

Regular Article

Neural activity during negative self-evaluation is associated with negative self-concept and depressive symptoms in adolescent girls

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Abstract

Self-concept becomes reliant on social comparison, potentially leading to excessive self-focused attention, persistently negative self-concept and increased risk for depression during early adolescence. Studies have implicated neural activation in cortical midline brain structures in self-related information processing, yet it remains unclear how this activation may underlie subjective self-concept and links to depression in adolescence. We examined these associations by assessing neural activity during negative vs. positive self-referential processing in 39 11- to 13-year-old girls. During a functional neuroimaging task, girls reported on their perceptions of self-concept by rating how true they believed positive and negative personality traits were about them. Girls reported on depressive symptoms at the scan and 6 months later. Activation in the dorsomedial and ventrolateral prefrontal cortexes (dMPFC; VLPFC), and visual association area was significantly associated with subjective self-concept and/or depressive symptoms at the scan or 6 months later. Exploratory models showed higher activation in the dMPFC to Self-negative > Self-positive was indirectly associated with concurrent depressive symptoms through more negative self-concept. Higher activation in the visual association area to Self-positive > Self-negative was associated with lower depressive symptoms at follow-up through more positive self-concept. Findings highlight how differential neural processing of negative versus positive self-relevant information maps onto perceptions of self-concept and adolescent depression.

Keywords: Neural self-referential processes; self-concept; depression; adolescence

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Risk for major depressive disorder increases substantially during adolescence, with prevalence rates rising to approximately 14–20% (see reviews by Birmaher et al., 1996; Costello et al., 2011; Hankin, 2006). Adolescence is also a crucial period during which self-concept, a complex construct encompassing self-perceptions about personal qualities, competence, and worth (Marsh & Shavelson, 1985), begins to stabilize (Cole et al., 2001; Shapka & Keating, 2005). Although fluctuations in self-concept during adolescence are normative (Cole et al., 2001), persistent negative beliefs about the self are clinical characteristics of depression and, according to cognitive theory, are causal and maintaining factors of depression (Beck, 1967; Harter & Jackson, 1993; Sowislo & Orth, 2013). Early-to-mid adolescents are especially vulnerable to more negative self-concept due to major social and biological transitions during this period and adolescents' high reliance on others' perceptions for validation (Cole et al., 2001; Rankin et al., 2004; Sontag et al., 2011). Therefore, this may be an important period to investigate the neural underpinnings of negative self-concept that could contribute to depressive symptoms. The current study aims to examine these links.

Cognitive models of depression emphasize that individuals who experience depression likely have trait-like, cognitive predispositions or biases as a function of biological vulnerabilities and/or prior salient experiences (Coyne & Gotlib, 1983; Kovacs & Beck, 1978). Due to these cognitive vulnerabilities, by early adolescence, some youth exhibit more negative and less positive biases in self-related cognitions/schemas, increasing susceptibility to the development of depression. Affective neuroscience literature in both adolescents and adults suggests that self-related information biases may be driven by neural processing. Specifically, the medial prefrontal cortex (MPFC; including dorsal and ventral regions), anterior cingulate cortex, posterior cingulate cortex/precuneus (precuneus), and inferior parietal lobe extending into the temporoparietal junction may be core regions particularly important to processing self-relevant information (reviews by Frewen et al., 2020; Northoff et al., 2006; Pfeifer & Peake, 2012). In fact, adolescents show greater activation than adults in these brain regions when attending to self-relevant information and experiencing feelings of self-consciousness (Blakemore et al., 2007; Pfeifer et al., 2007, 2009; Somerville et al., 2013), suggesting that self-relevant information may be especially salient during adolescence.

Altered functional activation patterns during self-referential processing are reported in adolescents with depression. Specifically, research shows that when attending to negatively valenced self-related stimuli (e.g., negative social feedback, negative situations and related emotions), adolescents with depression or remitted

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depression exhibit greater activation in the precuneus, anterior cingulate cortex, and middle and superior temporal gyrus, compared to healthy adolescents (Burkhouse *et al.*, 2017; Silk *et al.*, 2014, 2017). Findings are more mixed when examining neural activation to positively valenced self-related information. Some research suggests that adolescents with clinical depression show less activation in regions of the limbic system, MPFC, precuneus, and dACC during the self-referential processing of positive stimuli, such as social feedback (Silk *et al.*, 2017), happy facial expressions (Quevedo, Ng, Scott, Martin, *et al.*, 2016), and positive trait adjectives (Quevedo, Ng, Scott, Smyda, *et al.*, 2016). Similarly, youth at high risk for depression, as a function of maternal depression, have exhibited reduced activity in similar regions (*i.e.*, dACC, caudate, and inferior frontal gyrus) during positive social feedback processing (Olino *et al.*, 2015). However, studies have also found opposite effects, suggesting that adolescents with clinical depression (Bradley *et al.*, 2016) or at high-risk for depression (Liu *et al.*, 2020; Olino *et al.*, 2015) may recruit more activation in the posterior cingulate/precuneus, inferior parietal, temporal, ventrolateral and medial prefrontal cortex regions than healthy or low-risk youth while processing positive self-judgments and socially rewarding feedback. Such mixed findings may be due to differences in study tasks or design and/or symptom severity.

