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Adolescent neighborhood quality predicts adult dACC response to social exclusion

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Neuroimaging studies using the social-exclusion paradigm Cyberball indicate increased dorsal anterior cingulate cortex (dACC) and right insula activity as a function of exclusion. However, comparatively less work has been done on how social status factors may moderate this finding. This study used the Cyberball paradigm with 85 (45 females) socio-economically diverse participants from a larger longitudinal sample. We tested whether neighborhood quality during adolescence would predict subsequent neural responding to social exclusion in young adulthood. Given previous behavioral studies indicating greater social vigilance and negative evaluation as a function of lower status, we expected that lower adolescent neighborhood quality would predict greater dACC activity during exclusion at young adulthood. Our findings indicate that young adults who lived in low-quality neighborhoods in adolescence showed greater dACC activity to social exclusion than those who lived in higher quality neighborhoods. Lower neighborhood quality also predicted greater prefrontal activation in the superior frontal gyrus, dorsal medial prefrontal cortex and the middle frontal gyrus, possibly indicating greater regulatory effort. Finally, this effect was not driven by subsequent ratings of distress during exclusion. In sum, adolescent neighborhood quality appears to potentiate neural responses to social exclusion in young adulthood, effects that are independent of felt distress.

Keywords: dACC; fMRI; social exclusion; neighborhood SES; Cyberball

INTRODUCTION

Developmental social context, including socioeconomic factors, can impact socio-emotional processing, social network formation and cultural norms (Pretty, 2002; Sampson *et al.*, 2002; Hill *et al.*, 2005). Lower neighborhood socioeconomic status (SES) is associated with difficult socio-emotional development (Evans and English, 2002; Leventhal and Brooks-Gunn, 2000;), lower self-efficacy (Boardman and Robert, 2000), and less resourceful social-networks (Rankin and Quane, 2000). This broader context may be particularly influential in adolescence—a unique period of social development where peer relationships take the center stage and sensitivity to social exclusion can be acute (Downey *et al.*, 1998). Moreover, peer relationships experienced in adolescence are predictive of adult relationship patterns (Hartup, 1996). However, little is known about how adolescent social context may impact neural processing in adulthood.

Social exclusion is a common yet distressing experience often related with negative mood, distress, and even aggressive behavior (for review see Williams, 2007). The dorsal anterior cingulate cortex (dACC) and anterior insula are associated with the experience and distress of exclusion in adulthood (Eisenberger *et al.*, 2003; Kawamoto *et al.*, 2012) and in adolescence (Masten *et al.*, 2009; Bolling, 2011). Given the importance of social context to socio-emotional development we investigated how neighborhood quality in adolescence might impact neural activation to social exclusion in adults using functional magnetic resonance imaging (fMRI).

SES and social threat sensitivity

Low SES is consistently associated with lower physical and psychological health, and neighborhood SES independently predicts variance in many of the same outcomes (Jones and Duncan, 1995; Gould and Jones, 1996; Krieger *et al.*, 1997; Robert, 1998; Eaton *et al.*, 1999). The impact of neighborhoods may be heavily weighted toward the perceived availability of resources (Lynch *et al.*, 2000), but psychosocial variables are also likely to play a role (Adler and Snibbe, 2003; Gallo and Matthews, 2003).

Neighborhoods provide an important context for socialization and the development of social networks (Sampson, 1997; Pretty, 2002). Low SES neighborhoods are often characterized by both poverty and social disorder thus limiting a child's exposure to positive relationships and role models, even while increasing exposure to victimization (Taylor and Shumaker, 1990; Ross and Jang, 2000). Low neighborhood SES is associated with greater felt discrimination, higher hostility, and, in conjunction with other SES variables, greater social vigilance (Chen and Paterson, 2006). Importantly, individuals from low SES neighborhoods are more likely than their higher SES counterparts to interpret ambiguous social interactions as threatening (Taylor and Shumaker, 1990; Wandersman and Nation, 1998; Chen and Matthews, 2001; Chen *et al.*, 2004; Chen and Paterson, 2006).

