Child Psychiatry Hum Dev. Author manuscript; available in PMC 2024 February 01.

Published in final edited form as:
Child Psychiatry Hum Dev. 2023 February ; 54(1): 213–222. doi:10.1007/s10578-021-01242-2.

Cognitive and Affective Empathy as Indirect Paths Between Heterogeneous Depression Symptoms on Default Mode and Salience Network Connectivity in Adolescents

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Abstract

Depression amongst adolescents is a prevalent disorder consisting of heterogeneous emotional and functional symptoms—often involving impairments in social domains such as empathy. Cognitive and affective components of empathy as well as their associated neural networks (default mode network for cognitive empathy and salience network for affective empathy) are affected by depression. Depression commonly onsets during adolescence, a critical period for brain development underlying empathy. However, the available research in this area conceptualizes depression as a homogenous construct, and thereby miss to represent the full spectrum of symptoms. The present study aims to extend previous literature by testing whether cognitive and affective empathy indirectly account for associations between brain network connectivity and heterogeneous depression symptoms in adolescents. Heterogeneous functional and emotional symptoms of depression were measured using the child depression inventory. Our results indicate that cognitive empathy mediates the association between default mode network functional connectivity and emotional symptoms of depression. More specifically, that adolescents with a stronger positive association between the default mode network and cognitive empathy show lower emotional depression symptoms. This finding highlights the importance of cognitive empathy in the relationship between brain function and depression symptoms, which may be an important consideration for existing models of depression in adolescents.

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Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10578-021-01242-2.

Keywords

Cognitive empathy; Affective empathy; Functional connectivity; Depression; Adolescence

Introduction

Depression is a prevalent disorder involving decrements in social emotional functioning [1] that is typically examined as a homogenous construct [2, 3]. Adolescence is when depression commonly has its onset [4] with 13% of adolescents experiencing at least one episode of depression [5]. Depression symptoms in adolescents can be divided into heterogeneous sub-domains of emotional (e.g., negative mood and negative self-esteem) and functional symptoms (e.g., ineffectiveness and interpersonal problems) [6]. The common practice of examining depression as a homogenous construct misses important nuances of this disorder [2, 3]. For example, after assessing a variety of diverse symptoms (e.g., mood, suicidal ideation, weight loss/gain, insomnia/hypersomnia, anxiety) any combination may be classified as depression but they each describe divergent presentations [2, 3, 7]. Moreover, Fu [8] assert that neural underpinnings of depression symptom heterogeneity are not well understood and that further investigation into this heterogeneity can improve our understanding of depression. Which opens the question whether investigating depression heterogeneity in adolescent brains as they relate to social emotional processes could yield new insights into early depression?

Depression associates with impaired social emotional domains such as empathy [for review: 9]; and, because adolescence is a critical period for empathy development [10, 11], empathy is an important social domain for understanding adolescent depression. Empathy is a psychological response that involves understanding another's thoughts and feelings via cognitive and affective processes [12]. *Cognitive empathy* (i.e. perspective taking) is adopting another's point of view to understand their thoughts and feelings, whereas *affective empathy* is sharing of another's affective state, which may include *empathic concern,* or the concern for their emotional wellbeing [13, 14]. Empathy impairments are present in adults and adolescents with depression; but, where adults mainly show impairments in cognitive empathy [for meta-analysis see: 15], adolescents show potentially complex impairments in both cognitive and affective empathy with different studies showing linear and non-linear associations as well as sex effects [16–18]. This underscores the importance of examining these associations in adolescents. However, previous adolescent studies model cognitive and affective empathy in separate analyses with depression as a homogenous outcome. This approach may bias results from not modeling the shared variance of empathy components or capturing the heterogeneity of depression symptoms.

Underlying neural mechanisms of depression and empathy have been examined; but current knowledge can be advanced by examining functional connectivity underlying depression in adolescent brains in relation to cognitive and affective empathy. During empathic tasks, cognitive empathy positively associates with activation in the *default mode network* (*DMN*; medial prefrontal and posterior cingulate cortex), whereas affective empathy positively associates with activation in the *salience network* (*SAL*; anterior insula, anterior cingulate, and rostral prefrontal cortices) [19–23]. Interestingly, some work indicates that adolescent depression (when considered as a homogenous construct) associates with differences in these same networks [24, 25] and adolescence is a critical age for the neural development underlying empathy [26–28]. However, existing studies have mainly examined brain activations during empathic task performance, capturing brain activity during a specific state. Functional connectivity has emerged as an important method for examining brain function, which may reflect psychological processes in a trait-like condition. Thereby, this approach characterizes unique features of adolescent brain—task-independent function [29].

