UC Berkeley
UC Berkeley Previously Published Works

Title

"Loser" or "Popular"?: Neural response to social status words in adolescents with major depressive disorder

Permalink

https://escholarship.org/uc/item/6320j0vq

Authors

Silk, Jennifer S
Lee, Kyung Hwa
Kerestes, Rebecca
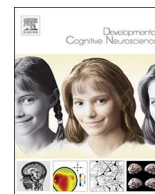et al.

Publication Date

2017-12-01

DOI

10.1016/j.dcn.2017.09.005

Peer reviewed

CrossMark

"Loser" or "Popular"?: Neural response to social status words in adolescents with major depressive disorder

Jennifer S. Silk[a,b,*,1], Kyung Hwa Lee[a,1], Rebecca Kerestes[b], Julianne M. Griffith[a], Ronald E. Dahl[c], Cecile D. Ladouceur[b,a]

[a] Department of Psychology, University of Pittsburgh, United States
[b] Department of Psychiatry, University of Pittsburgh School of Medicine, United States
[c] School of Public Health, University of California, Berkeley, United States

ARTICLE INFO

ABSTRACT

Concerns about social status are ubiquitous during adolescence, with information about social status often conveyed in text formats. Depressed adolescents may show alterations in the functioning of neural systems supporting processing of social status information. We examined whether depressed youth exhibited altered neural activation to social status words in temporal and prefrontal cortical regions thought to be involved in social cognitive processing, and whether this response was associated with development. Forty-nine adolescents (ages 10–18; 35 female), including 20 with major depressive disorder and 29 controls, were scanned while identifying the valence of words that connoted positive and negative social status. Results indicated that depressed youth showed reduced late activation to social status (vs neutral) words in the superior temporal cortex (STC) and medial prefrontal cortex (MPFC); whereas healthy youth did not show any significant differences between word types. Depressed youth also showed reduced late activation in the dorsolateral prefrontal cortex and fusiform gyrus to negative (vs positive) social status words; whereas healthy youth showed the opposite pattern. Finally, age was positively associated with MPFC activation to social status words. Findings suggest that hypoactivation in the "social cognitive brain network" might be implicated in altered interpersonal functioning in adolescent depression.

1. Introduction

"Sticks and stones may break my bones but words will never hurt me." Despite this old adage, we all know that words can hurt, especially during the precarious teen years. Teenagers between the ages of 13 and 17 send and receive an average of 67 text messages a day and more than 70% of teens are active on two or more social networking platforms (Lenhart, 2015). Teens extract beliefs about their own social status from the positive and negative messages and comments sent whirling through cyberspace by other teens. Little is known about the underlying neural processes involved in processing text that conveys information about social status. Given the high frequency with which this process occurs during adolescence, gaining a better understanding of individual differences in how the teen brain processes social status words may be important in understanding social and emotional adjustment during this period.

Nelson et al. (2005) outline a social information processing brain network that undergoes significant remodeling during adolescence. We anticipated that viewing social status words would activate brain regions within this network that are typically implicated in social cognitive processing, including perceiving and making attributions about another person's thoughts and feelings, as well as perceiving the self-relevance of social information. This includes the medial PFC (MPFC), the superior temporal sulcus (STS), temporoparietal junction (TPJ), and posterior cingulate cortex (PCC) (Blakemore, 2008; Frith and Frith, 2007). The STS in particular seems to play a role in integrating social perception and mentalizing, and serves as a central hub for social information processing (Yang et al., 2015). Healthy adolescents show elevated activity in this "social brain network" during tasks that require social perception or thinking about or imagining others' mental states (i.e. 'mentalizing'; Blakemore and Mills, 2014; Burnett et al., 2010). Pfeifer et al. (2009) have shown that when adolescents are asked to engage in self-appraisal, not only do they recruit regions involved in self-perception, such as the MPFC, but they also activate regions

---

* Corresponding author at: 210 S. Bouquet Street, Pittsburgh, PA 15260, United States.
E-mail address: jss4@pitt.edu (J.S. Silk).
[1] These authors contributed equally to this work.

involved in social perception and mentalizing, such as the TPJ and STS. Engagement of the social cognitive brain network during self-appraisal is elevated in adolescents compared to adults, suggesting that social comparison processes may play a particularly strong role in self-perception during adolescence (Pfeifer et al., 2009).

One important question is the extent to which individual differences in activation of neural networks involved in social cognitive processing may play a role in adolescent depression. Rates of depression increase dramatically during adolescence, especially in adolescent girls, who show increased sensitivity to interpersonal feedback during the adolescent years (Rudolph, 2002; Shih et al., 2006). Depression during adolescence is often triggered by the experience of social rejection (Nolan et al., 2003; Rudolph and Conley, 2005). Neuroimaging studies of simulated social interaction with peers have shown that adolescents with and at risk for depression show elevated activation of regions of the brain involved in monitoring and evaluating emotional salience, such as the subgenual anterior cingulate cortex (sgACC), in response to peer exclusion or rejection (Masten et al., 2011; Silk et al., 2014). Regions of the affective salience network, especially the amygdala and ACC, have also been consistently shown to be elevated among depressed compared to healthy adolescents during the processing of negative emotional stimuli, such as affective faces (Kerestes et al., 2014). Despite this clear evidence of perturbed functioning of affective salience networks during social information processing in adolescent depression, it is not known whether perturbed functioning of social cognitive brain networks might also play a role.

There is little existing literature to guide expectations about potential alterations in social cognitive brain function in adolescent depression. Based on behavioral evidence of interpersonal sensitivity in adolescent depression (Prinstein et al., 2005; Rudolph and Conley, 2005; Shih et al., 2006), we might expect that regions of the brain that detect and interpret social information would be hyper-reactive to social status information in youth who are depressed. On the other hand, social withdrawal is a core clinical feature of depression (Agoston and Rudolph, 2013; Hames et al., 2013). This social withdrawal might be driven by or reflected in a blunted (hypoactive) response among brain regions that process social information. Consistent with this possibility, one imaging study in adults showed that those with remitted depression exhibited hypoactivity in response to both positive and negative social interaction images in the MPFC compared to healthy adults (Elliott et al., 2012). These differences were present in the absence of depressive symptoms, and were not seen for achievement images used as comparison stimuli, suggesting that MPFC hypoactivity to social stimuli might function as a trait-like vulnerability factor for depression. Another study in adults revealed reduced activation in the STS, a region implicated in social perception and language processing, among depressed compared to healthy adults in response to reading sad words (Canli et al., 2004). Given limited research on this topic in adolescents with depression, we tested competing hypotheses that depressed youths' neural response in temporal and prefrontal cortical regions to social status words might be hypoactive vs. hyper-reactive compared to non-social neutral words.

We also explored whether the time-course of brain activation in response to social status information differed between depressed adolescents and healthy controls. A key feature of depression is the tendency to engage in perseverative self-referential thought, such as rumination (Nolen-Hoeksema et al., 2008), which is thought to result in sustained activation of regions involved in affective and self-referential processing (Burkhouse et al., 2017; Mandell et al., 2014). For example, Siegle et al. (2002) found that depressed adults show a sustained amygdala response to negative words up to 25 s after word presentation, which was correlated with the tendency to engage in perseverative self-referential thought. Similarly, Silk et al. (2014) found that depressed youth showed sustained dorsal ACC activation in response to simulated peer rejection relative to healthy youth 8–11 s after receiving feedback. However, it is not known whether depressed youth similarly

show sustained activation over time to social status stimuli in regions of the brain involved in social cognitive processing. Given the potential for perseverative self-referential thought following display of social status words, we hypothesized that group differences in brain activation to social status words would emerge in the latter half of trials, presumably reflecting alterations in elaborative processing of social stimuli.

We also explored whether activity in these neural regions would be modulated by word valence, specifically, whether the words connoted positive or negative social status. Elliott et al. (2012) found that MPFC activity in response to social interaction images was attenuated in depressed compared to healthy adults regardless of whether the images were of positive or negative valence. On the other hand, Silk et al. (2017) found that depressed adolescents showed a blunted MPFC and precuneus response to audio clips conveying maternal praise but not maternal criticism (relative to neutral statements). Thus, we explored the possibility of valence effects in social cognitive processing of social status words.