Though disruptions in neural self-referential processing in the context of adolescent depression have been repeatedly shown in the literature, to our knowledge only two studies have reported associations between neural self-referential processing and subjective self-concept in the context of adolescent depression. One reported that less dACC activation during self-referential processing of positive self-descriptors, compared to negative self-descriptors, was related to lower reported self-esteem and self-compassion across both healthy and depressed adolescents (Quevedo, Ng, Scott, Smyda, *et al.*, 2016), whereas the second reported that heightened activity in the ventrolateral prefrontal cortex (VLPFC) during self-reflection on positive traits mediated the positive association between depression risk (*i.e.*, maternal depression) and child depressive symptoms only in youth endorsing less positive self-descriptors (Liu *et al.*, 2020). Of interest, a few studies in healthy young adults and adolescents have shown that higher activation in the MPFC while self-evaluating on positive traits, relative to negative traits, was associated with higher endorsement of positive traits and with traits individuals rated as higher in importance (Van de Groep *et al.*, 2021; van der Cruysen *et al.*, 2017, 2018). With such little current research, there remains a need to continue investigating how negative versus positive self-concept is differentiated in the adolescent brain and how these differentiations may contribute to depression. Therefore, the current study aimed to: (1) Examine associations between neural activation during self-evaluation on negative versus positive self-traits (and vice versa) and depressive symptoms, (2) Examine understudied associations between neural activation during self-evaluation and adolescent girls' subjective self-concept, and (3) Explore to what extent subjective self-concept explains associations between neural activation during self-evaluation of negative versus positive self-traits (and vice versa) and depressive symptoms. These associations were examined in a female sample, as girls are known to be at a higher risk for depression during adolescence than boys (Hankin, 2006). Additionally, adolescent girls are especially vulnerable to having low self-worth and heightened self-consciousness (Kling, Hyde, Showers, & Buswell, 1999; Rankin *et al.*, 2004; F. R. Rosenberg & Simmons, 1975; Walker & Greene, 1986).

Given that heightened neural activation during the processing of negative self-related information has been consistently linked to adolescent depression, we hypothesized that (1) higher activity in brain regions that activate more to negative versus positive self-evaluation would be associated with higher depressive symptoms both concurrently and approximately 6 months later, (2) higher activity in regions of the brain that activate more to positive versus negative self-evaluation would be associated both with lower depressive symptoms both concurrently and approximately 6 months later. We also hypothesized that higher activity in brain regions that activate more to negative versus positive self-evaluation would be associated with more negative subjective self-concept, while higher activity in brain regions that activate more to positive versus negative self-evaluation would be associated with less negative subjective self-concept. Based on existing research and theory (*e.g.*, Beck, 1967; Harter & Jackson, 1993; Sowislo & Orth, 2013), we hypothesized that more negative self-concept would be associated with higher depressive symptoms both concurrently and approximately 6 months later.

Finally, we tested a possible indirect effect of subjective self-concept on the link between neural activity and depressive symptoms in exploratory mediation models. This exploratory aim is based on neurobiological theories suggesting that cognitive predispositions or biases underlying self-related, internally focused processing are, at least in part, the function of neurobiological vulnerability (see reviews by Butterfield *et al.*, 2023; Crone *et al.*, 2022; Marchetti *et al.*, 2012). As reviewed above, previous research provides evidence that greater activation in self-referential processing regions while attending to negatively valenced self-related stimuli is associated with adolescent depression. Therefore, we hypothesized that more negative subjective self-concept would statistically mediate the link between greater neural activation during self-evaluation of negative traits (relative to positive traits) and higher depressive symptoms reported both concurrently and approximately 6 months later. Though results in previous studies have been less consistent with regard to the association between positive self-related neural processing, various measures of subjective self-concept, and depression in adolescents, behavioral literature links more positive self-concept and biases to lower depression risk (Beck, 1967; Sowislo & Orth, 2013). Further, affective neuroscience literature reviews suggest that emotionally charged, self-related information is generally associated with greater activation of brain regions involved in self-referential and social cognitive processes (Andrews-Hanna *et al.*, 2010) and that depression is typically associated with hypoactivation of neural regions underlying attentional and salience processing of positively valenced stimuli (Groenewold *et al.*, 2013). Therefore, we also hypothesized that more positive adolescent self-concept would mediate the link between greater neural activation during self-evaluation on positive traits (relative to negative traits) and lower depressive symptoms, as this could suggest that adolescent girls who are biased more towards positively valenced self-relevant information, relative to negatively valenced information, are more likely to endorse more positive self-concept and less depression.

Neural activation during self-evaluation was examined using a whole-brain analytic approach. We chose this approach because, although there have been several core neural regions implicated in self-referential processing, many of the studies assessing adolescent neural activation during valence-specific, self-related information processing presented results that spanned across broader fronto-limbic and temporal areas (Liu *et al.*, 2020; Olino *et al.*, 2015; Quevedo, Ng, Scott, Martin, *et al.*, 2016; Quevedo, Ng, Scott, Smyda,

et al., 2016; Silk et al., 2017). Therefore, we aimed to capture all brain regions that may be important to test our primary hypotheses with.

Method

Participants

Forty-eight 11-to-13-year-old girls ($M_{\text{years}} = 12.19$, $SD = .80$) were recruited from a larger longitudinal study examining biosychosocial risk factors for social anxiety and depression in adolescence. Participants were recruited from the community and oversampled for high risk for social anxiety and depression based on fearful and shy temperament (as described in Sequeira et al., 2021). Exclusionary criteria included: a current or past DSM-5 diagnosis of an anxiety (except specific phobia), major depressive, psychotic or autistic spectrum disorder, $IQ < 70$ (assessed using the Wechsler Abbreviated Scale of Intelligence), lifetime presence of a neurological or serious medical condition, presence of magnetic resonance imaging contraindications, uncorrected visual disturbance ($< 20/40$ Snellen visual acuity), left handedness, presence of head injury or congenital neurological anomalies (based on parent report), taking medications that affect the central nervous system and endocrine function (e.g., SSRI's, oral steroids, oral contraceptives), being acutely suicidal or at risk for harm to self or others. Stimulant medications were permitted, as long as participants were able to refrain from taking them for 36 hr preceding the scan.