In the current study we aim to determine whether differences in cognitive and affective empathy mediate relationships between functional connectivity and heterogeneous depression symptoms in adolescents. We extend previous work by testing the relationships between brain function and dispositional-empathy in one model with heterogeneous depression symptoms as the outcome. Empathy is a plausible indirect path between neural mechanisms underlying depression. Contemporary thought suggests the brain drives behavior [30], the brain independently predicts both empathic behavior [21] and depression [for review: 9]; and, empathy predicts depression [16–18]. Therefore, we will model an indirect pathway using brain parameters as the independent variable; emotional and functional depression symptoms as the dependent; and both cognitive and affective empathy as the indirect pathway.

We expect higher levels of cognitive and affective empathy will associate with lower levels of both functional and emotional symptoms. Lower cognitive empathy associates with poorer social functioning [31, 32] and involves the DMN in processes such as thinking about emotions and perspective of self and others [33, 34], which is impaired in depression [35–37]; thus we hypothesized that a stronger association between the DMN and cognitive empathy would associate with lower levels of depression symptoms. Lower affective empathy associates with social impairments such as antisocial behavior [38] and mood symptoms [39], while SAL impairments underly emotional reactivity in depression [40]; thus we hypothesized that a stronger association between the SAL and affective empathy would associate with lower levels of both emotional and functional symptoms. Moreover, research suggests differences in self-reports of depression [41] and empathy [42–44] between sexes—therefore we expect to see sex differences in these associations. Because the literature is unclear in relation to non-linear relationships, we explore non-linear associations to determine non-linear terms (e.g., quadratic) are necessary for the final model.

Methods

Participants

The sample was drawn from the Nathan Kline Institute's Rockland dataset [45] using the 1000 connectomes project website (www.nitrc.org/projects/fcon_1000/). The dataset consisted of a general population sample from Rockland, New York. We included all participants in our study from this sample if they were mid to late adolescence [i.e. ages 13–17; 46] which totaled 122 participants. To ensure participants could understand self-report measures, we excluded 10 participants for having an IQ less than 80 assessed by the WAIS-II [$\alpha = 0.96$; 47]. Participants were not excluded based on clinical diagnosis, use of substances, or taking medication. The remaining sample consisted of 112 participants (Supplementary Fig. 1) that were predominantly White (63%, Black = 24%, Asian = 9%, Indian = 1%, other = 3%), balanced sex (female 45%), and a mean age of 14.59 ± 1.35. There were no clinically relevant diagnoses in the sample, 28 (25%) reported having used at least one substance in their lives (tobacco 9%, alcohol 21%, cannabis 13%, and 0 for stimulants, cocaine, narcotics, or hallucinogen), and 21 (18.7%) reported taking medications regularly. The studies procedures such as sampling, ethical considerations, and informed consent are outlined in Nooner, Colcombe [45].

Assessments

Interpersonal Reactivity Index (IRI)—As is common practice [48], subscales of the interpersonal reactivity index were used to assess affective empathy (empathic concern) and cognitive empathy (perspective taking) [42, 49]. The affective empathy subscale included seven-items ($\alpha = 0.74$), which measured the tendency to experience other's feelings and have concern for them (e.g. "When I see someone being taken advantage of, I feel kind of protective towards them"). The cognitive empathy subscale consisted of seven items ($\alpha = 0.79$), which measured the tendency to adopt the psychological point of view of others (e.g. "I try to look at everybody's side of a disagreement before I make a decision"). Participants rated items on a five-point scale ranging from 0 ("does not describe me") to 4 ("describes me well"). Both scales include some reverse coded items; all items were recoded prior to scale calculations so that higher scores indicate higher levels of empathy.