Finally, we examined whether neural response to social status words in social cognitive brain networks varied as a function of development. Adolescence is defined as the transitional period between puberty and adulthood in human development. Given the typical onset of the early stages of pubertal maturation at ages 9–10 (Herman-Giddens, 2006), we operationalize adolescence in this study as beginning at age 10 and ending at age 18. This developmental period encompasses marked changes in social affiliation and social behavior (Nelson et al., 2005; Steinberg and Morris, 2001) that correspond with advances in social-cognitive abilities as well as structural changes and functional reorganization of brain regions important for social-cognitive processes (Blakemore, 2008; Burnett et al., 2010). For example, a recent longitudinal study demonstrated reductions in gray matter volume and cortical thickness in the dorsomedial PFC (dmPFC), TPJ, and posterior STS (pSTS) from childhood through early adulthood (Mills et al., 2014). These structural changes during adolescence are thought to reflect synaptic reorganization and/or increased integrity of white matter (Paus et al., 2008). In terms of functional changes, imaging studies in typically developing youth have shown age-related increases between childhood and adolescence in MPFC activation during the processing of emotional faces (Pfeifer et al., 2011) and in response to social evaluation (Gunther Moor et al., 2010; Pfeifer et al., 2013). There is also evidence of a decrease in dmPFC activation during mentalizing tasks from adolescence to adulthood (see Blakemore, 2008), as well as enhanced connectivity of the MPFC with the pSTS/TPJ when thinking about social emotion scenarios in adolescents compared to adults (Burnett and Blakemore, 2009). Developmental theorists have argued that these changes may constitute a sensitive period for adapting to the social environment (Blakemore and Mills, 2014), or a period of enhanced flexibility in responding to social and motivational input (Crone and Dahl, 2012).

Recently investigators have also begun to examine the extent to which developmental changes in neural response to social stimuli are driven by the influence of pubertal increases in adrenal and gonadal hormones or chronological age. Existing data have linked pubertal maturation to increases in sensation-seeking (Martin et al., 2002), physiological reactivity to emotional words (Silk et al., 2009), neural response to monetary reward (Forbes et al., 2010; van Duijvenvoorde et al., 2014), affective faces (Forbes et al., 2011; Moore et al., 2012) and peer rejection (Silk et al., 2014). Only a few neuroimaging studies have focused on the role of pubertal maturation in social cognitive processing. Pfeifer et al. (2013) found that ventromedial PFC activation while processing social self-evaluative words increased with both age and pubertal development. In another study, Goddings et al. (2012) found that greater circulating levels of the pubertal hormone testosterone were associated with greater activation in the left anterior temporal cortex (ATC) during a mentalizing task, above and beyond the effects of age. However, little is known about the specific effects of puberty on social cognitive brain function. In the present study, we examined

whether age and/or pubertal status were associated with neural response to social status words in temporal and prefrontal cortical regions. We hypothesized that chronological age would be more strongly associated with response to social status words in prefrontal regions involved in social cognitive processing (i.e. MPFC), while pubertal status would be more strongly related to neural response in the temporal cortex (i.e. STS, TPJ). We also explored whether the relationship between development and neural response to social status words differed for depressed and healthy youth, given one recent report of attenuated associations between pubertal development and neural response to peer rejection in depressed compared to healthy youth (Silk et al., 2014).

2. Method

2.1. Participants

Fifty-eight very young adolescents to late adolescents (42 female, aged 10–18 years [M = 15.01, SD = 1.86]) were recruited from community advertisements, pediatrics offices, and existing research projects. Two participants were excluded due to poor task performance (e.g., no responding and accuracy rate < 60%) and seven participants were excluded due to excessive head movement (over 30% of scans with greater than ± 5 mm and ± 5° movement from a reference image and ± 1 mm and ± 1° incremental (scan-to-scan) movement). Forty-nine participants (35 female, aged 10–18 years [M = 15.14, SD = 1.82]) were included for our final analysis.

Twenty adolescents had a current primary diagnosis of major depressive disorder (MDD) based on DSM-IV (American Psychological Association, 1994) criteria and 29 were typically developing controls (CON) with no psychiatric history. Adolescents' lifetime and present DSM-IV diagnoses were assessed using the Schedule for Affective Disorders and Schizophrenia in School-Age Children—Present and Lifetime version (K-SADS-PL) (Kaufman et al., 1997). MDD adolescents were allowed to participate in the study if they were on a stable dose of SSRI medication (N = 2). Participants were excluded if they were taking psychoactive medications other than SSRI's or had metal braces or other metal objects in their body. CON adolescents were excluded if they met current or lifetime DSM-IV diagnosis for any Axis 1 disorder. MDD adolescents were excluded if they had a current diagnosis of obsessive-compulsive disorder, post-traumatic stress disorder, conduct disorder, substance abuse or dependence, ADHD combined type or predominantly hyperactive-impulsive type, or a lifetime diagnosis of bipolar disorder, psychotic depression, schizophrenia, schizoaffective disorder, or an autism spectrum disorder. Eleven MDD adolescents had a current diagnosis of one or more comorbid anxiety disorders, including panic disorder (N = 2), specific phobia (N = 4), generalized anxiety disorder (N = 6), social phobia (N = 2), separation anxiety disorder (N = 1), and agoraphobia (N = 1). One MDD youth had a comorbid diagnosis of oppositional defiant disorder.

2.2. Procedure

The parents provided informed consent and participants provided assent using forms approved by the University of Pittsburgh Institutional Review Board. They then completed two laboratory visits. During the first visit, participants completed a structured diagnostic interview and questionnaires to assess self-reported depressive symptoms and pubertal status. The fMRI assessment was completed during their second visit.

2.2.1. Structured diagnostic interviews

On their first visit to the lab, each adolescent and his or her parent (s) were interviewed to determine the youth's mental health history using K-SADS-PL (Kaufman et al., 1997). Parents and youth were interviewed separately, with clinicians integrating data from both

informants to arrive at a final diagnosis. All interviews were carried out by trained BA- and MA-level clinicians. 15% of interviews were double coded and there were no diagnostic disagreements.

2.2.2. fMRI assessment and debriefing

Participants underwent an fMRI scan. They were asked to lay as still as possible during the structural imaging acquisition and then to perform a word valence identification (WVID) task during the functional imaging acquisition. After the fMRI assessment, participants were asked to complete a post-scan valence rating of each word, ("How emotional is this word for you?") on a 7-point scale ranging from 1 (very negative) to 7 (very positive)?". To confirm that the social status words were considered relevant words to describe adolescent social status, participants were also asked to answer two questions: 1) Is this a word that kids your age would use to describe another kid they admire or look up to (high social status rating)? and, 2) Is this a word that kids your age would use to describe another kid they do NOT admire or do NOT look up to (low social status rating)? The response was 'yes' or 'no'. Participants were carefully debriefed following completion of the scan.

2.3. Experimental task and stimuli

During fMRI assessment, participants were asked to complete a WVID task, which has been used to examine physiological and neural activity in adults and youth with MDD (Siegle et al., 2007; Silk et al., 2007) The task was modified to incorporate words connoting social status. Participants were instructed to identify the emotional valence of 26 social status words (13 positive and 13 negative) and 13 neutral words by pressing a corresponding button for each valence (positive, negative, and neutral) using a Psychology Software Tools glove. Stimuli were displayed in black on a grey background via a back-projection screen (.88° visual angle) and presented using E-prime 1.0 software (Psychology Software Tools, Pittsburgh, PA). The social status words were generated by a focus group of 6 adolescents who were asked to generate a list of words that could be used to describe a person who the adolescent admired or looked up to (positive social status words; e.g., accepted, popular, liked, invited) or a person they did not admire or look up to (negative social status words: e.g., ignored, loser, disliked, unwanted). We selected social status words with multiple nominations across adolescents that could be balanced with neutral words for word length and frequency of use in the English language. As described below (see post-scan rating results), these words were validated based on post-scan ratings by participants in the present study. Neutral words were chosen from a corpus of words normed for use with youth (Neshat-Doost et al., 1999). Both social status words and neutral words are reported in Table S1 (see Supplementary materials).

A slow event-related paradigm was used to allow examination of the time-course of event-related neural responses (Fig. 1). Each trial began with a cue (a row of Xs) for 1000 ms, followed by presentation of the word for 5000 ms, and followed by a mask (another row of Xs) for 5690 ms. A 5690 ms inter-trial interval (duration was determined by multiples of our TR, 1.67 s) was used to provide sufficient time to assess sustained elaborative processing between trials. There were 26 trials presented with social status words (13 positive social status and 13 negative social status) and 13 trials with neutral words. Trials were shown in a randomized order.
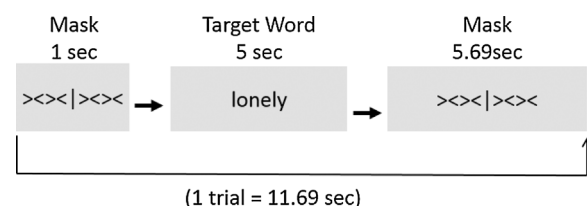

Fig. 1. Example of the experimental paradigm.

2.4. Self-report measures

Child and parent report of child depressive symptom severity were obtained using the long version of the Mood and Feelings Questionnaire (Angold et al., 1995), which is a widely used self-report measure of children and adolescents' depressive symptoms. The MFQ includes 33 items (child version) or 34 items (parent version).

