al., 2015). Since the FPN is densely connected with many other large-scale networks (Marek et al., 2015; Power et al., 2013), its connections with attention networks such as the dorsal attention network and the DMN enable it to regulate the balance between external and internal attention resources (Dixon et al., 2018; Vincent et al., 2008). Therefore, reduced connectivity between the FPN and the DMN may reflect weak top-down FPN regulation of internally-oriented attention, leading to depressive symptoms such as excessive attention diverted to internal thoughts as opposed to the external environment (Kaiser et al., 2015; Marchetti et al., 2012; Nejad et al., 2013).

In summary, previous rs-fcMRI research has provided empirical support for heightened within-DMN connectivity, diminished within-FPN connectivity, and diminished connectivity between DMN and FPN as neural correlates of MDD. A previous study (Gaffrey et al., 2012) examined DMN connectivity seeded at the posterior cingulate cortex in a sample of young

adolescents from the same longitudinal cohort as the current study (i.e. the Preschool Depression Study). It found hyperconnectivity between posterior cingulate seed and medial prefrontal regions in children with a history of MDD diagnosis during preschool age relative to healthy controls, and reduced connectivity between posterior cingulate seed and lateral cortical regions. However, most of the previous adolescence literature have focused on cross-sectional associations, with only few longitudinal studies conducted (Connolly et al., 2013; Davey et al., 2015; Ellis et al., 2017; Hirshfeld-Becker et al., 2019; Jin, Narayanan et al., 2017; Jin, Van Snellenberg et al., 2020; P.M. Pan et al., 2017; Strikwerda-Brown et al., 2014). As such, these associations could not be used to establish a temporal relationship between functional connectivity and depression. Furthermore, research studying links between depression and functional connectivity prior to adolescence has been lacking (Luby et al., 2009). As a result, it is still unclear if mechanisms and neural correlates of childhood depression differ from those of adolescent and adult depression (Tang et al., 2018).

Preschool-onset depression has been found to be a strong predictor of developing MDD in later childhood (Luby et al., 2014) and thus requires further research and clinical attention.

The aim of this study was to test associations between *a priori* functional connectivity (i.e. within-DMN, within-FPN and between FPN-DMN connectivity) and youth depression both cross-sectionally and longitudinally. A sample from the Preschool Depression Study (PDS) was used to test the preregistered hypotheses that concurrent depression severity, assessed as the mean of parental and child reports, is positively associated with functional connectivity during rest within the DMN and negatively associated with functional connectivity during rest within the FPN. These associations, if significant, would lend support to the theory that adolescent depression results from excessive internal attention to self-referencing thoughts due to deficient frontal control. Additional preregistered analyses were conducted on the cross-sectional relationship between concurrent depression severity and inter-network functional connectivity. Longitudinal analyses tested whether any of the three functional connectivity metrics (i.e., within-DMN, within-FPN, and inter-network DMN-FPN) predicted change in concurrent depression severity over three subsequent assessments. On top of the preregistered analyses, follow-up analyses which were not preregistered assessed the same associations using a) concurrent depression severity reported

separately by parents and children and b) past depression severity as alternative outcome variables in all analyses.

Methods

1.1 Participants

Two hundred and sixteen 6 to 12-year-olds who had been followed longitudinally since preschool-age and 42 healthy controls (9 to 14-years-old) were eligible for the fMRI assessment. Of the 258 eligible subjects, 124 participants completed the fMRI and had usable functional connectivity data. Of those, 116 had available child-reported concurrent depression data, 117 had available parent-reported concurrent depression, and 82 participants had an available measure of past depression severity at time of scan. Mahalanobis distance was calculated for each multivariate relationship to be examined (e.g., within-network functional connectivity of the DMN and concurrent depression severity) and used to identify and exclude multivariate outliers with a threshold of $p < 0.001$ ($N=3$ for mean parent and child reported concurrent depression and within-network functional connectivity of the DMN or FPN; $N=2$ for mean parent and child reported concurrent depression and between DMN-FPN functional connectivity, and for concurrent depression reported by child alone and within-network functional connectivity of the DMN or FPN; $N=1$ for concurrent depression reported by parents alone and both within-network functional connectivity of the DMN or

FPN and between DMN-FPN connectivity, and for concurrent depression reported by child alone and between DMN-FPN connectivity;). Detailed demographic information can be found in Table 1. Parental written consent and child assent were obtained before participation and the local Institutional Review Board approved all procedures.