Given that lower status is associated with increased threat sensitivity, neighborhood quality in adolescence could correspond with greater ACC activity via greater felt distress, greater threat vigilance, or both. Activation of the ACC has been associated with the affective components of physical pain both in human (Rainville *et al.*, 1997) and animal (Johansen *et al.*, 2001) studies. Proponents of the social pain hypothesis suggest that the neural system for social pain has 'piggy-backed' on the neural system for physical pain (Panksepp, 1998; Eisenberger, 2008). Indeed, the presence of attachment figures and time spent with friends corresponds with attenuated neural responding in both the ACC and insula during pain stimulation (Eisenberger *et al.*, 2011; Masten *et al.*, 2012)

But recent work casts doubt on the social pain interpretation. For example, Cacioppo and colleagues' (2013) meta-analysis of Cyberball studies (12 studies, $N = 244$) failed to show unambiguous overlap between the nociceptive pain matrix and the neural correlates of social pain, including dACC activity. The authors claim that perhaps low statistical power is to blame for the persistent dACC exclusion findings in individual studies. They further suggest that ACC activity

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is related to distress more generally, including social uncertainty (Cacioppo *et al.*, 2013). Similarly, Iannetti and colleagues (2013) have argued that neural activity common to both physical and social forms of pain are not in fact even pain-specific—that they instead reflect the detection of change, relevance, and novelty involved in physical and social infractions. Indeed, some have suggested that dACC activity associated with the Cyberball task in particular may be more related to expectancy violations than social pain (Somerville *et al.*, 2006; Bolling *et al.*, 2011). Moreover, contemporaneous theories cast the ACC as broadly supporting in error detection (Holroyd *et al.*, 2005) and conflict monitoring (Botvinick *et al.*, 2001, 2004).

The consistent finding of insula activation in response to social exclusion is less contested. For example, the previously mentioned meta-analysis reported right anterior insula activation in response to exclusion both from the Cyberball paradigm and from a reliving rejection paradigm (Cacioppo *et al.*, 2013). The insula is thought to be sensitive to somatic states and thus to be a precursor to emotional experiences within an embodied framework (Craig, 2002, 2004). Within the context of social exclusion, the insula is seen as a partner to the dACC in processing the distress (Eisenberger *et al.*, 2003; for conceptual model, Eisenberger 2008). The insula may also take part in an environmental monitoring or ‘saliency’ network, along with middle areas of the cingulate cortex (Seeley *et al.*, 2007; Taylor *et al.*, 2009). However it is unclear what part it plays in conflict monitoring, error detection, or expectancy violations.

SES, executive function and emotion regulation

Executive function varies consistently by SES. Children from lower SES backgrounds perform below their higher SES counterparts in tests of executive function and related tasks of attention and working memory (Mezzacappa, 2004; Lipina *et al.*, 2005; Noble *et al.*, 2005; Farah *et al.*, 2006; Noble *et al.*, 2007). For example, childhood poverty and chronic stress predict lower working memory capacity in young adults (Evans and Schamberg, 2009). These and similar so-called ‘executive’ processes have long been associated with the prefrontal cortex (PFC) (Diamond, 1988; for review see Miller and Cohen, 2001). And individuals from low-SES backgrounds show evidence of prefrontal irregularities associated with both visual (Kishiyama *et al.*, 2009) and auditory attention (D’Angiulli *et al.*, 2008). Other studies suggest a maturational lag in childhood PFC development among impoverished children (Otero, 1997; Otero *et al.*, 2003). Although executive functions associated with the PFC have traditionally emphasized cognition, both play a substantial role in emotion and emotion regulation (Urry *et al.*, 2009; Gross and Barrett, 2011; Opitz *et al.*, 2012). For example, directed attention and cognitive reappraisal are antecedent-focused cognitive strategies for emotional regulation that rely on prefrontal structures to up or down-regulate emotional experiences (Gross, 1998; Ochsner *et al.*, 2002; Urry, 2010). Furthermore, greater pre-frontal activity in the VMPFC and the VLPFC is inversely related to felt rejection and/or lower dACC activity during the Cyberball task (Eisenberger *et al.*, 2003, 2007; Onoda *et al.*, 2010). Thus, prefrontal areas may regulate dACC activity and the subjective social pain it putatively indexes (Eisenberger and Lieberman, 2004). In combination with what we know about the effect of low SES on other forms of executive function, these emotion-regulation observations—especially those associated with the Cyberball task—suggest to us that lower neighborhood quality may impair PFC processes that regulate the impact of social exclusion.