Adolescents or parents rate how true each item has been with regard to the adolescent's symptoms over the past two weeks (0 = *not true*, 1 = *sometimes true*, 2 = *true*). Internal consistency of this scale in the study sample was excellent (child version: α = 0.98, parent version: α = 0.95). Self-reported pubertal status was also obtained using the Pubertal Development Scale (PDS; Petersen et al., 1988) scored to provide two 5-point scales that differentially capture gonadal and adrenal hormonal signs of pubertal development (Shirtcliff et al., 2009). Physical maturation in humans is marked by independent maturation of the adrenal glands (adrenarche) and the gonads (gonadarche). It is not yet clearly understood how adrenal and gonadal aspects of pubertal maturation may differentially influence neural changes during adolescence; therefore, we tested the potential influence of adrenal and gonadal signs of pubertal maturation separately. Scoring takes into account different signs of pubertal development in boys and girls. Scores ranged from 2 to 5 in the present sample.

2.5. Imaging acquisition and preprocessing

2.5.1. Imaging acquisition

Images were acquired on a 3T Trio scanner (Siemens, Erlangen, Germany) at the Magnetic Resonance Research Center, University of Pittsburgh. Thirty-two 3.2-mm slices were acquired parallel using a posterior-to-anterior echo planar (EPI) pulse sequence (T2*-weighted imaged depicting BOLD signal; TR = 1670 ms, TE = 29 ms, FOV = 205 mm, flip angle = 75). Each image was acquired in 1.67 s, allowing 7 scans per 11.69 s trial (determined by multiples of our TR). High-resolution T1-weighted MPRAGE images (1 mm, axial) were also collected for use in cross-registration.

2.5.2. fMRI data preprocessing

fMRI analyses were conducted using locally developed NeuroImaging Software (NIS) (Fissell et al., 2003) and Analysis of Functional Neuroimaging (AFNI) software (Cox, 1996). Functional imaging data were corrected for motion using 3dVolReg implemented in AFNI using the first image as a reference. Linear and quadratic trends within runs were regressed out of fMRI time-series to eliminate effects of scanner drift, unrelated to brain activity using niscorrect from NIS. This procedure also reduces the impact of outliers by Windsorizing or clipping outliers over 1.5 interquartile range (IQR) from the 25th or 75th percentiles to the nearest value within this range. Data were temporally smoothed using a 4-point Gaussian filter and converted to percent-change based on the median of all imaging data. Data were co-registered to the Colin-27 Montreal Neurological Institute (MNI) template using the Automated Image Registration package's (AIR; Woods et al., 1993) 32 parameter non-linear automated warping algorithm and spatially smoothed using a 6 mm full width at half maximum (FWHM) filter.

2.6. Statistical analyses

2.6.1. Post-scan ratings and behavioral data

Post-scan valence ratings and behavioral data (reaction time and accuracy) were analyzed using repeated measures ANOVAs with group as a between-subject factor and valence as a within-subject factor. Post-scan ratings of social status words were analyzed using chi-square to test whether words classified as "social status" words by the focus group were also considered indicators of social status by participants.

2.6.2. Group X Time X Condition (social status vs. neutral words) effects on neural activity during word valence identification

To test our primary hypothesis, we conducted a Group (CON vs. MDD) X Time (7 scans spanning 11.69 s, the duration of each trial) X Condition (social status words vs. neutral words) random effects whole-brain analysis of variance (ANOVA) with participant as a random factor, and group, time, and condition as fixed factors. Time was modelled in the analysis rather than assuming the shape of the HRF because it has been shown that the shape of the HRF varies as a function of both task and brain region (see Handwerker et al., 2004; Siegle et al., 2007). Incorporating time as a factor in our analysis also allowed us to explore whether group and condition differences in processing social status words were driven by initial reactivity to the stimuli or more sustained elaborative processing.

To follow up Group X Time X Condition interactions, we extracted each participant's time-series from the functional ROIs that remained significant after correcting for multiple comparisons. We used Guthrie and Buchwald (1991)'s method to control for Type I error across the many evaluated temporal samples (0 ~ 11.69 s) within functional ROIs. As a temporal analog of contiguity thresholding, this technique restricts statistical significance to temporal windows in which there are more consecutive scans each statistically significant at p < 0.05 than would be expected by chance given the temporal autocorrelation of the data (*r* = 0.50–0.66 after removing 2 principal components, which accounted for ~75% of the variance in the time-series). Using this technique, Monte Carlo simulations suggested that post hoc Group X Condition interactions significant for 2 or more consecutive scans would be considered to have a temporal window significant at p < 0.05. We averaged the level of activation (signal% change from baseline [the first scan of each trial] in both word conditions separately) across the time points in the significant temporal windows (as determined by the Guthrie and Buchwald method) for each functional ROI and each participant. Then, we used this averaged level of activation in follow-up repeated measures Group X Condition ANOVAs and post-hoc pairwise comparisons using paired *t*-tests to compare conditions within each group, as appropriate.

2.6.3. Group differences in neural activity modulated by word valence

To further examine whether group differences in neural response to social status words were modulated by social status word valence, we conducted a Group (CON vs. MDD) X Time (7 scans spanning 11.69 s, the duration of each trial) X Valence (Negative social status words vs. Positive social status words) random effects whole-brain analysis of variance (ANOVA) with participant as a random factor, and group, time, and valence as fixed factors. We used the same Guthrie and Buchwald (1991) method to control for Type I error across the many evaluated temporal samples (0 ~ 11.69 s) within functional ROIs and the same methods for subsequent repeated measures ANOVAs and paired *t*-tests.

2.6.4. Effect of developmental factors on neural response to social status words

We next examined associations between developmental factors (i.e., age and pubertal maturation) and neural activity in response to social status words vs. neutral words, and whether their associations were moderated by diagnostic group (MDD vs. CON). Separate regression models were run for age, PDSA, and PDSG on brain activity in response to social status words in the functional ROIs that showed significant Group X Time X Condition (social status vs. neutral) interaction effects in the ANOVA. We extracted mean level of activation in the three functional ROIs (i.e., bilateral STS and MPFC) that were significant, averaging across the temporal windows that survived the temporal contiguity thresholding (8.35–11.69 s for all three regions). We tested main effects of age or pubertal status, and their interactions with group, on neural activity in response to social status words vs. neutral words. Multiple comparisons were controlled using a Bonferroni correction

(p < 0.017) for regression analyses on the three functional ROIs. Age and pubertal maturation were significantly correlated (age and PDSA: r = 0.45, p = 0.002; age and PDSG: r = 0.38, p = 0.009); therefore, to test for specificity of age or puberty effects, analyses were recomputed with age added as a control variable in the puberty models and puberty added as control variables in the age model.

2.6.5. Type I error control for whole-brain analyses

All group-level and interaction statistical maps were thresholded at voxel-wise $p < 0.005$ and corrected for multiple comparisons by using an empirically determined minimum cluster size to achieve a brain-wise corrected $p < 0.05$, via AFNI's 3dClustSim with smoothing estimated via AFNI's 3dFWHMx, version 16.1.04 "acf" procedure. Our cluster sizes were determined using 5000 Monte Carlo simulations, third-nearest neighbor (NN3) clustering. Because we tested interactions using F-tests, which are one-sided, we specified one-tailed tests in the parameters for the 3DClustSim; however, follow-up analyses to test directional effects (e.g., social status words vs. neutral words in each group) were tested using two-tailed paired t-tests. Both the uncorrected voxel-wise p value and contiguity threshold necessary to achieve a brain-wise corrected $p < 0.05$ are reported with each test described below.

3. Results

3.1. Demographic information

As shown in Table 1, MDD and CON adolescents did not differ in age, pubertal status, gender, race, or maternal education level (all p's > 0.47).

3.2. Post-Scan ratings and behavioral data results

A repeated measures ANOVA on post-scan valence ratings revealed that there was a significant main effect of valence ($F[1.50, 66] = 547.57$, $p < 0.001$, $\eta_p^2 = 0.93$ with Huynh-Feldt correction used for sphericity). Positive social status words were rated more positively ($M = 5.65$, $SD = 0.55$) than neutral words ($M = 4.04$, $SD = 0.44$) and negative social status words were rated as more negatively ($M = 2.11$, $SD = 0.51$; lower ratings signify greater negativity) than neutral words ($M = 4.04$, $SD = 0.44$). However, there was no significant main effect of Group ($F[1,44] = 0.07$, $p = 0.80$) or Group X Valence interaction (Huynh-Feldt corrected $F[1.50, 66] = 0.83$, $p = 0.41$ on post-scan valence ratings). Chi-square tests showed that social status words (both positive and negative) were more likely to be endorsed by participants as words they would use to describe social status compared to neutral

Table 1
Demographic characteristics of participants.