1.2 Measure of depression severity

There were two measures of depression severity used in the current study. Raw total scores from the Children's Depression Inventory (CDI) (Kovacs, 1985) were used to measure concurrent and longitudinal depression severity. The mean of child and parent report on the CDI was calculated for each assessment wave. CDI scores from three subsequent waves were used for longitudinal analyses. Of the 124 participants included in the longitudinal analyses, 119, 106, 94 and 94 had available CDI scores in the first to the fourth annual assessments, respectively.

Because the CDI scores had not been collected prior to the scan, mean number of core symptoms of depression endorsed from the beginning of the PDS study (i.e., at preschool age) to the time of scan was used to measure past depression severity. For all measures of depression, higher scores indicate greater depression severity.

1.3 Covariates

The following covariates were dummy coded: child's race (dummy coded using two variables: variable 1: White=1, Black=0; variable 2: Black=1, White=0), sex (male = 1, female= 0), past of MDD diagnosis (present = 1, absent = 0). The following continuous covariates were included: child's age at scan, income-to-needs ratio, concurrent anxiety severity at time of scan, and past anxiety severity. Concurrent anxiety severity was calculated as the number of core symptoms of generalized, social, and separation anxiety disorders, as well as post-traumatic stress disorder reported on the Child and Adolescent Psychiatric Assessment (CAPA; Angold & Costello, 1995; Angold et al., 1995) at the time of scan. Similar to the measure of past depression severity, past anxiety severity was calculated as the mean number of anxiety symptoms endorsed from start of the PDS study (i.e., at preschool age) to the time of scan on the Preschool Age Psychiatric Assessment (PAPA; Egger & Angold, 2004; Egger et al., 2006) when children were less than 8-years-old, and on the CAPA when youth were 8-years-old or older. The income-to-needs ratio was measured as the total family income divided by the federal poverty level based on family size (McLoyd, 1998).

1.4 Neuroimaging

1.4.1 Data acquisition

Functional magnetic resonance imaging (fMRI) data were acquired using a 3.0T Siemens Prisma scanner. Resting-state functional MRI (rsfMRI) was acquired with an echoplanar imaging sequence (TR=720ms, TE 33ms, FOV=216mm, flip = 52 degrees, voxel size 2.4 x 2.4 x 2.4, 63 slices, Multiband=7). A T1-weighted anatomical image was acquired for spatial normalization and functional localization (TR=2400ms, TE 2.22ms, flip angle=8 degrees, 208 slices, FOV=240mm, voxel size 0.8 x 0.8 x 0.8).

1.4.2 Functional connectivity preprocessing

A combination of FSL and in-house MATLAB scripts were used for functional connectivity data preprocessing and analysis. EPI images were corrected for gradient distortions, readout distortions, and bias field using fieldmap correction. Images were realigned from multi-band functional frames to a single-band reference image, and resampled to 2mm isotropic and registered to the MNI152 atlas. High motion volumes were censored (0.2 mm frame displacement). Respiratory artifacts in head motion estimates were corrected using a 2nd order bandstop filter (0.31 Hz and 0.43 Hz). Volumes were demeaned and de-

trended using betas from low-motion frames. Signals of non-interest, including 24 motion regressors (6 head motion parameters, their derivatives and squares), the first five PCA components from white matter and CSF, whole brain global signal, and the global signal derivative, were entered as regressors, with betas computed from low-motion frames. Data were interpolated across censored frames and bandpass filtered at $0.009 \text{ Hz} < f < 0.08 \text{ Hz}$. Finally, data were smoothed using 4mm FWHM Gaussian kernel. Participants with at least 5 minutes of low-motion fcMRI data were included in analyses.

1.4.3 Extracting estimates of functional connectivity

Functional connectivity during rest was measured as the temporal correlation of BOLD signal activities within the FPN network and DMN network separately, as well as the correlation between the FPN and DMN networks. Networks were defined by the parcellation from Power et al. (2011). Pearson r correlations were calculated between mean timeseries for all voxels in each ROI forming subject-specific connectomes.

1.5 Statistical Analyses

Confirmatory and follow-up analyses and hypotheses are specified, with confirmatory analyses and hypotheses preregistered post data collection but prior to data analysis

(osf.io/zjpqu). Confirmatory analyses tested the preregistered hypotheses that concurrent depression severity, assessed as the mean of parental and child reports, would be positively associated with functional connectivity during rest within the DMN and negatively associated with functional connectivity during rest within the FPN. These hypotheses were tested using multiple regression models. Other preregistered analyses without specific hypotheses included testing the association between inter-network (i.e. between DMN-FPN) functional connectivity and concurrent depression severity using multiple regression models.