Child Depression Inventory 2—Reference [50] is a 28-item self-report screening tool ($\alpha = 0.84$) that measures two components of depression over the previous two weeks. The emotional subscale ($\alpha = 0.72$) constitutes negative mood and self-esteem, whereas the functional subscale ($\alpha = 0.68$) constitutes interpersonal functioning/ineffectiveness and engagement in social activities. Each item is rated on a scale of 0 (does not describe me) to 2 (describes me very well). This scale has been validated for use in youth aged 8–18 [51].

Covariates and Demographics—Self-report of age, sex, and tanner stage were included as nuisance covariates. Pubertal development was measured by the genital and breast development subscales of the Tanner assessment ($\alpha = 0.77$), in which parents rated pictures representing development of secondary sex characteristics on a scale of 1 (pre-pubertal) to 5 (full maturity) [52]. Higher scores indicate greater pubertal development.

Imaging Analyses

Imaging Acquisition and Preprocessing—A Siemens TimTrio 3 T scanner was used to collect images using a blood oxygen level dependent (BOLD) contrast with an interleaved multiband echo planar imaging (EPI) sequence. During resting state scanning, participants were instructed to keep their eyes closed without falling asleep and to not think of anything in particular while they let their mind wander. A resting state fMRI scan (260 EPI volumes; repetition time (TR) 1400 ms; echo time (TE) 30 ms; flip angle 65°; 64 slices, Field of view (FOV) = 224 mm, voxel size 2 mm isotropic, duration = 10 min) and a magnetization prepared rapid gradient echo (MPRAGE) anatomical image (TR = 1900 ms, flip angle 9°, 176 slices, FOV = 250 mm, voxel size = 1 mm isotropic) were acquired for each participant.

Scan removal for T1 stabilization is unnecessary due to the Siemens sequence collecting images after saturation is achieved.

Statistical Parametric Mapping [SPM version 12; 53] with the CONN toolbox [version 18b; 54] were used to preprocess the data. The Artifact Detection Tools (ART; http://www.nitrc.org/projects/artifact_detect) was used to inspect each participant's time series for motion. Motion outliers were flagged for correction if > 0.5 mm and regressed out using binary motion covariates. Participants were excluded if motion was > 3 mm in any direction or > 20% invalid scans. No slice timing correction was used because of the short TR and multiband sequence used at acquisition.

Anatomic component-based noise correction method (aCompCor) [54] was used to reduce psychologic noise from the BOLD signal. This method regresses out CSF and white matter noise unrelated to neural processes while mitigating motion effects [55]. An additional advantage to this approach is that aCompCor does not artificially induce anticorrelations [56]. Co-registered MPRAGE and EPI images were normalized to an MNI template. Smoothing of images were conducted using a 6 mm Gaussian kernel. Finally, to preserve meaningful resting state associations, the data was bandpass filtered to between 0.008 and 0.09 Hz [57].

Region of Interest Selection—Networks were selected a priori on previous investigations of empathy [19–23] and depression [24, 25]. Based on these studies we identified regions of interest (ROI) using the Harvard Oxford Atlas available within CONN with the coordinates predefined as belonging to the respective network. Based on the atlas and previous studies we selected regions making up the DMN (e.g., medial prefrontal cortex, posterior cingulate cortex, and angular gyri) and the SAL (e.g., bilateral anterior insulae, anterior cingulate, and bilateral rostral prefrontal cortices) as seed regions (MNI coordinates: Supplementary Table 1).

Participant-Level Analysis—The CONN toolbox [version 18b; 54] was used to conduct participant level analyses. The time-series of each pairwise within network ROI connection was averaged and extracted for analyses. Prior to extraction, each pairwise connection was converted to a Z-value using Fisher's r-to-z transformation for use in group-level comparisons.

Statistical Analysis

The statistical software R [Version 3.6.3; 58] was used to conduct group level analyses. A path analysis model was fit using the lavaan package in R [59]. We modeled the extracted averaged DMN and SAL within-network connectivity parameters as independent variables and depression subcomponent scores as outcomes in relation to cognitive and affective empathy as the indirect paths. Because substance use [60] and medications [61, 62] may effect outcomes, we conducted an analysis removing participants reporting they used substances at some point in their life or are regularly taking medication. This analysis did not change estimated parameters (Supplementary Table 2) therefore we only report on the analysis with all participants included.