Participants who provided written informed parental consent and youth assent for future contact from the parent study were eligible for the current supplemental study; subsequent informed consent and assent were obtained from participating primary caregivers and adolescents for the current study.

Procedure

As part of the parent study, participants completed clinical interviews, laboratory interaction tasks, functional neuroimaging visits, and questionnaires. Participants and their primary caregivers completed an additional 1.5 hr visit for the current supplement study at the Magnetic Resonance Research Center in the local university hospital. During this assessment (T1), primary caregivers and youth completed questionnaires assessing adolescents' anxiety and depressive symptomatology and a 30-min functional magnetic resonance imaging (fMRI) scanning session. As part of the 1-year follow-up visit for the parent study, girls reported on their depressive symptoms which was used as the longitudinal outcome (T2) measure in the current study. T2 was approximately 6 months ($M = 6.37$, $SD = 1.46$) following T1 (i.e., the initial supplement study visit). Nine adolescent girls were excluded due to excessive fMRI motion artifacts (see fMRI Data Analysis section) and an additional participant was excluded from longitudinal analyses, due to missing follow-up data. Thirty-nine participants are included in cross-sectional analyses, 38 in the longitudinal analyses (Table 1 for final sample characteristics).

Measures

Mood and feelings questionnaire, child report (Costello & Angold, 1988)

The Mood and feelings questionnaire, child report assesses depressive symptoms in youth 8–18 years old via a 33-item self-report questionnaire. Participants rate how true each item is of their mood and behavior within the past 2 weeks on a three-point Likert scale (0 = "not true," 1 = "sometimes," 2 = "true"). Mood

Table 1. Participant demographics at time of scan (T1)

<i>N</i> = 39 female participants	<i>M</i> (<i>SD</i>)	Range
Age	12.27 (.80)	11–13
Race [<i>n</i> (%)]		
White, non-Hispanic	24 (61.5)	
Black	9 (23.1)	
Bi-racial	4 (10.3)	
Asian	1 (2.6)	
Native American	1 (2.6)	
Head of household education [<i>n</i> (%)]		
High school graduate	4 (10.3)	
Some college	10 (25.6)	
College degree	7 (17.9)	
Graduate training	18 (46.2)	
Pubertal status ^a	3.54 (1.19)	1.00–5.00
Self-concept ratings		
Positive self-concept	79.74 (6.46)	64.00–92.00
Negative self-concept	66.69 (7.29)	53.00–82.00
Total self-concept ^b	146.44 (12.60)	120.00–172.00
T1 depressive symptoms [<i>M</i> (<i>SD</i>)] ^c	5.82 (4.51)	0.00–15.00
T2 depressive symptoms [<i>M</i> (<i>SD</i>)] ^d	9.20 (7.88)	0.00–30.50

^aAssessed using Pubertal Development Scale.

^bTotal Self-Concept Ratings used for study analyses.

^cSymptoms assessed using Mood and Feelings Questionnaire-Child Report.

^dData from 38 participants.

and feelings questionnaire, child report total scores assessed at T1 and T2 were used as outcome measures. Higher total scores reflect greater symptomatology. Reliability for the Mood and feelings questionnaire in the current sample was high ($\alpha = .90$) at both timepoints.

Pubertal development scale (Petersen, Crockett, Richards, & Boxer, 1988)

The Pubertal development scale is a five item self-report that assesses physical development associated with pubertal changes. The current study used an adapted scoring system (Shirtcliff, Dahl, & Pollak, 2009) that captures gonadal and adrenal hormonal signals of physical development on a 5-point scale. As part of the parent study, pubic/body hair and skin changes were assessed in girls, as they are associated with adrenal hormones; gonadal hormonal signals are measured using questions about growth spurt, breast development, and menarche. Total score (range = 1–5) was used as covariate in study analyses ($\alpha = .74$).

fMRI assessment

Self-versus-change task (adapted from Jankowski et al., 2014)

During the task, participants were presented with positively ($n = 27$) and negatively valenced ($n = 23$) trait adjective words. Trait adjectives were representative of prosocial, insecure, and aggressive characteristics encompassing social, physical, and global aspects of self (e.g., "friendly," "trustworthy," "boring," "pushover," "depressed," "selfish," "rude," and "ugly"). Stimuli were presented using E-Prime software (Psychology Software Tools, Pittsburgh,

PA) and behavioral responses were collected using a Psychology Software Tools™ glove. Each of the 50 trait adjectives were presented twice, once during the self-evaluative condition in which adolescents rated how true the trait adjective was about them and once during a malleability-evaluative (i.e., change) condition in which adolescents rated how much the trait could change in people during their lives; ratings were completed using a 4-item Likert scale (1 = “not at all,” 2 = “a little,” 3 = “mostly,” or 4 = “definitely”). The task was a mixed block/event-related design that included 20 blocks (10 blocks/condition). A mix of positive and negative trait adjectives were included in each condition block. Each block (31.3 s) began with a brief instruction screen (3,000 ms), followed by five trials (4,500 ms/trial) during which participants made rating responses. Each block ended with a 4,500 ms rest interval (blank screen). Participants were randomly and evenly assigned to a task version (one that began with a self-evaluative block type or one that began with a change block type).