Longitudinal analyses also tested the relationship between baseline within-network and inter-network functional connectivity metrics and individual trajectories of depression severity using hierarchical linear modeling. Linear mixed effect models from the lme4 package in Rv3.6.0 (Bates, Mächler, Bolker, & Walker, 2015) were used to model fixed and random effects of intercept and slope parameters over four assessment waves. These models were used to test for associations between within-network and inter-network connectivity at time of scan and the slope of depression severity trajectories over the following three waves. In addition to the aforementioned covariates, psychotropic medication use was included as an additional covariate in supplementary analyses. The same set of cross-sectional and

longitudinal associations were re-analyzed in follow-up analyses using alternative outcome variables (i.e. past depression severity, concurrent depression severity reported by parents, and concurrent depression severity reported by children).

All analyses controlled for age, sex, race, ethnicity, income-to-needs ratio, past MDD diagnosis and anxiety severity. All continuous predictor and outcome variables were standardized to make regression estimates more interpretable. False discovery rate (FDR) multiple comparison correction was applied across models.

Results

2.1 Association between functional connectivity and concurrent depression severity

Neither within-DMN nor within-FPN functional connectivity were associated with concurrent depression severity at the time of scan (see Table 2). Inter-network functional connectivity between the DMN and the FPN was also not significantly associated with concurrent depression severity. All findings were consistent when child and parent reported concurrent depression severity were examined separately, and when psychotropic medication use was included as a covariate in analyses. When the same analyses were rerun examining past depression severity, findings were consistent, showing no significant associations with functional connectivity metrics.

2.2 Association between functional connectivity and depression severity trajectories

No function connectivity metrics of interest (i.e. within-DMN, within-FPN and between DMN-FPN functional connectivity metrics) were significantly associated with the slope of depression symptom trajectories (see Table 3). All findings were consistent when child and parent reported concurrent depression severity were examined separately, and when psychotropic medication use was included as a covariate in analyses.

Discussion

Neither preregistered analyses nor follow-up analyses found support for the hypotheses of the current study. Specifically, within-DMN functional connectivity, within-FPN functional connectivity, and DMN-FPN functional connectivity were not significantly associated with concurrent or past depression severity, nor predicted future change in individual depression severity trajectories.

Although we are cautious in drawing conclusions from null results, these results provide important caution for propositions that DMN, FPN, or between network functional connectivity during rest is a neural correlate of depression or depression risk across the lifespan. This is key information in evaluating support for theories that suggest that weak regulation from cognitive control networks to the extended medial prefrontal DMN network may underlie deficits in regulating excessive internally-oriented attention in depression. Such theories propose that imbalanced connectivity between the DMN and the FPN, coupled with a hypo-connected FPN and hyper-connected DMN, may underlie ineffective top-down regulation of negative emotions and attention, resulting in persistent negative mood and cognitive bias, dysfunctions across cognitive domains, as well as excessive internally-

oriented attention at the expense of attending to the external world in depressed patients

(Brzezicka, 2013; Kaiser et al., 2015; B. J. Li et al., 2017; Marchetti et al., 2012; Nejad et al., 2013).

The current study, then, may provide some insight into boundaries of this theory. For example, this theory was developed in large part using data from adult participants.

Clinically, depression in youth differs from adult manifestations of depression in important ways, such as greater irritability (Stringaris et al., 2013) which is classified as a core mood symptom for children and adolescents in the DSM-IV and DSM-5 (American Psychiatric Association, 2000, 2013). Neurally, basic science research shows that the DMN is sparsely functionally correlated during childhood, while it has developed into a tightly integrated network by the age of 21 (Fair et al., 2008) and that the FPN continues to change during preadolescence (Sherman, et al., 2014). Therefore, ongoing network development may lead to key differences in the neural correlates of childhood and adult depression. Cognitively, children may be continuing to develop cognitive control abilities and acquire more complex cognitive emotion regulation abilities into adolescence and adulthood (Larsen & Luna, 2018; Luna et al., 2015). Therefore, there are many reasons to believe that some of the brain

correlates of depression in youth may differ from those in adults. This question warrants future studies, in particular large-scale longitudinal studies such as the currently ongoing Adolescent Brain Cognitive Development study.