Missing Data Analysis—Data missingness was assessed using the Visualization and Imputation of Missing Values "VIF" package in R [63]. A test for missing completely at random (MCAR) outlined by [64] was conducted using the 'MissMech' package in r [65]. Then, a dichotomous variable was created for missing values (missing = 1 and not missing = 0) then both chi-square and t tests were used to assess if any systematic reasons for missing values were present [66].

Out of the 112 participants, 28 (25%) participants had motion issues or > 20% of invalid scans and this data was removed, leaving 84 (75%) with full data. We then assessed missingness for the 28 participants who did not have full data and could not find any systematic reasons for the missing values. The test for missingness was not significant ($p = 0.43$) suggesting data were missing at random and follow up analyses revealed no need for ancillary variables to account for missingness. Thus, we used full information maximum likelihood was used to obtain maximum likelihood estimates for the 28 (25%) missing values [67].

Assumption Checking—Prior to analysis, we assessed whether to include linear or non-linear relationships by visually examining scatterplots and residual plots of x and y relationships to determine nonlinearity. We then checked assumptions of: multicollinearity, multivariate normality, linearity, skewness, kurtosis, and heteroscedasticity for the model using the Global Validation of Linear Models Assumptions package in r [68].

Contrary to previous research, our pre-modeling investigation of scatterplots and residual plots revealed no evidence for non-linear relationships. Assumption checks indicated the depression variables did not meet the assumption of normal distribution and further univariate investigation indicated a potential problematic skew (emotional skew = 0.94; functional skew = 1.06) under Bulmer [69] criteria (cutoff close to 1), but all other assumptions were met—including linearity. Thus, we fit the formal model with the assumption of linearity using the robust variant of maximum likelihood to account for nonnormal distribution of the outcome variables [70].

Outlier Detection—Outliers were detected using Cook's D cutoff criteria (D(i) > 4/n; [71] that was calculated using the R package "influence.SEM" [72]. Cook's D revealed 9 outliers that were removed leaving a final sample of 103 male and female adolescents (40% female, Mean age = 14.55 ± 1.34) in the final analysis.

Model Fitting—Model fit was assessed using criteria for adequate fit of CFI and TLI ≥ 0.90, and RMSEA and SRMR ≤ 0.08 [73, 74]. A priori we specified a covariation between cognitive and affective empathy; age and tanner assessment; and between the outcome variables. To statistically support chosen paths using cross-sectional data, we compared the fit statistics of the hypothesized model against an alternative model that reversed the placement of variables in the analysis, to assess if the originally hypothesized model best fit the data. This was done to support directional paths that fit the data, not to assert causality. A 95% confidence interval was calculated using 5,000 bootstrap samples to test the mediation effect.

Finally, we constrained model parameters to examine indirect paths independence of direct paths and conducted a multigroup modeling approach to examine sex differences in magnitude across regression parameters and for differences in intercepts. To probe indirect paths independence from direct paths, we used a likelihood ratio tests that compared a model that constrained relevant direct paths to a model where it was unconstrained. For sex effects across intercepts and regression parameters, we conducted a likelihood ratio test using multigroup models grouped by sex that was compared against a model that constrained intercepts and another that constrained regression parameters across sexes.

Results

The model with directional paths as hypothesized fit the data adequately ($X^2(8) = 9.57$; CFI = 0.987; TLI = 0.940; RMSEA = 0.044, SRMR = 0.051) and fit better than a model with the directional paths reversed, which did not meet a priori fit criteria ($X^2(11) = 19.35$; CFI = 0.923; TLI = 0.753; RMSEA = 0.087, SRMR = 0.077). Thus, we report on the hypothesized model with full results reported in Table 1 and the model depicted in Fig. 1. Moreover, multigroup models by sex were not significantly different on intercepts or regression parameters (see sex effects section below).

Within-Network Functional Connectivity Associating with Empathy

Empathy regressed on predictors reveal that DMN within-network connectivity positively associated with cognitive empathy ($\beta = 8.40$, $p = 0.004$, bootstrapped CI95%[8.285, 8.459]) and SAL within-network connectivity positively associated with affective empathy ($\beta = 7.86$, $p = 0.008$, bootstrapped CI95%[7.597, 7.771]). Regarding the covariates, higher levels of pubertal stage associated with higher cognitive empathy (Table 1).