	CON group	MDD group	Sig
N	29	20	
# Female	20 (69%)	15 (75%)	n.s.
# Caucasian	24 (83%)	16 (80%)	n.s.
Age M (SD)	15.17 (1.89)	15.11 (1.75)	n.s.
Pubertal status			
Adrenal PDS M(SD)	4.29 (0.94)	4.50 (0.86)	n.s.
Gonadal PDS M(SD)	3.93 (0.66)	3.72 (0.73)	n.s.
Maternal education M(SD)	5.81 (0.83)	5.61 (1.15)	n.s.
Self-report measures			
Child-reported MFQ M(SD)	4.03 (4.46)	37.10 (12.84)	p < 0.001
Parent-reported MFQ M(SD)	2.50 (2.18)	19.37 (11.00)	p < 0.001

Note. M = Mean, SD = standard deviation, Maternal education levels (1: less than seventh grade, 2: junior high school (9th grade), 3: partial high school (10th or 11th grade), 4: high school graduate, 5: partial college (at least 1 year) or specialized training, 6: standard college or university graduate, and 7: graduate professional training (graduate degree)). n.s. = not significant.

words (high social status rating: $\chi^2 [1] = 664.68$, $p < 0.0001$ and low social status rating: $\chi^2 [1] = 512.44$, $p < 0.0001$). Given that behavioral data (reaction time and accuracy) were not a primary focus of this study, results from these data are reported in Supplementary Materials (see S-I).

3.3. fMRI results

3.3.1. Group X Time X Condition (social status vs. neutral words) effects on neural activity during word valence identification

As presented in Table 2, significant Group X Time X Condition interactions were observed in 7 clusters, including the bilateral superior temporal cortex (STC) extending to the insula, the MPFC extending to the lateral PFC (LPFC), the medial parietal cortex including PCC and precuneus, and prefrontal regions, such as the bilateral superior frontal gyrus and middle frontal gyrus ($p < 0.005$ and 76 voxels contiguity). Given the broad clusters identified, we further restricted our regions of interest (functional ROIs) by delineating areas of STC, MPFC, PCC and precuneus from entire clusters (i.e., bilateral STC extending to insula, MPFC extending to LPFC, and medial parietal cortex), as these areas are implicated in social cognitive processing. To do this, we created anatomically defined ROIs using AFNI's Talairach atlas including the bilateral STC, MPFC, PCC, and precuneus, and found overlapping areas between anatomically defined ROIs and the entire clusters. Post-hoc analyses on these ROI's revealed that, in the bilateral STC and MPFC, MDD youth showed lower activation in the latter part of the time-course in response to social status words compared to neutral words (8.38 s–11.69 s), while CON youth did not show significant differences in activation to social status vs. neutral words at any time points (Fig. 2). Temporal contiguity thresholding revealed that the PCC and precuneus effects were not significant for 2 consecutive scans, so these regions were not included in the subsequent analyses.

3.3.2. Group differences in neural activation to social status words modulated by word valence

Group X Time X Valence (positive vs. negative social status words) interactions were observed in a widespread brain network, including the retrosplenial cortex (RSC) extending to the thalamus and the left DLPFC, as well as temporal and occipital regions ($p < 0.005$ and 51 voxels contiguity) (Table 3). Within the RSC/thalamus, MDD youth showed reduced activation in response to negative social status words compared to positive social status words, but CON youth did not differ significantly over time in activation to positive vs. negative social status words (Fig. 3). As depicted in Fig. 3, there were also differences in patterns of neural activation modulated by valence in brain regions that were not included as part of our hypothesized regions. Specifically, MDD youth showed reduced DLPFC activity in response to negative social status words compared to positive social status words, whereas CON youth showed elevated DLPFC in response to negative social status words compared to positive social status words (Fig. 3). The same pattern was observed in the right fusiform gyrus (Fig. 3).

3.3.3. Effect of developmental factors on neural response to social status words

Finally, we explored whether developmental factors were associated with neural activity in response to social status vs. neutral words in the social cognitive regions identified in the omnibus ANOVA (i.e., bilateral STC and MPFC), and whether their associations differed for depressed youth and healthy controls. Functional ROI-based regression analyses revealed a significant main effect of chronological age on MPFC activity in response to social status words vs. neutral words indicating that age was positively correlated with MPFC activity ($\beta = 0.34$, $t = 2.49$, $p = 0.016$; see Fig. 4). However, the main effect of age on MPFC activity did not remain significant at the Bonferroni-corrected threshold ($p < .017$) after controlling for adreneracheal and gonadarcheal pubertal maturation scores ($\beta = 0.34$, $t = 2.03$, $p = 0.049$), suggesting

Table 2
Group differences in neural response to social status words *vs.* neutral words over time.

Brain region	BA	k	Tal coordinates of centroid			F value of centroid	Temporal windows: Group x Condition	Repeated measures Group x Condition ANOVA	Pairwise comparisons	
			x	y	z				MDD (Soc vs. Neut)	CON (Soc vs. Neut)
Superior Frontal Gyrus	8	136	−25	26	48	4.65	6.68 ~ 11.69 s	$F_{(1, 47)} = 12.25$, $p = 0.001$, partial $\eta^2 = 0.21$	$t_{(19)} = -4.94$, $p = 0.000$	n.s.
Superior Frontal Gyrus	6	118	23	18	52	4.67	8.35 ~ 11.69 s	$F_{(1, 47)} = 11.89$, $p = 0.001$, partial $\eta^2 = 0.20$	$t_{(19)} = -3.09$, $p = 0.006$	n.s.
Parietal cortex	30	2298	4	−49	15	3.97	8.35 ~ 11.69 s	$F_{(1, 47)} = 14.05$, $p = 0.000$, partial $\eta^2 = 0.23$	$t_{(19)} = -3.65$, $p = 0.002$	n.s.
Posterior Cingulate Cortex	30	95	2	−48	21	4.66	n.s.	–	–	–
Precuneus	7	421	−7	−67	34	4.84	n.s.	–	–	–
Superior Temporal Cortex extending to insula	41/42	294	−57	−20	8	3.28	6.68 ~ 11.69 s	$F_{(1, 47)} = 19.78$, $p = 0.000$, partial $\eta^2 = 0.30$	$t_{(19)} = -4.21$, $p = 0.000$	n.s.
Superior Temporal Cortex	41/22	78	−56	−21	4	4.48	8.35 ~ 11.69 s	$F_{(1, 47)} = 12.46$, $p = 0.001$, partial $\eta^2 = 0.21$	$t_{(19)} = -3.14$, $p = 0.005$	n.s.
Medial Prefrontal Cortex extending to Lateral PFC	10	262	4	55	10	3.88	8.35 ~ 11.69 s	$F_{(1, 47)} = 8.46$, $p = 0.006$, partial $\eta^2 = 0.13$	$t_{(19)} = -2.30$, $p = 0.033$	n.s.
[a]Medial Prefrontal Cortex	10	81	6	52	6	4.91	8.35 ~ 11.69 s	$F_{(1, 47)} = 6.81$, $p = 0.012$, partial $\eta^2 = 0.13$	$t_{(19)} = -2.09$, $p = 0.050$	n.s.
Superior Temporal Cortex extending to insula	22	275	57	−7	6	3.72	6.68 ~ 11.69 s	$F_{(1, 47)} = 11.69$, $p = 0.001$, partial $\eta^2 = 0.20$	$t_{(19)} = -3.20$, $p = 0.005$	n.s.
[a]Superior Temporal Cortex	22/21	159	58	−8	5	3.68	8.35 ~ 11.69 s	$F_{(1, 47)} = 12.23$, $p = 0.001$, partial $\eta^2 = 0.21$	$t_{(19)} = -3.31$, $p = 0.004$	n.s.
Middle Frontal gyrus	47	84	−28	34	−4	3.45	6.68 ~ 11.69 s	$F_{(1, 47)} = 13.17$, $p = 0.001$, partial $\eta^2 = 0.22$	$t_{(19)} = -4.15$, $p = 0.001$	n.s.

Note. Whole-brain Group X Time X Condition ANOVA ($p < 0.005$, 76 voxels contiguity). Tal = Talairach; BA = Brodmann area; k = number of voxels (voxel size = $3.20^3 \times 3.20^3 \times 3.2$ mm^3); repeated measures ANOVA Fs = Huynh-Feldt corrected Fs for possible violations of sphericity; MDD = major depressive disorder; CON = healthy control; Soc = social status words; Neut = neutral words; n.s. = no significance.