Participant self-evaluative ratings during the fMRI task were used to create the “Self-Concept” variable for analyses. To confirm participants’ perceptions of the valence of each trait, adolescents completed a post-task valence identification worksheet following their scan session. Participants circled whether they considered each of the 50 trait words to be a “positive (good) or negative (bad/not so good) way to be described.” This worksheet was added to the study protocol approximately halfway through the study; therefore, ratings were completed by a subsample of 20 participants. Trait words that did not meet an 80% confirmation rate on valence were not included in the “Self-Concept” variable for study analyses. Participant ratings indicated mixed ratings on valence for “shy” (50% negative rating), “flirty” (60% positive rating), “risky” (60% negative rating), and “assertive” (55% positive rating), so these words were excluded. There were 21 remaining negative trait words and 25 remaining positive trait words. Negative trait word ratings were reverse coded, so that lower scores represented more negative/less positive self-concept and higher scores represented less negative/more positive self-concept. Self-evaluative ratings on negative and positive words were strongly correlated ($r = .678, p < .001$), so were summed into one self-concept score. Using this sum, the Self-Concept variable ratings could range from 46 (most negative) to 184 (most positive). See Table 1 for statistical information on negative, positive, and total self-concept ratings.

fMRI data acquisition

Multiband images were acquired on a 3T Siemens Trio scanner. Stimuli were projected using a color high-resolution LCD projector. Each volume consisted of 60 slices (3.2 mm thick). Volumes were acquired parallel to the anterior-posterior commissure line using a T2*-weighted echo planar imaging pulse sequence with multiband = 3, 1,500 ms repetition time, 30 ms echo time, 55° flip angle, $3.2 \times 3.2 \times 3.2$ mm voxels, 220×220 field of view, 96×96 matrix size. Scanning began on the instruction screen of the first block. A total of 150 volumes were collected for each block condition (self and change). Four hundred and nineteen volumes were acquired throughout the entire 10.5-min task. One hundred and ninety-two high-resolution, inversion time-weighted MPRAGE images were also acquired (repetition time = 2,300 ms, echo time = 3.93 ms, TI = 900 ms, field of view = 256×256 , voxel size = $1.0 \times 1.0 \times 1.0$ mm, flip angle = 9°, slice thickness = 1 mm) for co-registration pre-processing procedures.

fMRI pre-processing

Images were pre-processed using SPM12 (<http://www.fil.ion.ucl.ac.uk/spm>). Volumes were oriented to the AC-PC line and realigned to correct for head motion. Images were segmented and co-registered to the first functional image. Realigned images were spatially normalized to a standard MNI template (Montreal Neurological Institute template) using a fourth degree B-spline interpolation method. Normalized images were smoothed with a 6 mm full-width at half-maximum Gaussian filter. Voxels were resampled to be 2 mm^3 . If participants exhibited absolute motion greater than $2 \text{ mm}/2^\circ$ and global intensities more than 3 SD from the mean for more than 25% of volumes, they were excluded from analyses ($n = 9$). Six motion parameters were included as regressors in the first level generalized linear model design to correct for slow-drift motion.

The first level generalized linear model included 11 regressors – self-positive, self-negative, change-positive, and change-negative conditions, the rest intervals, and six motion parameters. There were 20, 3.0-s rest periods during which participants were presented with a brief screen stating which condition they would be presented with (self or change) which were not modeled and used as baseline. The Self-Negative > Self-Positive and Self-Positive > Self-Negative contrasts were used for data analyses.

Data analysis

To compare differences in neural activation between the negative self-evaluative and positive self-evaluative task conditions, within-sample *t*-tests were computed in SPM12 using the Self-Negative > Self-Positive and Self-Positive > Self-Negative contrasts. Clusters passing a voxelwise, $p_{\text{uncorr}} < .001$ threshold and $p_{\text{FWE}} < .05$ family-wise, cluster-level error correction were considered significant. Parameter estimates from significant clusters were extracted for each participant using the MarsBaR toolbox for SPM. Bivariate correlations (with Pearson correlation coefficients) between neural activity, subjective self-concept, and depressive symptoms were run in SPSS.

Indirect effects were assessed in SPSS with the PROCESS macro, using 5,000 bootstrapped samples, to test the final study hypotheses. We consider these models exploratory due to the small sample and fact that most variables were measured concurrently and, further, hope that preliminary findings may inform future longitudinal studies in this area. Extracted neural activation values for each significant cluster were entered into separate PROCESS models as independent variables, adolescents’ self-concept ratings were entered as mediating variables, and adolescent depression scores were included as dependent variables. Indirect effects were only explored if significant direct associations between neural activation, self-concept and depressive symptoms were found. No more than two indirect models could be run for each brain region, one per each time point (T1 and T2), so we did not correct for multiple tests at this level. All measures included as independent variables in analyses were assessed for outliers. Eight outlying data points, including four T1 depression scores, one T2 depression score, and three neural activation parameter estimates, were winsorized to $25^{\text{th}}\%ile/75^{\text{th}}\%ile \pm 1.5 \times IQR$.

Results

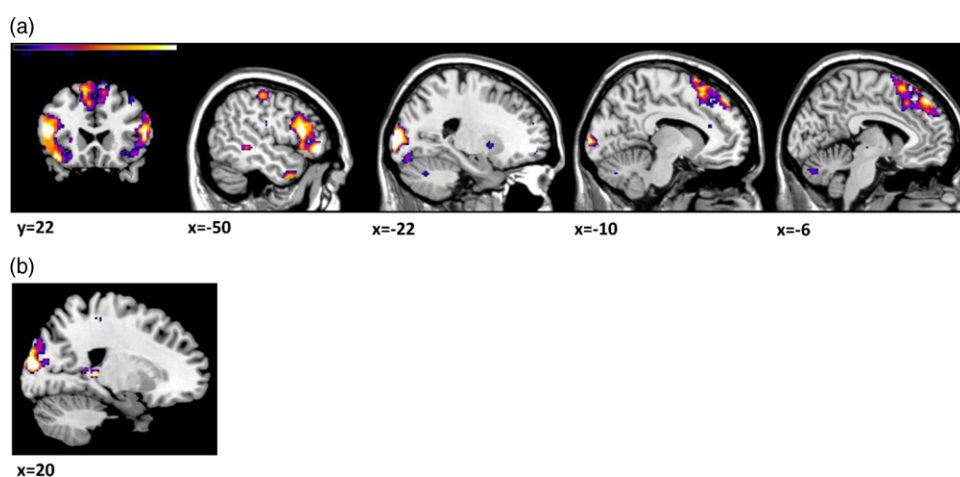
Self-Negative vs. Self-Positive activation