Empathy Mediating Functional Connectivity Underlying Depression

Emotional depressive symptoms regressed on predictors revealed that both DMN within-network connectivity ($\beta = -5.212$, $p = 0.042$) and cognitive empathy ($\beta = -0.143$, $p = 0.034$) negatively associated with emotional depression symptoms, which were further supported by the bootstrapped confidence intervals (Table 1). For indirect paths, the DMN indirectly negatively associated with emotional symptoms via cognitive empathy (indirect: $\beta = -1.197$, $p = 0.046$, bootstrapped CI95%[− 2.37, − 0.017]) and significant negative total effects (total: $\beta = -5.71$, $p = 0.035$, bootstrapped CI95%[− 11.02, − 0.413]). The model accounted for 18% of the variance in emotional symptoms ($R^2 = 0.181$).

Functional depressive symptoms regressed on predictors revealed no significant associations with predictors of interest. However, bootstrapped confidence intervals suggest negative confidence intervals for DMN, SAL, and both cognitive and affective empathy (Table 1). Similarly no significant indirect paths but there were significant total effects (total: $\beta = -9.72$, p = 0.006, bootstrapped CI95%[− 16.65, − 2.75]). The model accounted for 22% of the variance of functional symptoms ($R^2 = 0.223$).

Indirect Effects of Functional Connectivity via Empathy

Because we found a significant indirect effect of DMN on emotional depression symptoms via cognitive empathy, we empirically tested if this indirect path was independent of a direct effect of DMN on emotional depression symptoms. We conducted a likelihood ratio test comparing a model with the parameter between DMN and emotional depression symptoms constrained to a model where this was freely estimated. The model with the constrained direct parameter was not significantly different from the model that freely estimated the direct effect ($\Delta X^2 = 3$, $p = 0.074$, bootstrapped $p = 0.597$). This insignificant change in model fit after removing the direct parameter suggests that cognitive empathy explains the negative association between DMN and emotional symptoms independent of a direct association.

Sex Effects on Empathy and Depression Symptoms

In the formal model, females were more likely the report higher mean levels of cognitive and affective empathy (cognitive: $\gamma = -2.11$, $p = 0.021$; affective: $\gamma = -2.15$, $p = 0.021$) as well as higher emotional and functional depression symptoms (emotional: $\gamma = -1.92$, $p = 0.001$, functional: $\gamma = -2.21$, $p = 0.01$). However, when comparing multigroup models there were no significant differences in intercepts ($\Delta X^2 = 11.6$, $p = 0.16$) or magnitude of regression parameters ($\Delta X^2 = 11.7$, $p = 0.17$) between males and females.

Discussion

The present results demonstrate differences in the association between the DMN within-network connectivity and subcomponents of depression in relation to empathy. The current analysis extends previous work by showing that: (1) DMN within-network connectivity and cognitive empathy associates linearly with emotional symptoms of depression in adolescents; (2) affective empathy does not associate with either subcomponents of depression; and (3) the DMN indirectly associates with emotional depression symptoms via a covariation with cognitive empathy.

The present study extends the field of early depression by pulling together separate lines of research indicating that DMN connectivity positively associates with cognitive empathy in adolescents [21] and cognitive empathy negatively associates with symptoms of depression [24, 25]. Contrary to previous findings, we found no association of affective empathy with depression when examining heterogeneous symptoms, and no evidence of non-linear associations.

Within-Network Functional Connectivity Underlying Empathy

Consistent with our hypotheses drawn from previous literature, stronger DMN within-network connectivity associates with higher levels of cognitive empathy. Likewise, stronger SAL within-network connectivity associates with greater affective empathy as expected. These associations evidence the neural underpinnings of empathy in adolescence.