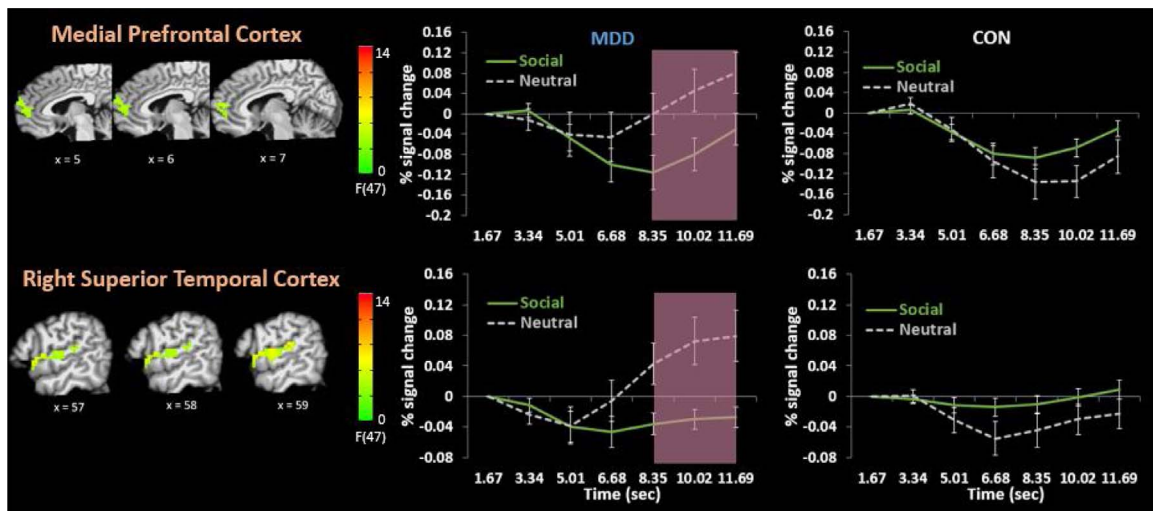[a] Activation over time in these regions is plotted in Fig. 2.

Fig. 2. Time-courses of neural activation in regions (medial prefrontal cortex [MPFC] and superior temporal cortex [STC]) involved in social cognitive processing that showed Group X Time X Condition interaction effects. Significant differences in time-courses between social status words and neutral words are highlighted in red; areas shaded in red indicate $p < 0.05$ across the temporal windows.

that this effect cannot be specifically attributed to chronological age above and beyond pubertal maturation. There were no significant main effects of Puberty (adrenarche or gonadarche) or Group X Age or Group X Puberty interactions.

4. Discussion

The results of the present study suggest that there may be a neural basis to differences in social cognitive processing between depressed and healthy adolescents. Specifically, when presented with words conveying social status, depressed youth showed reduced activation to social status relative to neutral words in key temporal and prefrontal cortical regions thought to be part of a social cognitive processing network (Frith and Frith, 2007), including the STC and MPFC. Healthy youth, on the other hand, did not differ in response to social status compared to neutral words in either of these regions. A similar pattern of reduced activation was observed in the DLPFC and fusiform gyrus in response to negative relative to positive social status words among depressed, but not healthy youth. Healthy control youth showed an opposite pattern of elevated activation to negative relative to positive social status words. With regard to developmental factors, we found greater mPFC response to social status words in older adolescents, although this finding was attenuated when controlling for pubertal status.

We tested competing theoretical models predicting hyper-reactivity vs. hypoactivity in temporal and prefrontal cortical regions in response to social status information relative to neutral information in depressed compared to healthy youth. Our finding that depressed adolescents exhibited lower activation of the STC and MPFC when presented with both positive and negative social status words compared to neutral words supports the hypoactivation model. This is consistent with Elliott et al.'s (2012) study in adults with remitted depression, which reported evidence of hypoactivity in the MPFC among depressed compared to healthy adults in response to social interaction images, regardless of valence. The MPFC is a key region implicated in self-related processing in adolescence (Pfeifer et al., 2009). Hypoactivity within this region among depressed individuals may indicate blunted processing of the self-relevance of social status words.

We also found reduced activation in the anterior STC to social status words relative to neutral words among depressed youth only. Our finding is consistent with a study in adults showing hypoactivation of the anterior STC in response to sad words among depressed compared to healthy individuals (Canli et al., 2004). The majority of studies of social cognition have focused on the posterior portion of the STC,

whereas our findings centered on a more anterior portion of the STC. Evidence supports an anterior-posterior organization of the social perception functions of the STC, with more posterior portions involved in theory of mind and the detection of biological motion, and more anterior portions of STC involved in voice processing and language perception (Deen et al., 2015; Hein and Knight, 2008). Thus, our findings may reflect reduced lexical/semantic processing in social compared to neutral words in depressed youth. This pattern was not modulated by social status word valence (positive vs. negative), consistent with the idea that the STC primarily processes the social aspects of stimuli (Frith and Frith, 2007; Saxe, 2006; Yang et al., 2015).

It is not clear whether this pattern of hypoactivation within the social cognitive brain network in depressed youth is a correlate or cause of depression. It could be that reduced neural processing of social status information contributes to alterations in social behavior and/or self-perception that in turn contribute to the development and maintenance of depressive symptoms. For example, reduced processing of social information could contribute to the social withdrawal symptoms that typically present as a key feature of the clinical phenomenology of adolescent depression. To support this interpretation, future research is needed to clearly link this pattern of blunted social cognitive brain response to real-world indices of social withdrawal, such as ecological momentary assessment indices of social interaction. Alternatively, individuals who are experiencing symptoms of depression, such as social withdrawal and interpersonal sensitivity, may implicitly or explicitly disengage from processing the self- and social-relevance of social status words. Such disengagement might function as a protective mechanism in daily life, given high rates of interpersonal dysfunction in adolescents with depression (Rudolph et al., 2009). Additional research using more direct measures of attention, such as eyetracking, could be helpful in testing the potential role of attentional disengagement in contributing to hypoactivity of social cognitive brain regions during social information processing. Future prospective longitudinal research is also needed to disentangle whether this altered social cognitive brain response to social status information is a mechanism underlying depression, or a correlate of the behavioral symptoms that accompany the disorder.

Consistent with our hypotheses, differences among depressed youth in brain activation to social status words compared to neutral words emerged only in the later stages of processing, from approximately 8–11 s after word presentation. This is consistent with the idea that depressed individuals show alterations in elaborative processing that occur after the initial processing of social stimuli (Siegle et al., 2002;

Table 3
Group x Time effects modulated by social status word valence (positive vs. negative).

Brain region	BA	k	Tal coordinates of centroid x	y	z	F value of centroid	Temporal regions: Group x Valence	Repeated measures Group x Valence ANOVA	Pairwise comparisons MDD (Pos vs. Neg)	CON (Pos vs. Neg)
Paracentral Lobule	7	615	4	−48	53	4.33	3.34 ~ 11.69 s	$F(1, 47) = 17.84$, $p = 0.000$, partial $\eta^2 = 0.28$	$t(19) = 3.20$, $p = 0.005$	$t(28) = -2.88$, $p = 0.008$
[a] Middle Frontal Gyrus (Left Dorsolateral Prefrontal Cortex)	9/8	54	−33	38	41	6.38	5.01 ~ 11.69 s	$F(1, 47) = 15.70$, $p = 0.000$, partial $\eta^2 = 0.25$	$t(19) = -2.64$, $p = 0.016$	n.s.
[a] Retrosplenial Cortex extending to Thalamus	23	83	3	−29	18	5.04	6.68 ~ 11.69 s	$F(1, 47) = 9.47$, $p = 0.003$, partial $\eta^2 = 0.17$	$t(19) = 2.73$, $p = 0.013$	$t(28) = -2.87$, $p = 0.008$
Middle Temporal Gyrus	22	72	54	−57	8	4.91	6.68 ~ 11.69 s	$F(1, 47) = 10.12$, $p = 0.003$, partial $\eta^2 = 0.18$	$t(19) = 2.82$, $p = 0.011$	n.s.
Culmen	–	107	4	−68	−8	3.26	8.35 ~ 11.69 s	$F(1, 47) = 9.75$, $p = 0.003$, partial $\eta^2 = 0.17$	$t(19) = 2.28$, $p = 0.035$	$t(28) = -2.41$, $p = 0.023$
[a] Fusiform Gyrus	37	86	45	−61	−14	3.47	8.35 ~ 11.69 s	$F(1, 47) = 8.96$, $p = 0.004$, partial $\eta^2 = 0.16$	$t(19) = 2.67$, $p = 0.015$	$t(28) = -2.32$, $p = 0.028$
Culmen	–	236	−30	−48	−21	3.67	6.68 ~ 11.69 s	$F(1, 47) = 14.27$, $p = 0.000$, partial $\eta^2 = 0.23$	$t(19) = 3.17$, $p = 0.005$	$t(28) = -1.87$, $p = 0.072$

Note. Whole-brain Group X Time X Valence ANOVA ($p < 0.005$, 51 voxels contiguity). Tal = Talairach; BA = Brodmann area; k = number of voxels (voxel size = 3.20³ × 3.20³ × 3.20³ = 3.2 × 3.2 × 3.2 mm³), repeated measures ANOVA Fs = Huynh-Feldt corrected Fs for possible violations of sphericity; MDD = major depressive disorder; CON = healthy control; Pos = Positive social status words; Neg = Negative social status words; n.s. = no significance.