Although the current study failed to reject the null hypothesis, it had notable methodological strengths. It used a unique, longitudinal sample of youth prospectively assessed for depression severity, and accounted for covariates commonly associated with youth depression, such as socioeconomic status (Goodman et al., 2003; Pino et al., 2018). Furthermore, it was preregistered. There are inherent values in the publication of preregistered null results. Publication bias, which refers to the phenomenon that studies with negative results are more difficult to be published than those with positive results, have been found to increase over the years, especially in the field of social science (Fanelli, 2012; Nosek et al., 2018). Publication bias may encourage researchers to withhold their negative research findings, or even engage in questionable research practices such as p-hacking and HARKing (Hypothesizing After the Results are Known) (Head et al., 2015; John et al., 2012; Kerr, 1998). These practices may lead to increased false positive effects (Simmons et al., 2011) and poor replicability (Open Science Collaboration, 2015). Publication bias is also

detrimental to the development of knowledge, because hypotheses of new studies are crafted based on previous literature. If there is an inflated ratio of positive findings relative to negative findings, researchers may be misguided to believe that there is a robust relationship when there is not, and predicate their hypotheses on questionable theories (Jooper et al., 2012). In order to check the questionable research practices, preregistration has been proposed as a way to distinguish prediction and postdiction, and to restrict unwanted researcher's degree of freedom which can manipulate results (Silberzahn et al., 2018). Some studies have suggested that preregistration is associated with increased reproducibility (Swaen et al., 2001) and less publication bias (Kaplan & Irvin, 2015). Therefore, despite reporting null results, our preregistered study will make a valuable contribution to the literature.

There are also potential methodological reasons for why the current study did not mirror prior findings. Firstly, it is possible that this study failed to detect a true effect due to insufficient power. We conducted a power analyses (WebPower package; Cohen, 1988; Maxwell & Delaney, 2004; Zhang & Yuan, 2018) for all analyses which showed that the current study has 80% power to detect effect sizes (f^2) larger than between 0.09 and 0.075,

depending on the analysis. Secondly, most previous studies were conducted with adolescents over the age of 10, while about half of the participants in this study ranged from 6 to 9 years old. Therefore, these previous findings may not have been applicable to the subjects in the present study. Thirdly, some studies have identified hyperconnectivity among some regions and hypoconnectivity among other regions typically included in the DMN (Connolly et al., 2013; Gaffrey et al., 2012; Zhu, Wang et al., 2012). There is evidence of functional heterogeneity within the FPN (Dixon et al., 2018) and the DMN (Andrews-Hanna et al., 2010; Laird et al., 2009; Leech et al., 2011; Sambataro et al., 2014). In contrast, the current study computed DMN and FPN functional connectivity across all a priori regions. As such, it is possible that these opposing effects cancelled out in the current study. Finally, most previous studies used categorical measures of depression (e.g., comparing MDD and healthy controls) and ANOVA/ANCOVAs, while the present study used dimensional measures of depression and multiple regression analyses.

In conclusion, the present, preregistered study did not find significant cross-sectional or longitudinal associations between depression severity and intra-network functional connectivity within the DMN or FPN networks, nor between the two networks. Future studies

will further inform the presence or potential absence of any relationship between functional connectivity and depression in youth.

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Table 1. Sample Characteristics and demographics for cross-sectional and longitudinal analyses

Characteristic	Cross-sectional sample	Longitudinal sample
N	115	124
Age in years (mean $\pm$ SD)	10.03 $\pm$ 1.28	9.99 $\pm$ 1.31
Sex, % male	48.70%	48.39%
Race [#]		
Caucasian	66.09%	64.52%
African American	45.22%	46.77%
Others	11.30%	11.29%
Income-to-needs ratio ^a (mean $\pm$ SD)	1.72 $\pm$ 0.97	1.75 $\pm$ 0.98
Psychotropic medication use	20.87%	20.16%
Anxiety symptoms (mean $\pm$ SD)	2.11 $\pm$ 2.31	2.20 $\pm$ 2.44
Past MDD diagnosis	40.87%	41.13%

a. The income-to-needs ratio was measured as the total family income divided by the federal poverty level based on family size; # Race variables were coded as non-mutually exclusive dichotomous variables; as such, these numbers do not sum to 100% as participants could be included in multiple categories. MDD=Major Depressive Disorder. SD=standard deviation.