Results showed significant activation during the Self-Negative > Self-Positive, across all participants, in the left dorsal

Table 2. Whole-brain, within-sample, *t*-test results comparing Self-Negative and Self-Positive conditions (voxelwise threshold, $p_{\text{uncorr}} < .001$) using a with a family-wise error ($p_{\text{FWE}} < .05$) correction for multiple comparisons

	Hem.	Region	Brodmann area	Peak voxel coordinates			<i>k</i>	<i>t</i> -statistic (df = 38)
				<i>x</i>	<i>Y</i>	<i>Z</i>		
<i>Self-Negative > Self-Positive</i>	L	VLPFC	45/47	-50	20	14	990	5.62
	L	dMPFC	8	-8	44	48	140	5.03
	L	SMA/dMPFC	6/8	-10	20	60	184	4.60
	L	Visual association	18	-22	-100	6	737	6.90
<i>Self-Positive > Self-Negative</i>	R	Visual association	18	20	-92	12	198	5.87

Note. *k* = cluster size; R = right, L = left; VLPFC = ventrolateral prefrontal cortex; dMPFC = dorsal medial prefrontal cortex; SMA/dMPFC = supplementary motor area/dorsal medial prefrontal cortex.

**Figure 1.** Whole-brain activation ($p_{\text{uncorr}} < .001$ voxelwise threshold; $p_{\text{FWE}} < .05$ clusterwise threshold) during: (a) Self-Negative, greater than Self-Positive, condition; and (b) during Self-Positive, greater than Self-Negative, condition.

medial prefrontal cortex (dMPFC), VLPFC, supplementary motor area/dorsal medial prefrontal cortex (SMA/dMPFC) and left visual association area. Greater activation during the Self-Positive > Self-Negative was found in the right visual association area (Table 2; Figure 1).

Associations between neural activity, self-concept, and depressive symptoms

Correlations can be found in Table 3. Depressive symptoms at T1 and T2 were highly correlated ($r = .67$, $p < .001$); depressive symptoms were significantly higher at T2, compared to T1 ($t = -3.77$, $p < .001$). As hypothesized, depressive symptoms at T1 and T2 were significantly associated with girls' subjective self-concept (T1: $r = -.495$, $p = .001$; T2: $r = -.495$, $p = .002$). Further, differential neural activation in several regions during Self-Negative vs. Self-Positive conditions was associated with self-concept and/or depressive symptoms in hypothesized directions. Activation in the L dMPFC during Self-Negative > Self-Positive was significantly associated with self-concept ($r = -.313$, $p = .05$), such that more activation to Self-Negative compared to Self-Positive was linked to more negative self-concept; significant associations were not found in the L VLPFC, L SMA/dMPFC, and L visual association area (p 's = .12–.74). Activation in the right visual association area during Self-Positive > Self-Negative was significantly associated with self-concept ($r = .339$, $p = .04$); more

activation to Self-Positive, compared to Self-Negative was linked to more positive self-concept. More depressive symptoms was significantly associated with activation in the L VLPFC (T1: $r = .330$, $p = .04$; T2: $r = .405$, $p = .01$), L dMPFC (T1: $r = .357$, $p = .03$; T2: NS), and L SMA/dMPFC (T1: $r = .314$, $p = .05$; T2: $r = .435$, $p = .006$) during Self-Negative > Self-Positive, while less depressive symptoms was associated with activation in the right visual association area at T2 only ($r = -.333$, $p = .04$) during Self-Positive > Self-Negative.

Exploratory indirect effects models

Bivariate correlation analyses among behavioral variables of interest and potential covariates (see Table 3) indicated that neither age nor pubertal status were significantly correlated with other behavioral variables of interest, so they were excluded from final models.

T1

Given that neural activation in the L dMPFC was significantly associated with both self-concept and depressive symptoms, an indirect effect model was run to explore the possible indirect effects of self-concept on the relationship between neural activation and depressive symptoms. Greater dMPFC activation during Self-Negative > Self-Positive was associated with higher T1 depressive symptoms through less positive self-concept ratings (Effect = 3.162

Table 3. Correlations between demographic and behavioral variables of interest ($N = 39$)

	1.	2.	3.	4.	5.	6.	7.	8.	9.
1. Age	1								
2. Pubertal status	-.339*	1							
3. Self-concept	-.145	-.057	1						
4. T1 depressive Sx	.192	.193	-.495***	1					
5. T2 depressive Sx ^a	.018	.110	-.495***	.671***	1				
<i>Self-Negative > Self-Positive</i>									
6. L VLPFC	.038	-.144	-.251	.330*	.405**	1			
7. L dMPFC	.126	-.069	-.313*	.357*	.256	.816***	1		
8. L SMA/dMPFC	.044	.005	-.200	.314*	.435**	.800***	.702***	1	
9. L visual association	.335*	.009	-.055	.275 [†]	.202	.386*	.618***	.499***	1
<i>Self-Positive > Self-Negative</i>									
10. R visual association	-.088	-.084	.339*	-.154	-.333*	-.417**	-.498**	-.434**	-.447***

[†] $p < .10$; * $p \leq .05$, ** $p \leq .01$, *** $p \leq .005$.

^aCorrelations with T2 depressive symptoms with 38 participants.

Note. Sx = Symptoms.