[a] Activation over time in these regions is plotted in Fig. 3.

Silk et al., 2014). However, unlike these previous studies which focused on brain regions more strongly involved in emotional responding, we found support for hypoactivation rather than hyper-activation of brain response to social status words. Thus, our findings likely do not reflect ruminative or perseverative self-referential thought. Instead, results highlight reduced elaborative processing of social information following initial stimulus appraisal. Given that we observed reduced rather than increased activation of the prefrontal cortex, this is likely an implicit rather than an explicit or purposeful process.

Activation in the MPFC and STC was not modulated by social status word valence; however, we explored whether brain activity in other regions might differ for positive versus negative social status words. We found that depressed youth exhibited lower activation to negative compared to positive social status words in the DLPFC and fusiform gyrus. In contrast, healthy youth showed elevated activation in these regions to negative vs positive social status words. The DLPFC has been shown to be implicated in voluntary emotion regulation (Phillips et al., 2008) as well as during implicit and incidental emotion regulation that occurs during the processing of emotional stimuli, even in the absence of explicit emotion regulation instructions (Drabant et al., 2009). It is also one of the regions recruited when evaluating the valence of an emotional stimulus, which many consider as constituting a form of incidental emotion regulation (Burklund et al., 2014; Lieberman et al., 2011). Given that participants had to provide a judgement of valence of the social status words, one possible interpretation for the deactivation of the DLPFC to negative social status words could be altered implicit regulation among depressed youth. It should be noted that we cannot conclude that these valence effects are specific to social status words, as we did not compare them with positive and negative non-social words. Future research to examine implicit emotion regulation to stimuli high or low in social relevance and negative or positive valence is needed to determine the specific underlying neurocognitive processes that underlie processing social information in depressed youth.

The present findings also support our hypothesis that older adolescents would show greater activation of the MPFC when processing of social status information. This is consistent with recent studies pointing to age-related increases in MPFC activation among youth during social-cognitive tasks, such as processing social self-evaluative words (Pfeifer et al., 2013), emotional faces (Pfeifer et al., 2011), and social feedback (Gunther Moor et al., 2010). These findings may reflect an increased sensitivity to the self-relevance of social status information from early to late adolescence, which may, in turn, help to explain increased vulnerability to depression during this developmental period. However, we cannot be sure whether these findings are attributable to the effects of chronological age or pubertal development, as the results did not remain significant when controlling for pubertal status. This may be due to limited power to include both variables in the model given the small sample and high inter-correlation between age and puberty. Furthermore, in contrast to Pfeifer et al. (2013) and Goddings et al. (2012), we did not find support for pubertal influences on the processing of social status words. Additional research with larger samples, as well as direct measurement of pubertal hormones, is needed to more clearly differentiate the role of pubertal development from chronological age in social cognitive brain functioning.

The present study differs from most existing research in using words as social stimuli rather than faces or pictures. Words denoting social status may be particularly relevant for today's teens because much of the information that they process regarding social status is conveyed via text in social media and text messaging formats. Findings are consistent with a previous study that reported blunted pupil dilation among depressed youth compared to healthy youth when processing negative emotion words (Silk et al., 2007), as well as Canli et al.'s (2004) finding of reduced STC activation to sad words in depressed relative to healthy adults. Nevertheless, it is important to note that findings may not generalize to other types of social stimuli.

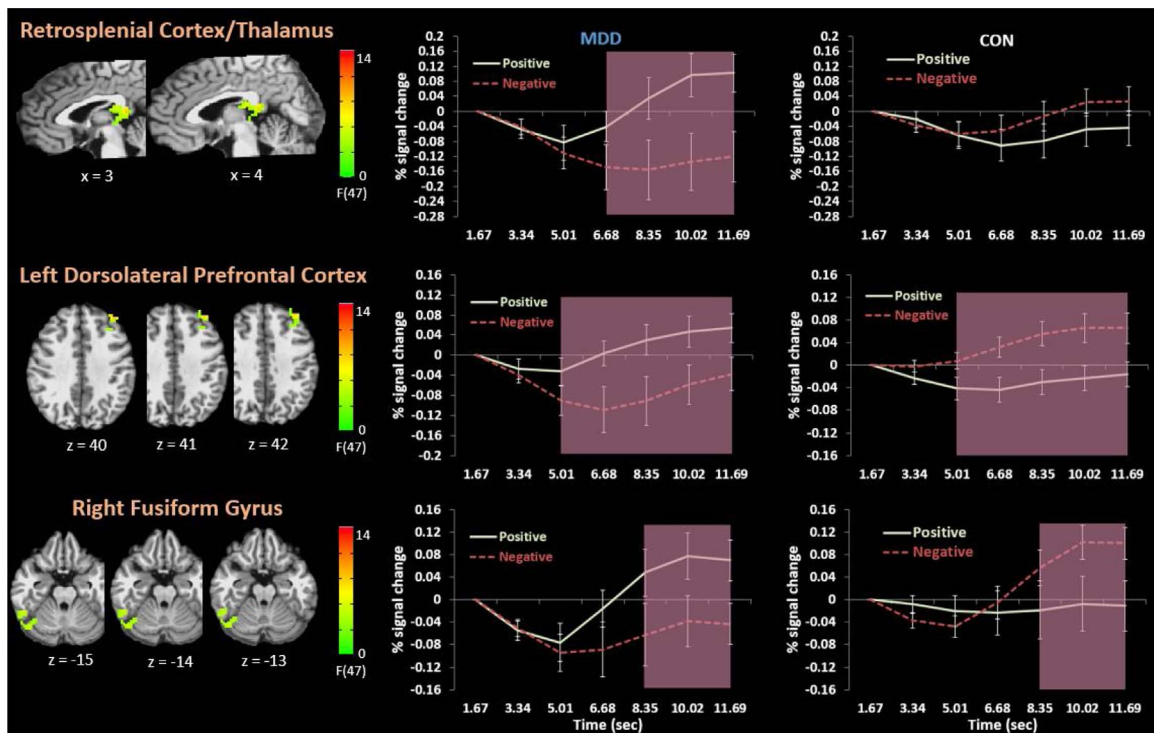Another limitation in the present study is that we were not able to

Fig. 3. Time-courses of neural activation in brain regions that showed Group X Time X Valence interaction effects. Significant differences in time-courses between positive social status words and negative social status words are highlighted in red; areas shaded in red indicate $p < 0.05$ across the temporal windows.

disentangle social versus emotional aspects of social status words. Although it would be challenging to generate social status words that do not have emotional connotation, future research using non-emotional social words and non-social emotional words may be helpful in explicating whether neural alterations in adolescent depression are more strongly driven by social or emotional features of the stimuli. Furthermore, although social status words were presented, adolescents were not instructed to think about how the words applied to themselves. Thus, the current study measures implicit but not explicit self-referential processing. Tasks that include more explicit social evaluation, such as simulated peer feedback tasks (Silk et al., 2014), may be useful in further probing altered social information processing in adolescents with depression. It should also be noted that this study's cross-sectional design limits understanding of the possible causal role that altered neural responses to social status words may play in the onset of depression. Future longitudinal imaging research is needed to address this question. Finally, gender differences are evident in rates of depression and social behaviors during adolescence (Cyranowski et al., 2000; Hankin and Abramson, 2001; Rudolph, 2002); however, our relatively small sample size (particularly for boys) did not allow us to explore possible gender differences in neural response to social status words. Furthermore, our largely female sample likely obscured our ability to observe any differential influences of puberty on the neural response to social status words among boys.

Despite these limitations, this study had several strengths, including the use of a well-characterized clinical sample of adolescents currently experiencing a depressive episode, as well as the incorporation of ecologically valid social status stimuli. Evidence of atypical social information processing in depressed youth could have implications for the social functioning of adolescents with depression. For example, hypoactivity in temporal and prefrontal regions of the brain that process socially salient information could alter social learning and real-world social interactions, which, in turn, could further influence brain development. Furthermore, findings suggest that novel interventions engaging social cognitive brain networks could be a valuable new direction in prevention and treatment of depression during adolescence.