Current study

With this study, we sought to understand how early adolescent neighborhood-quality corresponds with the neural response to social exclusion in adulthood. Because our subsample was part of a larger longitudinal study, we were able to assess neighborhood quality data when participants were approximately 13 years old. Participants then completed the fMRI Cyberball task at approximately 25 years of age—12 years later.

Our broadest hypothesis, given previous work on threat sensitivity in lower neighborhood SES populations, is that circuits typically associated with social exclusion will be more active among individuals from lower neighborhood SES backgrounds. Following this, it’s important to understand the kinds of psychological variables SES might be mediated through in understanding its association with social exclusion. Given the models reviewed above, we propose two competing hypotheses:

(i) From the social pain hypothesis perspective, dACC activation indexes felt distress—a form of subjective pain. If true, it should be possible to find evidence that felt distress might mediate the association between neighborhood quality and dACC activation.
(ii) From a social vigilance/ error detection/ or conflict monitoring perspective, increased dACC activation indexes violations of expectancy that may not correspond with felt distress. If true, we might expect the association between neighborhood quality and dACC activation to be unmediated by felt distress.

Finally, given that executive function varies by SES and, in turn, that many emotion regulation strategies rely on executive control, we thought it most likely that exclusion would result in greater PFC activity as a function of lower neighborhood quality.

METHODS

Participants

Participants were recruited from a larger longitudinal study (Kliff/VIDA Study; $N = 184$; cf., Hare *et al.*, 2011) via e-mail and phone calls to complete a set of neuroimaging tasks, including Cyberball. Following safety standards for fMRI practice, possible participants were excluded if pregnant, claustrophobic or if they had ferromagnetic items in their body. Participants were also excluded if they could not bring a well-known partner, either a friend, spouse, relationship partner or cohabitating relationship partner to the scanning session. This was due to the nature of another non-Cyberball scan completed in the same session (c.f., Coan *et al.*, 2012). Eighty-six healthy participants (45 females) completed the Cyberball scan. One participant was excluded due to abnormal neural activation resulting in a final sample of 85 participants.

The Kliff/VIDA study is a longitudinal study with yearly waves of data collection. Wave one of data collection for VIDA begun when participants were 13 years of age. At this time, parents completed demographic questionnaires and the neighborhood quality questionnaire. The median household income was between \$40 000 and \$50 000 and ranged between under \$5000 (4.81%) and \$60 000 and above (28.91%). For the subset of participants in this study, 55.29% of their parents endorsed having ever used public assistance with 10% indicating the use of unemployment assistance exclusively ($N = 83$, 2 did not respond). 36.47% of participant’s parents said that they had difficulty to a great difficulty paying bills each month and 20% said they did not have enough money to make ends meet each month ($N = 85$). Only 9.41% said they had more than enough money left over while most (43.52%) indicated that they had at least some money left over each month. fMRI data was collected between Waves 13 and 14. Participants were around 25–26 years-of-age ($M = 24.5$, s.d $= 1.35$). The sample was comprised of 56% (48) self-indentified Caucasian participants and 37% (32) self-identified African American participants. The remaining six participants comprise a diverse group that was collapsed into an ‘Other’ category (7%).