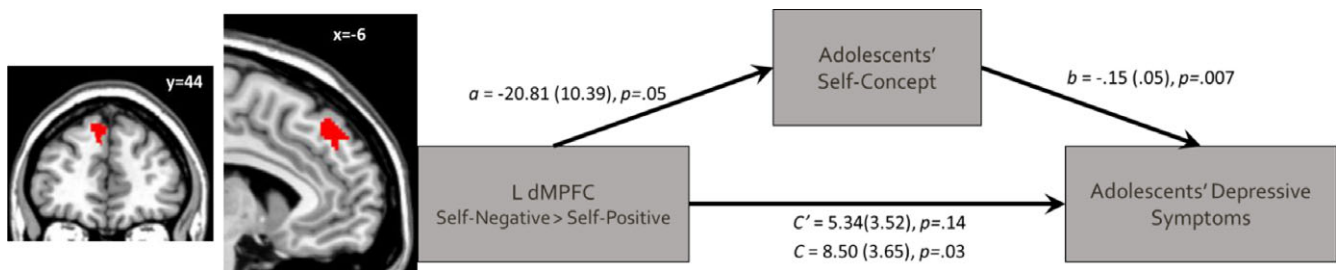


Figure 2. Neural activation associated with concurrent depressive symptoms through indirect effects of Self-Negative > Self-Positive activation in the left dorsal medial prefrontal cortex.

[BootSE = 2.027], 95%CI: 0.077, 7.801; Figure 2). Significant effects were probed to assess whether activation during the Self-Negative or Self-Positive conditions were driving the effects; to this end, we re-ran indirect effect models using data from only the Self-Negative > Baseline and only the Self-Positive > Baseline contrasts. Follow-up analyses indicate that activation specifically during the Self-Negative condition was driving this effect (Effect = 2.158 (BootSE = 1.272), 95%CI: 0.343, 5.255), as the indirect effect model using data from the Self-Positive condition was not significant (Effect = 1.600 (BootSE = 1.295), 95%CI: -0.844, 4.286). Table 4 for full model information.

Additionally, an alternative model was tested to assess whether subjective self-concept ratings would lead to self-referential neural function, and in turn be associated with depressive symptoms. No significant indirect effect was found (dMPFC: Effect = -.0251 [BootSE = .018], 95%CI: -.065, .004).

T2

Neural activation in the R visual association area was significantly associated with both self-concept and depressive symptoms at T2, therefore an indirect effect model was used to explore the possible indirect effects of self-concept on the relationship between neural activation and depressive symptoms. Greater neural activation in the right visual association area during Self-Positive > Self-Negative was

associated with lower levels of T2 depressive symptoms through more positive self-concept ratings (Effect = -7.344 [BootSE = 4.520], 95% CI: -18.072, -5.999; Table 5, Figure 3). Follow-up analyses showed that indirect effect models using data from only the Self-Positive condition or only the Self-Negative condition were not significant (Self-Positive > Baseline: Effect = -1.401 (BootSE = 1.558) 95%CI: -5.282, .867; Self-Negative > Baseline: Effect = .099 (BootSE = 1.234) 95%CI: -2.278, 2.864), suggesting that it was specifically the difference between the two conditions that was driving the effect. Importantly, however, this model was no longer significant after statistically adjusting for T1 depressive symptoms (Effect = -2.245 (BootSE = 2.202) 95%CI: -7.381, 1.195).

We also examined to what extent subjective self-concept ratings would lead to self-referential neural function, and in turn be associated with depressive symptoms. Indirect effects for this model were not significant (Effect = -.045 [BootSE = .042], 95% CI: -.127, .044).

Discussion

This study demonstrates the presence of brain-behavior associations supporting self-referential processing, subjective self-concept and depressive symptoms in adolescent girls. In general, early adolescent girls in the current study show greater activation in left frontal cortical regions and in the left visual association area

Table 4. Significant indirect effect models of neural activation on T1 depressive symptoms through adolescents' self-concept ratings

Independent variable	Coeff.	SE	t-statistic	p
<i>Self-negative > Self-positive</i>				
L dMPFC (BA8)				
Total effect model summary	$R^2 = .128, F(1, 37) = 5.414, p = .026$			
Effect of IV on mediator	-20.806	10.385	-2.004	.053
Direct effect of mediator on DV	-.152	.053	-2.874	.007
Direct effect of IV on DV	5.338	3.516	1.518	.138
Total effect of IV on DV	8.499	3.653	2.327	.026
Indirect effect of IV on DV	Effect = 3.162 (BootSE = 2.027), 95%CI: 0.077, 7.801			
Standardized indirect effect	Effect = 0.133 (BootSE = 0.078), 95%CI: 0.004, 0.305			

Bolded parameter = $p \leq .05$.

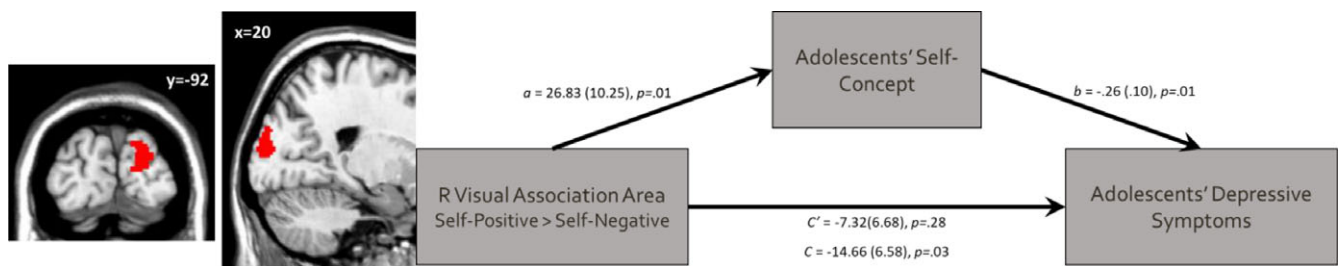
Note. IV = independent variable; DV = dependent variable; L = left; R = right, dMPFC = dorsal medial prefrontal cortex. All analyses were conducted with extracted mean BOLD response within each functionally derived ROI for Self-Negative vs. Self-Positive contrast.