Both DMN involvement in cognitive empathy and SAL involvement with affective empathy has strong support in the literature [19–23, 75]. The DMN involves self-referential cognitive processes including thinking about one's own and others thoughts and emotions [76–78], which are not specific to but are important for cognitive empathy [33, 34]. The SAL involves integration of sensory, affective, and cognitive information [for review see: 79], which supports empathic feelings [80, 81]. The present study extends previous research on empathy by providing evidence that functional connectivity within the DMN and SAL are associated with adolescent cognitive and affective empathy traits, respectively.

Empathy Mediates the Functional Connectivity Underlying Depression Symptoms

Our results show that adolescents with higher DMN within-network connectivity reported less emotional depression symptoms. In addition, we found that higher DMN connectivity was related to higher cognitive empathy, which in turn was associated with less emotional depression symptoms. This indirect association held after removing the direct association between DMN and emotional symptoms in the statistical model. This suggests that cognitive empathy is the process through which DMN functional connectivity affects emotional depression symptoms in adolescents.

The DMN is thought to be involved in social understanding and perceiving emotions [82]. Individuals with depressive (internalizing) symptoms showed altered connectivity in the DMN, which associated with an inability to recognize emotions in others [83] and in oneself [84]. Given that understanding another's emotions is important for understanding your own thought processes [85], it may be that greater DMN within-network connectivity associates with emotional understanding necessary for cognitive empathy, which, in turn, associates with lower levels of emotional depression symptoms.

Contrary to hypothesized, neither the SAL nor affective empathy associated with either of the depressive symptoms examined. Interestingly this finding is more consistent with adult studies [for meta-analysis see: 15] rather than previous studies on adolescents [16–18]; however these adolescent studies did not model the shared variance between cognitive and affective empathy and examined depression as a homogenous construct. This may indicate that the SAL and affective empathy are not implicated when considering shared variance between empathic components and heterogeneity of adolescent depression symptoms. Taken together, the present results extend previous literature by indicating the importance of DMN within-network connectivity and its covariation with cognitive empathy for emotional depression symptoms in adolescents.

Effects of Sex

On average, females reported higher levels of cognitive and affective empathy as well as higher levels of emotional and functional depression symptoms than males. However, when examining multigroup models that constrained parameters to be equal across groups, there were no differences in intercept or magnitude of regression parameters between males and females. And, importantly, we found no significant directional paths where neural parameters were independent variables. This is an important distinction because sex is a contentious topic in empathy research [86] with self-report studies suggesting females self-report higher levels of empathy [42–44], but some imaging studies involving empathic tasks have not demonstrated sex differences [21, 23, 87]. This may suggest self-reports are capturing social conditioning rather than empathic ability. The present results suggest that even though females self-reported higher empathy and depression, males and females did not significantly differ on associations between neural connectivity, self-reported empathy components, and depression heterogeneity.

Limitations

The present study must be interpreted under the following limitations. First, this is a cross-sectional design, thus causal paths cannot be determined. Because there were no temporal associations between variables, true mediation model could not be tested but rather the mediator covaried with the independent variable. Further testing is necessary to determine the causal direction of these relationships. Second, analyses did not reach the sample size necessary for adequate power. It is plausible that the current findings reflect reality given the statistically significant effects and confidence intervals. It is also worth noting the current analysis may not have detected all effects due to a lack of power; and the few bootstrap inconsistencies reported may reflect our analysis did not detect all effects. Third, ROIs were defined using a predefined atlas. This method may not accurately reflect the neural regions for the present sample that may impact results. However, these atlases are defined across larger sample sizes that evidence generalizability and mitigate researcher error in region definition. Fourth, some confounding variables were not ideal measurements; specifically, substance use was a binary measure; also, while there was data recorded whether they took medications, we did not have information on what medications they were taking. However, removing these participants did not change regression parameters, but future studies should consider severity and different medications impact. Finally, there are multiple other factors unaccounted for that may have impacted empathy and the brain (e.g. trauma [88, 89], comorbidity [90, 91]), but were outside the focus of the present study. Future studies could investigate the impact of trauma or comorbidity of clinical diagnoses. Despite these limitations, the present study evidence DMN within-network connectivity covariation with cognitive empathy in relationship to both functional and emotional internalizing symptoms.