Materials

Questionnaires

Neighborhood quality questionnaire. Participants' mothers completed the Neighborhood Quality Questionnaire (NQ) at wave 1 of the KLIFF/VIDA study when participants were 13 years old (Wave 1). The NQ is a 23-item composite of three scales each assessing different aspects of neighborhood quality (Buckner, 1988; Gonzales *et al.*, 1996). The scale assesses neighborhood connectedness (e.g. 'I believe my neighbors would help me in an emergency;' $\alpha = 0.76$), neighborhood crime and deterioration (e.g. 'In the past two years things in my neighborhood have gotten worse;' $\alpha = 0.78$), and neighborhood risk (e.g. 'violent crimes that involve weapons occur in my neighborhood;' $\alpha = 0.93$) as reported by the participant's mother (or father when mother was unavailable). Subscales were correlated at $r = 0.74$. We therefore created a composite neighborhood quality score by adding the sums of each subscale with items reflecting lower neighborhood quality being reverse coded. Finally, the scores were Z-transformed before continuing with the analyses. Two participants were missing an NQ score. Their scores were replaced at the centered mean of 0 and all analyses were replicated without their inclusion to the same results. This measure was previously used on a subset of the KLIFF sample as a moderator to neural activation (Coan *et al.*, 2012).

Need threat scale. Previous Cyberball studies have used the Need-Threat Scale to assess felt distress during the paradigm (cf., Eisenberger *et al.*, 2003). Our participants completed a 12-item version of the Need-Threat Scale based on work of Williams and his lab (Jamieson *et al.*, 2010) following Cyberball. The scale included 12 items and assessed states of belongingness ('I felt rejected'), self-esteem ('I felt good about myself'), control ('I felt powerful'), and meaningfulness ('I had a feeling that my presence during the game was important') experienced during the Cyberball paradigm. Participants endorsed items on a five-point likert scale ranging from 'Not at all' (1) to 'Very much so' (5). Statements endorsing positive feelings were reversed coded and items were added to create one score whose magnitude quantified the degree of felt rejection.

Procedure

Participants were told that they would be playing a virtual catch-game with other participants who were completing the same study at two different universities (cf., Eisenberger *et al.*, 2003). However, no such players existed. We then obtained informed consent in accordance with the University of Virginia's internal review board. Following informed consent, participants were asked to write a short biography for the other players to read. Before entering the scanner, the participants were shown two of four short autobiographies describing the two other hypothetical players. While they read the other player's biographies, participants were told that we were waiting for the systems to synch to add credence to our cover story.

After participants entered the scanner, we obtained a high-resolution anatomical scan. Following this, we collected two functional scans from the fMRI while the participant played Cyberball. The paradigm starts with a hand in the middle of the screen representing the participant in the scanner and two cartoon avatars in the upper right and upper left corner, each representing one of the two hypothetical players. The avatar in the upper left then begins the game by throwing the ball to either the participant or the second player. Per usual Cyberball methodology, tosses from the hypothetical players were lagged from 0.2 to 2 s randomly to give the illusion of human players. Participants tossed the ball to either the avatar to the left or the right through the use of an MR-compatible button box. During the first, 'inclusion' scan, each avatar tossed the ball to the participant about 50% of the time. The second scan was obtained immediately following the first one and comprised the 'exclusion' scan. During the 'exclusion' scan, the participant was tossed to 10 times and then ignored for the remainder of the session (~50–60 s) while he or she continued to watch the avatars toss to each other.

Following completion of both scans, participants exited the scanner and completed the NTS within a brief packet with other self-report measures not included in this analysis. The researchers then debriefed participants regarding all tasks completed, including the deception used in the Cyberball task. Participants were questioned on their experience and encouraged to ask questions themselves.

Image acquisition and data analysis

Data were acquired using a Siemen's 3.0 Tesla MAGNETOM Trio high-speed magnetic resonance imaging device at University of Virginia's Fontaine Research Park. Participants viewed the stimuli using the fMRI's CP transmit/receive head coil with an integrated mirror. One hundred and seventy-six high-resolution structural T1-weighted magnetization-prepared rapid-acquisition gradient echo images were obtained (1-mm slices, TR = 1900 ms, TE = 2.53 ms, flip angle = 9°, FOV = 250 mm, voxel size = 1 × 1 × 1 mm) before functional scans. Seventy-five functional T2-weighted Echo Planar images (EPI's) sensitive to BOLD contrast were collected during each of the two Cyberball games. Although the Cyberball paradigm is self-advancing, functional scans were of a fixed length, each lasting 2 min and 30 s, with rest periods extending shorter games. These functional images were collected in volumes of twenty-eight 3.5-mm transversal echo-planar slices covering the whole brain (1-mm slice gap, TR = 2000 ms, TE = 40 ms, flip angle =9 0°, FOV = 192 mm, matrix= 64 × 64, voxel size = 3 × 3 × 3.5 mm).