Table 5. Significant indirect effect model of neural activation on T2 depressive symptoms through adolescents' self-concept ratings

Independent variable	Coeff.	SE	t-statistic	p
<i>Self-positive > Self-negative</i>				
R visual association (BA18)				
Total effect model summary	$R^2 = .121, F(1, 36) = 4.968, p = .032$			
Effect of IV on mediator	26.827	10.246	2.716	.010
Direct effect of mediator on DV	-.264	.099	-2.668	.012
Direct effect of IV on DV	-7.320	6.676	-1.096	.280
Total effect of IV on DV	-14.664	6.579	-2.229	.032
Indirect effect of IV on DV	Effect = -7.344 (BootSE = 4.520), 95%CI: -18.072, -0.599			
Standardized indirect effect	Effect = -0.174 (BootSE = 0.087), 95%CI: -0.357, -0.017			

Bolded parameter = $p \leq .05$.

Note. IV = independent variable; DV = dependent variable; R = right, All analyses were conducted with extracted mean BOLD response within each functionally derived ROI for Self-Positive vs. Self-Negative contrast. $N = 38$.

**Figure 3.** Neural activation associated with T2 depressive symptoms at 6-month follow-up through indirect effects of Self-Positive > Self-Negative activation in the right visual association area.

during self-evaluation of negative traits, relative to positive traits, and greater activation in the right visual association area during self-evaluation of positive traits, relative to negative traits. Further, findings indicate that girls' neural activation during self-evaluation is associated with girls' self-concept and depressive symptoms. Additionally, exploratory mediation models show that higher neural activation in the dMPFC during self-evaluation of negative, relative to positive, traits is

linked to higher concurrent depressive symptoms through more negative self-concept ratings. Higher neural activation in the right visual association area during self-evaluation of positive, relative to negative, traits is also related to lower levels of depressive symptoms 6 months after baseline assessment, through more positive self-concept ratings. These mediation models provide preliminary data to inform future longitudinal research with larger sample sizes in this area.

With respect to study findings in the MPFC, results further highlight the important role that this region plays in self-referential processes. Consistent with evidence presented by Davey *et al.* (2016), the current results included two clusters in the dorsal region of the MPFC – one in the left dMPFC and the second slightly posterior spanning across both the dMPFC and SMA. The MPFC is believed to help guide how individuals perceive themselves, as well as direct and guide attention to either internal ongoing thought or external stimuli (Davey *et al.*, 2016; Whitfield-Gabrieli & Ford, 2012). The dMPFC has been involved in deciding whether specific traits (e.g., personality traits, autobiographical memories, and self-knowledge) are characteristic of one's self (Araujo *et al.*, 2013; Crone *et al.*, 2022; Molnar-Szakacs & Uddin, 2013). In addition, the dMPFC/SMA cluster spanned into regions of the anterior cingulate cortex which is shown to be involved in cognitive conflict monitoring, error detection, and affective attentional control (Bush *et al.*, 2000; Dolcos *et al.*, 2020; Eisenberger & Lieberman, 2004). This could potentially indicate that youth, in general, detect cognitive conflict and recruit more attentional control resources when asked to think of themselves from a negative perspective.

Of note, results of previous studies in healthy young adults and adolescents have indicated patterns opposite to our findings, showing that the MPFC is generally more activated during self-evaluation of *positive* traits, relative to negative traits (Van de Groep *et al.*, 2021; van der Crujisen *et al.*, 2017, 2018). It may be that our findings are related to the nature of our sample, such that two thirds of the girls were recruited to be high in shy or fearful temperament, placing them at higher risk for depression. In fact, previous studies conducted in depressed adolescents and adults have indicated similar patterns to the present study in that there is dMPFC hyperactivation during negative self-related processing and hypoactivation during positive self-related processing (Burkhouse *et al.*, 2017; Quevedo, Ng, Scott, Smyda, *et al.*, 2016; Yoshimura *et al.*, 2010). This interpretation may be further supported by significant associations presented in this study between greater dMPFC and SMA/dMPFC activation to Self-Negative, compared to Self-Positive, and more depressive symptoms concurrently and 6 months later (for SMA/dMPFC cluster only).

Additionally, as hypothesized, brain-behavior analyses in this study provided evidence of a direct link between dMPFC activity and subjective self-concept. While results of all of the prior studies assessing neural underpinnings of self-concept have been specific to neural function during self-evaluation in positive contexts, relative to negative (Liu *et al.*, 2020; Quevedo, Ng, Scott, Smyda, *et al.*, 2016; Van de Groep *et al.*, 2021; van der Crujisen *et al.*, 2017, 2018), the current findings add to the literature by providing evidence that higher neural activation during negative self-evaluation, relative to positive, in the dMPFC is related to more negative subjective reports of self-concept in adolescents. Based on the presumed function of the dMPFC described earlier, this result could suggest that greater activation in the dMPFC during negative self-evaluation is indicative of more entrenched feelings of negative self-concept. Interestingly, the exploratory indirect effect model demonstrated that adolescent subjective feelings of self-concept help to explain the relationship between greater activation in the dMPFC during self-evaluation of negative traits and higher levels of depressive symptoms. Therefore, our findings suggest that youth exhibiting heightened activation in the dMPFC while self-evaluating from a *negative* perspective, more so than from a positive perspective, may have a cognitive bias towards negative

attributes of the self which are known to play a role in depressive states (Kovacs & Beck, 1978).