Appendix A. Supplementary data

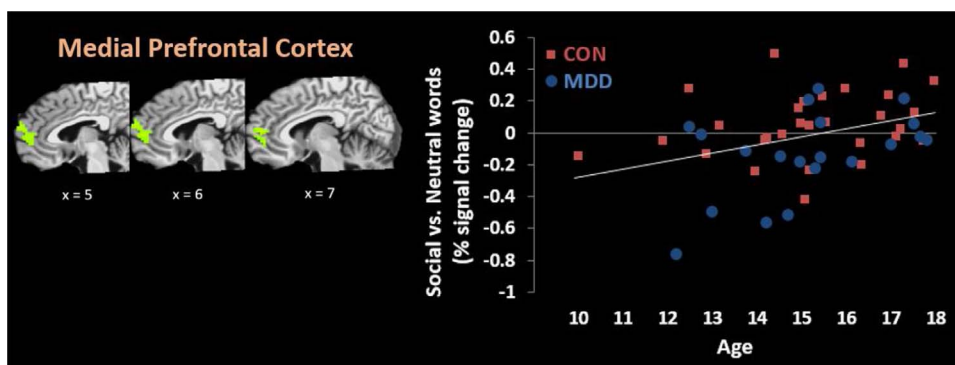Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.dcn.2017.09.005.

Fig. 4. Positive association between age and MPFC activity in response to social status words vs. neutral words ($r = 0.34$, $p = 0.016$).

References

Agoston, A.M., Rudolph, K.D., 2013. Pathways from depressive symptoms to low social status. J. Abnorm. Child Psychol. 41 (2), 295–308. http://dx.doi.org/10.1007/s10802-012-9675-y.

American Psychological Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (Washington, D.C.: Author).

Angold, A., Costello, E.J., Messer, S.C., Pickles, A., 1995. Development of a short questionnaire for use in epidemiological studies of depression in children and adolescents. Int. J. Methods Psychiatr. Res. 5 (4), 237–249.

Blakemore, S.J., Mills, K.L., 2014. Is adolescence a sensitive period for sociocultural processing. Annu. Rev. Psychol. 65, 187–207. http://dx.doi.org/10.1146/annurev-psych-010213-115202.

Blakemore, S.J., 2008. The social brain in adolescence. Nat. Rev. Neurosci. 9 (4). http://dx.doi.org/10.1038/nrn2353.

Burkhouse, K.L., Jacobs, R.H., Peters, A.T., Ajilore, O., Watkins, E.R., Langenecker, S.A., 2017. Neural correlates of rumination in adolescents with remitted major depressive disorder and healthy controls. Cogn. Affective Behav. Neurosci. 17 (2), 394–405. http://dx.doi.org/10.3758/s13415-016-0486-4.

Burklund, L.J., Creswell, J.D., Irwin, M.R., Lieberman, M.D., 2014. The common and distinct neural bases of affect labeling and reappraisal in healthy adults. Front. Psychol. 5, 221. http://dx.doi.org/10.3389/fpsyg.2014.00221.

Burnett, S., Blakemore, S.J., 2009. Functional connectivity during a social emotion task in adolescents and in adults. Eur. J. Neurosci. 29 (6), 1294–1301.

Burnett, S., Sebastian, C.L., Cohen Kadosh, K., Blakemore, S.-J., 2010. The social brain in adolescence: evidence from functional magnetic resonance imaging and behavioural studies. Neurosci. Biobehav. Rev. http://dx.doi.org/10.1016/j.neubiorev.2010.10.011.

Canli, T., Sivers, H., Thomason, M.E., Whitfield-Gabrieli, S., Gabrieli, J.D., Gotlib, I.H., 2004. Brain activation to emotional words in depressed vs healthy subjects. Neuroreport 15 (17), 2585–2588.

Cox, R., 1996. AFNI: software for analysis and visualization of functional magnetic resonance neuroimages. Comput. Biomed. Res. 29, 162–173.

Crone, E.A., Dahl, R.E., 2012. Understanding adolescence as a period of social-affective engagement and goal flexibility. Nat. Rev. Neurosci. 13 (9), 636–650. http://dx.doi.org/10.1038/nrn3313. (nrn3313 [pii]).

Cyranowski, J.M., Frank, E., Young, E., Shear, M.K., 2000. Adolescent onset of the gender difference in lifetime rates of major depression: a theoretical model. Arch. Gen. Psychiatry 57 (1), 21–27.

Deen, B., Koldewyn, K., Kanwisher, N., Saxe, R., 2015. Functional organization of social perception and cognition in the superior temporal sulcus. Cereb. Cortex 25 (11), 4596–4609. http://dx.doi.org/10.1093/cercor/bhv111.

Drabant, E.M., McRae, K., Manuck, S.B., Hariri, A.R., Gross, J.J., 2009. Individual differences in typical reappraisal use predict amygdala and prefrontal responses. Biol. Psychiatry 65 (5), 367–373. http://dx.doi.org/10.1016/j.biopsych.2008.09.007.

Elliott, R., Lythe, K., Lee, R., McKie, S., Juhasz, G., Thomas, E.J., et al., 2012. Reduced medial prefrontal responses to social interaction images in remitted depression. Arch. Gen. Psychiatry 69 (1), 37–45. http://dx.doi.org/10.1001/archgenpsychiatry.2011.13922213787.

Fissell, K., Tseytlin, E., Cunningham, D., Iyer, K., Carter, C.S., Schneider, W., Cohen, J.D., 2003. Fiswidgets: a graphical computing environment for neuroimaging analysis. Neuroinformatics 1 (1), 111–125.

Forbes, E.E., Ryan, N.D., Phillips, M.L., Manuck, S.B., Worthman, C.M., Moyles, D.L., et al., 2010. Healthy adolescents' neural response to reward: associations with puberty, positive affect, and depressive symptoms. J. Am. Acad. Child Adolesc. Psychiatry 49 (2), 162–172 e161-165. 00004583-201002000-00010 [pii].

Forbes, E.E., Phillips, M.L., Silk, J.S., Ryan, N.D., Dahl, R.E., 2011. Neural systems of threat processing in adolescents: role of pubertal maturation and relation to measures of negative affect. Dev. Neuropsychol. 36 (4), 429–452.

Frith, C.D., Frith, U., 2007. Social cognition in humans. Curr. Biol. 17, R724–R732.

Goddings, A.L., Burnett Heyes, S., Bird, G., Viner, R.M., Blakemore, S.J., 2012. The relationship between puberty and social emotion processing. Dev. Sci. 15 (6), 801–811. http://dx.doi.org/10.1111/j.1467-7687.2012.01174.x.

Gunther Moor, B., van Leijenhorst, L., Rombouts, S.A., Crone, E.A., Van der Molen, M.W., 2010. Do you like me? Neural correlates of social evaluation and developmental trajectories. Soc. Neurosci. 5 (5-6), 461–482 925873572 [pii].

Guthrie, D., Buchwald, J.S., 1991. Significance testing of difference potentials. Psychophysiology 28 (2), 240–244.

Hames, J.L., Hagan, C.R., Joiner, T.E., 2013. Interpersonal processes in depression. Annu. Rev. Clin. Psychol. 355–377. http://dx.doi.org/10.1146/annurev-clinpsy-050212-185553 23297787.

Handwerker, D.A., Ollinger, J.M., D'Esposito, M., 2004. Variation of BOLD hemodynamic responses across subjects and brain regions and their effects on statistical analyses. Neuroimage 21 (4), 1639–1651. http://dx.doi.org/10.1016/j.neuroimage.2003.11.029.

Hankin, B.L., Abramson, L.Y., 2001. Development of gender differences in depression: an elaborated cognitive vulnerability-transactional stress theory. Psychol. Bull. 127 (6), 773–796.

Hein, G., Knight, R.T., 2008. Superior temporal sulcus-It's my area: or is it? J. Cogn. Neurosci. 20 (12), 2125–2136. http://dx.doi.org/10.1162/jocn.2008.20148.

Herman-Giddens, M.E., 2006. Recent data on pubertal milestones in United States children: the secular trend toward earlier development. Int. J. Androl. 29, 241–246.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., et al., 1997. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. J. Am. Acad. Child Adolesc.

Psychiatry 36 (7), 980–988. http://dx.doi.org/10.1097/00004583-199707000-00021.

Kerestes, R., Davey, C.G., Stephanou, K., Whittle, S., Harrison, B.J., 2014. Functional brain imaging studies of youth depression: a systematic review. NeuroImage: Clin. 4 (0), 209–231. http://dx.doi.org/10.1016/j.nicl.2013.11.009.

Lenhart, A., 2015. Teens, Social Media & Technology Overview. (2015). http://www.pewinternet.org/files/2015/04/PI_TeensandTech_Update2015_0409151.pdf.

Lieberman, M.D., Inagaki, T.K., Tabibnia, G., Crockett, M.J., 2011. Subjective responses to emotional stimuli during labeling, reappraisal, and distraction. Emotion 11 (3), 468–480. http://dx.doi.org/10.1037/a0023503.

Mandell, D., Siegle, G.J., Shutt, L., Feldmiller, J., Thase, M.E., 2014. Neural substrates of trait ruminations in depression. J. Abnorm. Psychol. 123 (1), 35–48. http://dx.doi.org/10.1037/a0035834.