Data were preprocessed and analyzed using FMRIB Software Library (FSL) software (Version 5.98; www.fmrib.ox.ac.uk/fsl). The preprocessing pipeline corrected for motion artifacts using FMRIB's Linear Image Registration Tool (MCFLIRT; Jenkinson *et al.*, 2002). Slice-timing differences were adjusted for using temporal interpolation, and signal to noise ratio was increased via a high-pass filter with a cutoff point of 100 s. Non-brain tissues were removed using the BET brain extraction (Smith, 2002). We used a 5-mm full width at half-minimum Gaussian kernel, and grand-mean intensity normalizaiton for spatial smoothing. Finally, functional imaging was registered to the Montreal Neurological Institute (MNI) standard space using FLIRT (Jenkinson *et al.*, 2002). All registrations were checked manually and signal-to-noise ratios (SNR) collected for quality control. SNR across runs averaged at 57.63 with a standard deviation of 13.27. There were no SNR differences between Runs 1 and Runs 2 ($P > 0.05$).

As in previous studies, each round of Cyberball was modeled as a run with blocks of exclusion and inclusion. Using the second run only, we then created four planned linear contrasts for each participant: inclusion, exclusion, inclusion>exclusion, and exclusion>inclusion. Inclusion was modeled using the first inclusive 10 throws of the second run and exclusion was modeled on the remaining exclusion throws. The exclusion > inclusion lower level contrast was then used in a whole-brain corrected ($Z > 1.96$, $P < 0.05$) covariate cluster analysis with neighborhood quality Z scores as the covariate. One participant was removed due to abnormally high brain activation more than three times that of the average.

RESULTS

Descriptive statistics

Neighborhood quality at approximately 13 years of age as rated by the participants' parents was skewed left (−1.02) towards greater neighborhood quality (M = −5.93, s.d. = 11.70, Min = −41.96, Max = 8). *NTS scores* ranged from 12 to 47 and were fairly normally distributed (M = 29.01, s.d. = 7.67).

Exclusion

In a previous analysis of these data (Chango, 2012), Chango reported that compared to inclusion, participants had greater activity in the dACC, vACC and right insula during the exclusion period—all activations consistent with those reported before (Eisenberger *et al.*, 2003, 2007; Masten *et al.*, 2009, 2010). Social exclusion also corresponded with increased activity in the left and right VLPFC, and the VMPFC. For this analysis, we used standardized NQ scores in a whole-brain corrected ($Z > 1.96$, $P < 0.05$) covariate analysis of neighborhood quality and the exclusion-inclusion contrast. The full covariate model yielded a main effect of the exclusion-inclusion contrast in a large overlapping cluster including three local maxima with the dorsomedial PFC, and one each in the dACC/paracingulate and superior frontal gyrus (Table 1). Results do not deviate from main effect findings previously reported (Chango, 2012).

Exclusion and early neighborhood quality

Scores were centered and entered into FSL using a covariate analysis. Two neighborhood quality scores where not available. These were imputed at the center.[1]

Effects of neighborhood quality on neural correlates of ostracism

Regions with higher activation during rejection as a function of lower neighborhood quality are summarized in Table 2. Clusters where often connected and activation was heterogeneous (Figure 1). We therefore defined clusters both by structural probability maps in FSL and by the continuity of functional activation. Results indicated greater dACC/paracingulate activity as a function of lower neighborhood quality during adolescence. We also observed greater activity in DMPFC/Superior frontal gyrus, superior frontal gyrus and middle frontal regions as neighborhood quality decreased (Figure 2). Additional analyses were conducted to rule out ethnic identity and income as possible mediators. Neither variable explained the association between neighborhood quality and exclusion-related neural activation (see Supplementary Material for greater details).