Conclusions

This study, unlike the previous studies, modeled subcomponents of depression in adolescents as well as cognitive and affective empathy together in one model. Not only is it more realistic to model heterogeneous depression symptoms, but the components of empathy are important to model together because, even though they are separate constructs, they have some overlapping variance that if not accounted for may provide inaccurate results. Given our improved modeling considerations, the finding that cognitive empathy is the process through which the DMN negatively associated with emotional depression symptoms is both adequately supported and novel.

In conclusion, the present study examined the association between DMN and SAL within-network connectivity with heterogeneous depression symptoms in relation to cognitive and affective empathy. As supported in the literature, the DMN and cognitive empathy negatively associated with emotional and functional depression symptoms. The literature was extended with the finding that the DMN had an indirect association, via a covariation with cognitive empathy, on emotional depression symptoms. The present study provides evidence that healthy DMN within-network connectivity in relation to cognitive empathy are important for emotional symptoms of depression in adolescents.

Summary

Cognitive and affective components of empathy as well as neural underpinnings in the salience and default mode networks are known impairments in depression symptoms in adolescents; however, our knowledge is limited because previous studies did not account for shared variance between cognitive and affective empathy in one model and modeled depression as a homogenous construct. The present study extends this line of research by examining DMN and SAL connectivity underlying heterogenous emotional and functional symptoms of depression in relation to both cognitive and affective empathy in one model. The present study sampled adolescents between the ages of 13–18 from the Nathan Kline Institutes Rockland dataset. A total of 112 adolescents used in the present study underwent resting state MRI, completed the child depression inventory (for heterogenous depression symptoms), and the interpersonal reactivity index (cognitive and affective empathy). The CONN toolbox was used to preprocess and to first level analysis of imaging data. Then the statistical software R was used to conduct path analysis. Results indicate that cognitive empathy mediates the association between default mode network functional connectivity and emotional symptoms of depression. More specifically, that adolescents with a stronger positive association between the default mode network and cognitive empathy show lower emotional depression symptoms. This finding supports the importance of cognitive empathy in the relationship between brin function and depression symptoms; and that cognitive empathy is an important consideration for existing models for depression in adolescents.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

Drew E Winters, PhD. was supported by a training grant from National Institutes of Mental Health, T32MH015442.

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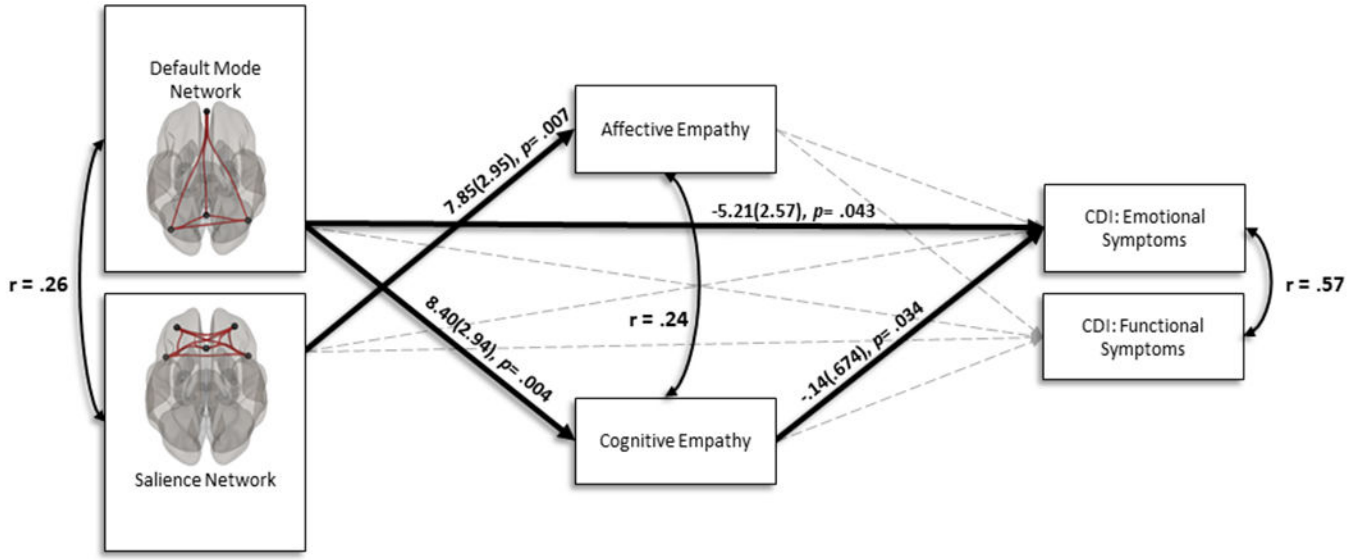

Fig. 1.