Martin, C.A., Kelly, T.H., Rayens, M.K., Brogli, B.R., Brenzel, A., Smith, W.J., Omar, H.A., 2002. Sensation seeking, puberty and nicotine, alcohol and marijuana use in adolescence. J. Am. Acad. Child Adolesc. Psychiatry 41 (12), 1495–1502.

Masten, C.L., Eisenberger, N.I., Borofsky, L.A., McNealy, K., Pfeifer, J.H., Dapretto, M., 2011. Subgenual anterior cingulate responses to peer rejection: a marker of adolescents' risk for depression? Dev. Psychopathol. 23 (1), 283–292.

Mills, K.L., Lalonde, F., Clasen, L.S., Giedd, J.N., Blakemore, S.J., 2014. Developmental changes in the structure of the social brain in late childhood and adolescence. Soc. Cogn. Affective Neurosci. 9 (1), 123–131. http://dx.doi.org/10.1093/scan/nss113.

Moore, W.E., Pfeifer, 3rd, Masten, J.H., Mazziotta, C.L., Iacoboni, J.C., Dapretto, M., 2012. Facing puberty: associations between pubertal development and neural responses to affective facial displays. Soc. Cogn. Affective Neurosci. 7 (1), 35–43. http://dx.doi.org/10.1093/scan/nsr066. nsr066 [pii].

Nelson, E.E., Leibenluft, E., McClure, E., Pine, D.S., 2005. The social re-orientation of adolescence: a neuroscience perspective on the process and its relation to psychopathology. Psychol. Med. 35 (2), 163–174.

Neshat-Doost, H.T., Moradi, A.R., Taghavi, M.R., Yule, W., Dalgleish, T., 1999. The development of a corpus of emotional words produced by children and adolescents. Personal. Ind. Differ. 27 (3), 433–451.

Nolan, S.A., Flynn, C., Garber, J., 2003. Prospective relations between rejection and depression in young adolescents. J. Personal. Soc. Psychol. 85 (4), 745–755.

Nolen-Hoeksema, S., Wisco, B.E., Lyubomirsky, S., 2008. Rethinking rumination. Perspect. Psychol. Sci. 3 (5), 400–424. http://dx.doi.org/10.1111/j.1745-6924.2008.00088.x.

Paus, T., Keshavan, M., Giedd, J.N., 2008. Why do many psychiatric disorders emerge during adolescence? Nat. Rev. Neurosci. 9 (12), 947–957.

Petersen, A.C., Crockett, L., Richards, M., Boxer, A., 1988. A self-report measure of pubertal status: reliability, validity, and initial norms. J. Youth. Adolesc. 17 (2), 117–133.

Pfeifer, J.H., Masten, C.L., Borofsky, L.A., Dapretto, M., Fuligni, A.J., Lieberman, M.D., 2009. Neural correlates of direct and reflected self-appraisals in adolescents and adults: when social perspective-taking informs self-perception. Child Dev. 80 (4), 1016–1038.

Pfeifer, J.H., Masten, C.L., Moore 3rd, W.E., Oswald, T.M., Mazziotta, J.C., Iacoboni, M., Dapretto, M., 2011. Entering adolescence: resistance to peer influence, risky behavior, and neural changes in emotion reactivity. Neuron 69 (5), 1029–1036 S0896-6273(11)00117-6 [pii].

Pfeifer, J.H., Kahn, L.E., Merchant, J.S., Peake, S.J., Veroude, K., Masten, C.L., et al., 2013. Longitudinal change in the neural bases of adolescent social self-evaluations: effects of age and pubertal development. J. Neurosci. 33 (17), 7415–7419. http://dx.doi.org/10.1523/jneurosci. 4074-12.2013.

Phillips, M.L., Ladouceur, C.D., Drevets, W.C., 2008. Neural systems underlying voluntary and automatic emotion regulation: toward a neural model of bipolar disorder. Mol. Psychiatry 13 (9) 829-829.

Prinstein, M.J., Cheah, C.S.L., Guyer, A.E., 2005. Peer victimization, cue interpretation, and internalizing symptoms: preliminary concurrent and longitudinal findings for children and adolescents. J. Clin. Child Adolesc. Psychol. 34 (1), 11–24. http://dx.doi.org/10.1207/s15374424jccp3401_2.

Rudolph, K.D., Conley, C.S., 2005. The socioemotional costs and benefits of social-evaluative concerns: do girls care too much? J. Personal. 73 (1), 115–138.

Rudolph, K.D., Flynn, M., Abaied, J.L., Groot, A., Thompson, R., 2009. Why is Past depression the best predictor of future depression? Stress generation as a mechanism of depression continuity in girls. J. Clin. Child Adolesc. Psychol. 38 (4), 473–485.

Rudolph, K.D., 2002. Gender differences in emotional responses to interpersonal stress during adolescence. J. Adolesc. Health 30 (4), 3–13.

Saxe, R., 2006. Uniquely human social cognition. Curr. Opin. Neurobiol. 16 (2), 235–239.

Shih, J.H., Eberhart, N.K., Hammen, C.L., Brennan, P.A., 2006. Differential exposure and reactivity to interpersonal stress predict sex differences in adolescent depression. J. Clin. Child Adolesc. Psychol. 35 (1), 103–115. http://dx.doi.org/10.1207/s15374424jccp3501_9.

Shirtcliff, E.A., Dahl, R.E., Pollak, S.D., 2009. Pubertal development: correspondence between hormonal and physical development. Child Dev. 80 (2), 327–337. http://dx.doi.org/10.1111/j.1467-8624.2009.01263.x.

Siegle, G.J., Steinhauer, S.R., Thase, M.E., Stenger, V.A., Carter, C.S., 2002. Can't shake that feeling: event-related fMRI assessment of sustained amygdala activity in response to emotional information in depressed individuals? Biol. Psychiatry 51 (9), 693–707.

Siegle, G.J., Thompson, W., Carter, C.S., Steinhauer, S.R., Thase, M.E., 2007. Increased amygdala and decreased dorsolateral prefrontal BOLD responses in unipolar depression: related and independent features. Biol. Psychiatry 61 (2), 198–209. http://dx.doi.org/10.1016/j.biopsych.2006.05.048.

Silk, J.S., Dahl, R.E., Ryan, N.D., Forbes, E.E., Axelson, D.A., Birmaher, B., Siegle, G.J., 2007. Pupillary reactivity to emotional information in child and adolescent

depression: links to clinical and ecological measures. Am. J. Psychiatry 164 (12). http://dx.doi.org/10.1176/appi.ajp.2007.0611181618056243.

Silk, J.S., Siegle, G.J., Whalen, D.J., Ostapenko, L., Ladouceur, C.D., Dahl, R.E., 2009. Pubertal changes in emotional information processing: pupillary, behavioral, and subjective evidence during emotional word identification. Dev. Psychopathol. 21 (1), 7–26.

Silk, J.S., Siegle, G.J., Lee, K.H., Nelson, E.E., Stroud, L.R., Dahl, R.E., 2014. Increased neural response to peer rejection associated with adolescent depression and pubertal development. Soc. Cogn. Affect. Neurosci. 9 (11), 1798–1807. http://dx.doi.org/10.1093/scan/nst175.

Silk, J.S., Lee, K.H., Elliott, R.D., Hooley, J.M., Dahl, R.E., Barber, A., Siegle, G.J., 2017. 'Mom-I don't want to hear it': brain response to maternal praise and criticism in adolescents with major depressive disorder. Soc. Cogn. Affect. Neurosci. 12 (5),

729–738. http://dx.doi.org/10.1093/scan/nsx014.

Steinberg, L., Morris, A.S.1, 2001. Adolescent development. Annu. Rev. Psychol. 52, 83–110. http://dx.doi.org/10.1146/annurev.psych.52.1.8352/1/83.

van Duijvenvoorde, A.C.K., Op de Macks, Z.A., Overgaauw, S., Gunther Moor, B., Dahl, R.E., Crone, E.A., 2014. A cross-sectional and longitudinal analysis of reward-related brain activation: effects of age, pubertal stage, and reward sensitivity. Brain Cogn. 89, 3–14. http://dx.doi.org/10.1016/j.bandc.2013.10.005.

Woods, R.P., Mazziotta, J.C., Cherry, S.R., 1993. MRI-PET registration with automated algorithm? J. Comput. Assist. Tomogr. 17 (4), 536–546.

Yang, D.Y.J., Rosenblau, G., Keifer, C., Pelphrey, K.A.1, 2015. An integrative neural model of social perception, action observation, and theory of mind. Neurosci. Biobehav. Rev. 51, 263–275. http://dx.doi.org/10.1016/j.neubiorev.2015.01.020.