Neighborhood quality, exclusion and the need threat scale

Need Threat Scale scores and neural correlates of ostracism

We tested the hypothesis that our neighborhood findings were mediated through felt distress following exclusion. First, we looked at covariation between NTS and neighborhood quality. Second, we looked at associations between the mean time series for the dACC/paracingulate identified in the full model and NTS scores. We used Featquery in FSL to extract the mean time series in the exclusion > inclusion contrast for the dACC/Paracingulate ROI mask created by accounting for anatomical and functional boundaries. These values were then exported, with NTS and NQ scores, into RStudio for additional analysis. NTS scores and neighborhood quality scores were not significantly correlated, $r = 0.17$, $P = 0.12$. We also conducted a linear regression between NTS scores and dACC activation. One case emerged as a model outlier as defined by Cook's Distance (leverage > 0.05) due to highly negative dACC/paracingulate activation. The model was re-run without this case. Results indicated no association between NTS scores and dACC/Paracingulate activation, $F(1,82) = 0.44$, $P = 0.51$. Analyses using the NTS subscale scores yielded the same conclusion (see Supplementary materials for greater detail).

[1] A subsequent reanalysis dropping these two individuals did not alter the pattern of results.

Table 1 Local maxima for the main effect of exclusion > inclusion in full model including neighborhood quality as a covariate

Regions	Z	Peak coordinates		
		x	*y*	*z*
DMPFC	8.98	0	54	32
	8.49	2	60	32
	8.30	2	44	36
	8.29	0	50	28
Paracingulate/dACC	8.98	6	50	12
Superior Frontal Gyrus	8.38	0	34	38

Table 2 Regions negatively correlated with neighborhood quality in exclusion > inclusion contrast

Regions	Z	Peak coordinates			Size (voxels)
		x	*y*	*z*	
			Frontal regions		
DMPFC	4.31	−18	40	38	204
Superior frontal gyrus	3.74	−26	28	50	297
	3.56	−16	38	30	
Middle frontal gyrus	3.74	−26	22	38	473
	3.33	−32	22	30	
			Cortical regions		
ACC/paracingulate cortex		−18	30	26	181

Notes. Results indicated one large heterogeneous cluster with local maxima at these coordinates. Voxel size for each region of interest were determined by creating functionally and structurally contiguous masks in FSLView. We then used FLS's FeatQuery to extract ROI size.

DISCUSSION

Our results suggest that lower childhood neighborhood quality is associated with increased activation in portions of the prefrontal and cingulate cortices during social exclusion. Furthermore, we were unable to find evidence that the association between neighborhood quality and dACC activation might have been mediated through subjective distress as measured by the NTS. These observations are noteworthy for several reasons. First, our measurements of neighborhood quality were obtained 12 years before our measurements of brain activity during social exclusion and crossed developmental milestones. Moreover, our neighborhood quality measurements were *parent-rated*, not derived from our participants themselves. Thus despite our primary measures of interest crossing not only great temporal distances, but also very different levels of analysis, we observed theoretically meaningful results. Below, we offer some conjectures on likely explanations for the associations we observed.

Neighborhood quality and social vigilance

Although these results do not permit causal conclusions, they are consistent with previous suggestions that individuals from lower quality neighborhoods are more sensitive to potential threats (Chen and Paterson, 2006). The ACC has been implicated in monitoring, cost-benefit analysis, and social salience in both human and animal studies (Rushworth *et al.*, 2007). The insula has also been implicated in a