Table 2. Results of multiple regression models of associations between concurrent and past depression severity and functional connectivity of DMN and FPN networks

Predictor	β (95% confidence interval)	p
Outcome		
Within-DMN		
Concurrent depression severity		
<i>Mean of parent & child report</i>	.07 (-.08, .22)	.36
<i>Parent report</i>	.01 (-.14, .16)	.90
<i>Child report</i>	.07 (-.12, .25)	.48
Past depression severity	-.06 (-.17, .05)	.26
Within-FPN		
Concurrent depression severity		
<i>Mean of parent & child report</i>	.07 (-.08, .22)	.34
<i>Parent report</i>	.00 (-.16, .15)	1.00
<i>Child report</i>	.12 (-.05, .30)	.16
Past depression severity	-.02 (-.13, .09)	.70
Between DMN-FPN		
Concurrent depression severity		
<i>Mean of parent & child report</i>	.01 (-.15, .16)	.95
<i>Parent report</i>	-.01 (-.17, .15)	.93
<i>Child report</i>	.06 (-.12, .24)	.50
Past depression severity	.09 (-.03, .21)	.12

All estimates are standardized. DMN=default mode network. FPN=fronto-parietal network.

Table 3. Results of hierarchical linear models of associations between depression severity trajectories and within-DMN and within-FPN functional connectivity

	DMN			FPN			DMN-FPN		
	Mean			Mean			Mean		
Predictor	parent & child report	Parent report	Child report	parent & child report	Parent report	Child report	parent & child report	Parent report	Child report
	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)	Beta (SE)
Time	-.0001 (.61)	-.46 (.80)	1.53* (.62)	1.04 (-.60)	1.54* (-.77)	2.34** (.58)	.43* (.21)	.44 (.28)	1.54** (.21)
Within-network FC	3.82 (8.74)	-7.82 (11.84)	1.25 (1.72)	6.03 (6.32)	2.41 (-8.60)	1.53 (7.57)	3.76 (9.32)	6.10 (12.64)	8.82 (1.18)
Income-to-need ratio	-.75* (-.33)	-.70 (-.46)	-.68* (.32)	-.79* (.33)	-.69 (-.46)	-.73* (.32)	-.77* (.33)	-.67 (.46)	-.71* (.32)
Sex	-.08 (-.58)	-.46 (-.82)	.09 (-.57)	-.09 (-.58)	-.51 (-.82)	.07 (-.58)	-.10 (.576)	-.44 (.82)	.04 (.57)
Anxiety symptoms	.89** (-.14)	1.18** (.19)	.82** (.14)	.90** (-.14)	1.19** (.19)	.83** (.14)	.92** (.138)	1.20** (.20)	.86** (.14)
African American	.82 (-.96)	.48 (-1.36)	1.15 (-.95)	.66 (-.97)	.61 (-1.36)	.89 (-.96)	.71 (.95)	.52 (1.35)	.97 (.94)
Caucasian	1.25 (-.96)	2.27 (1.37)	1.03 (-.95)	1.27 (-.98)	2.39 (-1.38)	1.03 (-.96)	1.44 (.97)	2.39 (1.37)	1.27 (.96)
Age at time of scan	-.09 (.22)	.20 (-.31)	-.18 (-.22)	-.05 (-.22)	.20 (-.31)	-.11 (-.21)	-.04 (.22)	.20 (.31)	-.09 (.21)

Past									
MDD	1.55*	2.39*	1.27	1.55*	2.34*	1.26	1.44*	2.29*	1.14
diagnos	(-.67)	(.95)	(-.66)	(.68)	(-.96)	(-.67)	(.69)	(.97)	(.68)
is									
Time:									
Within	2.65	6.52	.17	-3.86	-6.35	-4.48	2.65	.42	-.72
-	(-4.31)	(-5.59)	(-4.41)	(3.26)	(-4.20)	(3.19)	(4.62)	(5.98)	(4.59)
networ									
k FC									
Intercep	2.71	1.32	.13	1.91	-.27	-.76	2.84	.32	.95
t	(-2.72)	(-3.83)	(-2.81)	(2.75)	(-3.87)	(2.82)	(2.58)	(3.65)	(2.55)
Observ									
ations	411	407	815	411	407	815	411	407	815
Log									
Likelih	-	-	-	-	-	-	-	-	-
ood	1136.35	1244.85	2511.18	1136.79	1244.88	2511.72	1136.30	1245.23	2511.61
Akaike									
Inf.	2302.70	2519.70	5052.35	2303.58	2519.77	5053.44	2302.59	252.47	5053.23
Crit.									
Bayesia									
n Inf.	2362.98	2579.83	5122.90	2363.68	2579.90	5123.99	2362.87	258.60	5123.77
Crit.									

Note. *p<.05 **p<.01 FC=functional connectivity. DMN=default mode network. FPN=fronto-parietal network. SE=standard error. Association of interest is bolded.