The present study also showed the L VLPFC to be more activated during self-evaluation of negative traits, relative to positive traits, across the entire sample and that greater activation was associated with higher depressive symptoms, both concurrently and longitudinally. Prior research has reported VLPFC activation to be associated with child depressive symptoms in youth with less positive self-concept, though results were specific to neural processing during self-evaluation of positive traits (Liu *et al.*, 2020). The VLPFC is involved in regulation of negative emotion, resistance to emotional distractibility, emotional memory encoding, and semantic processing (Casey *et al.*, 2008; Dolcos *et al.*, 2020; Phillips *et al.*, 2003), as well as with the regulation of negative self-beliefs using reappraisal in healthy adults (Goldin *et al.*, 2009). Given that we found that greater activation in both the dMPFC and VLPFC during negative self-processing were associated with higher depressive symptoms, the pattern of elevated activation in the VLPFC could represent a potential compensatory mechanism through which negative, affectively charged self-directed perceptions may be processed, encoded, and regulated, in response to the demands of persistent internally focused attention, affective attentional control and monitoring demands, potentially reflected by the heightened dMPFC. Future studies should include a reappraisal condition and/or assess causal connectivity patterns between these regions to directly test this hypothesis.

Additionally, we found that greater activation in the left visual association area was associated with negative, relative to positive, self-evaluative processing, whereas the right visual association area was associated with positive, relative to negative, self-evaluative processing, across the entire sample. The visual association area is thought to underlie individuals' perceptual representations, initial focus, and attention to cues (Browning *et al.*, 2010; Dolcos *et al.*, 2020). Of note, part of our lateralized results align with a meta-analysis showing that activation in the *left* occipital cortex is more typical in response to *negative* stimuli (Lindquist *et al.*, 2015). Surprisingly, we found the right visual association area to activate more during the positive self-referential context, compared to the negative, which deviates from a meta-analysis showing that the visual association area activates to both negative and positive contexts (Lindquist *et al.*, 2015). It is unclear what might be driving the valence-specific result in the right visual association area in this study; however, we may speculate that this could be related to the early adolescent age of the sample and/or that the sample is majority high-risk for depression, though future studies are needed to investigate this.

Moreover, we found higher activation in the right visual association area during positive, relative to negative, self-evaluative processing was associated with less negative self-concept ratings and less depressive symptoms 6 months later, whereas activity in the left visual association area during negative, relative to positive, self-evaluative processing was not correlated with subjective self-concept or depressive symptoms. The exploratory indirect effect model further showed that the link between right visual association area activation in the positive context and lower levels of depressive symptoms is mediated by girls' reports of more positive self-concept. Another important consideration is that higher right visual association area activation during positive vs. negative self-evaluation was only associated with lower 6-month depressive symptoms through less negative self-concept when baseline depressive symptoms were not statistically adjusted for. This could suggest that the relationship between brain activity and

subjective self-concept is associated with current, or more stable, depressive symptoms but is not sensitive to changes in depressive symptoms over time.

Despite promising findings, the current study had several limitations. First, neural function and self-concept ratings were assessed at the same timepoint for exploratory study models and T1 indirect effect models were fully cross-sectional. Therefore, directional relationships between constructs, particularly for the indirect effect models are preliminary and speculative. Further, we recognize that these relationships are bidirectional such that persistent negative self-concept and self-cognitions could impact neural function and, in turn, subsequent risk for depression. Of note, however, the models testing the effects of self-concept biases on patterns of neural function, and in turn depressive symptoms, were not supported. Nevertheless, it is possible that pre-existing depressive symptoms prior to baseline assessment may be driving the variance in the T1 models. This is relevant because our T2 model results were not maintained when T1 symptoms were added as a covariate. Future studies should be conducted to confirm these exploratory findings.

Another limitation was that we had a relatively small sample of all females. The relatively small sample may have limited the power to detect small effects. The sample size also precluded testing of moderating factors, such as whether youth's beliefs regarding the stability of personality characteristics (as assessed during the "change" conditions of the fMRI task) would have a moderating effect on the associations between neural activation, self-concept and depressive symptoms. The study only included girls given their high risk for depression and low self-concept, compared to boys (Costello et al., 2003), and these girls were oversampled to be at higher risk for social anxiety and depression based on temperament. Therefore, it is important to consider that the presented results may not generalize to girls with lower levels of shy and fearful temperament or to boys due to potential gender differences in self-concept and depression risk. The sample was also 61% White, indicating a need to expand this research using more diverse samples. Further, although depressive symptoms significantly increased between assessments, on average, symptoms levels were not within the clinical range. However, this is not necessarily a limitation because predicting subclinical symptoms is important, as these symptoms can be functionally impairing and confer risk for more severe depression in the future, when rates peak around ages 15–16 (Costello et al., 2003). Therefore, these girls may still develop clinical depression in a couple of years. Overall, future studies should further test this model's predictive ability in larger, more diverse samples that include adolescents with clinical levels of depression.

This study provides new insights into the relation between self-related evaluative neural processing and depression in adolescents using an fMRI task that enabled specific conclusions regarding the neural underpinnings of self-concept. Early adolescence is an important period when self-concept and risk for depression begin to develop (Costello et al., 2011; Shapka & Keating, 2005), therefore this study provides evidence for a model hypothesizing that neural processing during negative and positive self-evaluations may subserve cognitive, self-related biases that are related to depressive symptoms. This may have important clinical applications. For example, research has begun establishing the use of neurofeedback paradigms that engage self-focused processing (i.e., happy self-face stimuli) for depressed adolescents (Quevedo et al., 2019). Present findings may help in the continued development of novel neurofeedback and other neurobehavioral interventions by

offering insight into specific neural targets for the reduction of negative self-concept and, in turn, risk for adolescent depression.

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