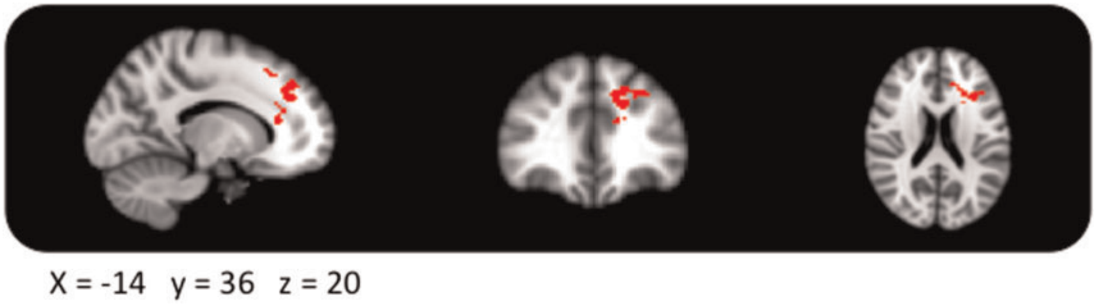

Fig. 1 Sagittal, coronal, and axial view of significant cluster negatively correlated with neighborhood quality in the exclusion > inclusion contrast as part of the whole brain cluster analysis ($Z = 1.96$, $P > 0.05$). MNI coordinates ($x = -14$, $y = 36$, $z = 20$) reflect a central location to better illustrate the scope of the cluster and is not a peak voxel.Cluster size is 1140 voxels large ($P = 0.006$). True activation and extent cannot be determined given the anatomical boundary crossing (Woo *et al.*, 2014).