Figure depicting significant path coefficients. This model also controlled for age, sex, and tanner stage (not shown). Dotted lines indicate insignificant paths and solid like indicate significant paths. The bolded paths indicate significant indirect effects independent of the direct effect. All path coefficients reported in Table 1

Table 1

Path analysis results

	Unstandardized estimate	Standard error	Standardized estimate	Z score	P value	Bootstrapped CI95%	
						Lower CI95%	Upper CI95%
Cognitive empathy							
DMN	8.404 *	2.9496	0.2709	2.8492	0.0044	8.285	8.459
Tanner	0.999 *	0.4453	0.2174	2.2434	0.0249	0.986	1.012
Sex (male)	−2.109 *	0.9187	−0.2152	−2.2957	0.0217	−2.140	−2.086
Age	−0.347	0.3266	−0.096	−1.0624	0.288	−0.361	−0.341
Affective empathy							
SAL	7.846 *	2.950	0.280	2.660	0.008	7.597	7.771
Tanner	0.318	0.432	0.070	0.736	0.462	0.310	0.335
Sex (male)	−2.152 *	0.936	−0.222	−2.300	0.021	−2.189	−2.136
Age	0.137	0.349	0.038	0.391	0.696	0.118	0.138
CDI emotional							
DMN	−5.212 *	2.567	−0.243	−2.030	0.042	−5.405	−5.250
SAL	0.698	1.925	0.036	0.363	0.717	0.691	0.810
Cognitive empathy	−0.143 *	0.067	−0.206	−2.115	0.034	−0.138	−0.134
Affective empathy	−0.001	0.064	−0.001	−0.013	0.990	−0.010	−0.006
Tanner	0.119	0.375	0.037	0.317	0.752	0.098	0.120
Sex (male)	−1.920 *	0.611	−0.283	−3.145	0.002	−1.946	−1.910
Age	0.091	0.285	0.036	0.317	0.751	0.075	0.092
CDI functional							
DMN	−5.251	3.389	−0.225	−1.549	0.121	−5.475	−5.273
SAL	−3.374	2.393	−0.158	−1.410	0.159	−3.224	−3.077
Cognitive empathy	−0.131	0.077	−0.174	−1.706	0.088	−0.127	−0.122
Affective empathy	0.000	0.060	0.000	−0.004	0.997	−0.007	−0.003
Tanner	−0.080	0.385	−0.023	−0.207	0.836	−0.110	−0.087
Sex (male)	−2.212 *	0.703	−0.300	−3.147	0.002	−2.200	−2.158
Age	0.214	0.250	0.079	0.857	0.392	0.210	0.225

	Unstandardized estimate	Standard error	Standardized estimate	Z score	P value	Bootstrapped CI95%	
						Lower CI95%	Upper CI95%
Indirect effects							
DMN—CE—emotional	−1.197*	0.602	−0.056	−1.989	0.047	−2.377	−0.017
DMN—CE—functional	−0.007	0.503	−0.001	−0.013	0.989	−0.992	0.978
SAL—AE—emotional	−1.100	0.609	−0.047	−1.808	0.071	−2.293	0.093
SAL—AE—functional	−0.002	0.472	−0.000	−0.004	0.997	−0.927	0.924
Total effects							
Emotional symptoms	−9.727*	3.537	−0.429	−2.750	0.006	−16.659	−2.795
Function symptoms	−5.718*	2.707	−0.263	−2.112	0.035	−11.023	−0.413

Model Fit: Chi-square(df) = (8) = 9.57; CFI = .987; TLI = 0.940; RMSEA = .044, SRMR = .051)

Confidence intervals bootstrapped at 5000 resamples

* $p < .05$

CDI child depression inventory, DMN default mode network, SAL salience network, CE cognitive empathy, AE affective empathy