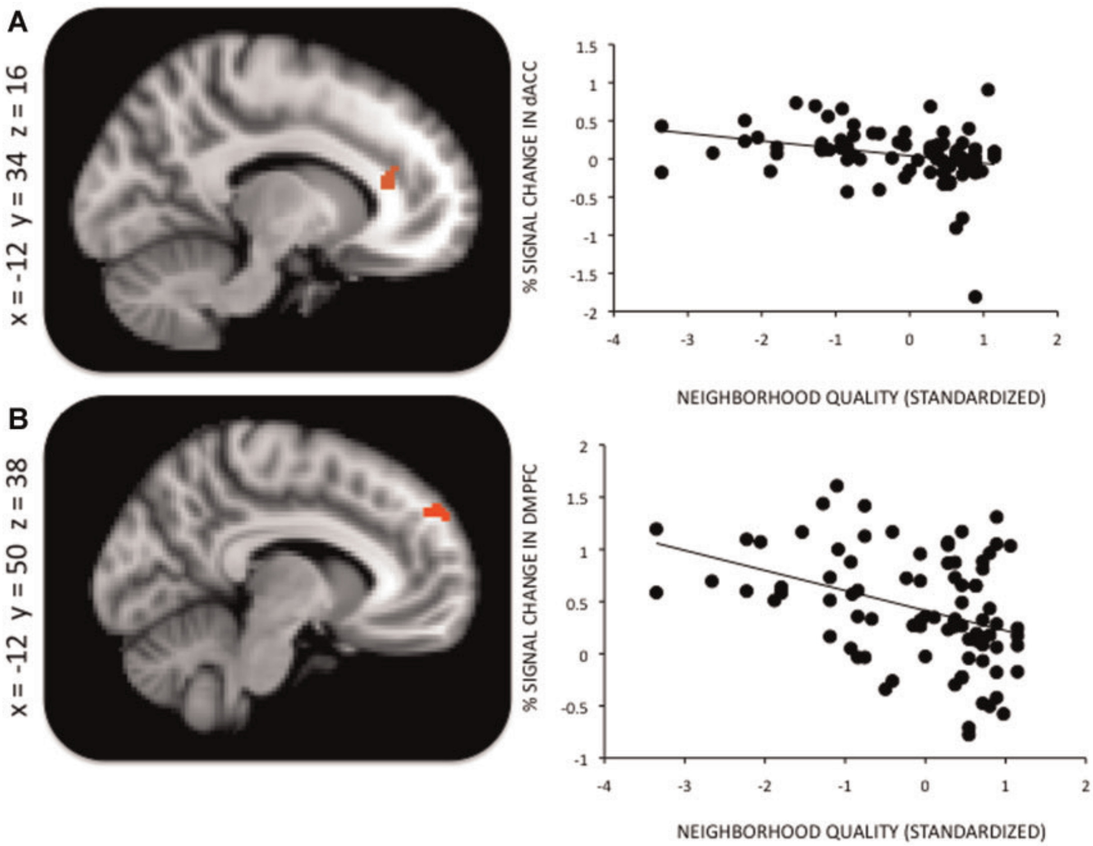

Fig. 2 Percent signal change in the dACC/Paracingulate and DMPFC during exclusion as a function of adolescent neighborhood quality. **A**) Cluster in red depicts activation in the dACC/Paracingulate cortex during exclusion as a function of neighborhood quality. Cluster is a mask defined by both functional activation and structural boundaries as defined by the Harvard Cortical Atlas in FSL. Scatter plot depicts the percent signal change for each participant in the dACC/Paracingulate ($x = -12$, $y = 34$, $z = 16$) as defined by the group level analysis (*Y* axis) and standardized neighborhood quality scores at 13 years of age (*X* axis). **B**) Cluster in red depicts activation in the DMPFC during exclusion as a function of neighborhood quality. Cluster is a mask defined by both functional activation and structural boundaries as defined by the Harvard Cortical Atlas in FSL. The scatter plot depicts percent signal change for each participant (*Y* axis) in the DMPFC ($x = -8$, $y = 50$, $z = 38$) and standardized neighborhood quality scores (*X* axis). As adolescent neighborhood quality increases, activations in the dACC/paracingulate and the DMPFC decrease.

general 'saliency' network in conjuction with middle portions of the ACC (including dACC) using resting state fMRI analysis (Seeley *et al.*, 2007; Taylor *et al.*, 2009). Although insula activation was significant both in the main effects of exclusion (Chango, 2012) and in the main effects with the covariate as part of a large cluster, it was not correlated with adolescent neighborhood quality. Although the insula is implicated in social saliency it is perhaps more about integration of physiological feelings (Craig, 2009). Its lack of covariation in our model supports the hypothesis that the greater neural activation we observed as a function of lower neighborhood quality is less about hurt feelings and more about vigilance. Possibly, the greater ACC activity we see as a function of lower neighborhood quality is an index of greater social monitoring effort and not greater distress. Lower quality neighborhoods are often rife with social disorder, including victimization and crime, placing a premium on familiarity and predictability in social relationships (Willmott & Policy Studies Institute, 1987; Argyle, 1994).

However, a counter hypothesis is that exposure to lower-quality neighborhoods should lead to habituation to its aversive components, including felt discrimination or threat. This is not found in children and adults with a history of physical abuse—arguably a more extreme analog to neighborhood quality. Experience of abuse does not attenuate but rather increases perceptual and physiological sensitivity to the antecedents of violence (Pollak *et al.*, 2001, 2002). From this perspective, the potentiated dACC sensitivity we observed during exclusion among individuals from low-quality neighborhoods can be viewed as an adaptive strategy aimed to fit a predictive model to a developmental context (cf., Friston, 2010).

This interpretation is consistent with the error likelihood hypothesis regarding the ACC. According to this theory, the ACC (and the dACC in particular) is activated as a function of both the likelihood of error and the predicted magnitude of error consequences (Brown and Braver, 2007). In this case, the 'error' is failure to receive the ball around one third of the time or, generally, failure to be included. The predicted magnitude of such an error is partially determined by experience, with participants from lower quality neighborhoods perhaps predicting more severe consequences. But our results are not completely incompatible with the conflict-monitoring hypothesis, which suggests that the dACC is part of a larger monitoring network and serves to detect conflict (Botvinick *et al.*, 2004). In this case, participants monitored what was expected (receiving the ball fairly equally) and what was experienced (exclusion). Violation of the expectations set by the first inclusion game creates uncertainty at the micro and at the macro level. At the micro level, probabilistic expectations are violated (e.g. you fail to receive the ball one-third of the time). At the macro level, social expectations of goodwill are violated (e.g. the expectation of social inclusion is contradicted). It may be that early experience with troubled neighborhoods sensitizes the dACC to conflicts between socially relevant predictions and outcomes.

Some have suggested that the ventral ACC (vACC) indexes negative affect and arousal while the dACC indexes conflicts between expected and observed outcomes (Somerville *et al.*, 2006; Onoda *et al.*, 2009; Bolling *et al.*, 2011; Kawamoto *et al.*, 2012). Interestingly, only dACC covaried as a function of adolescent neighborhood quality. Furthermore, we did not observe any association between adolescent neighborhood quality and either vACC activation or subjective feelings of distress. Thus, our data do not suggest that the connection between dACC activation and neighborhood quality is mediated through felt distress. In our view, it is more likely that the dACC is indexing salience in this case and as other have suggested more broadly. The dACC is also involved in approach/ avoidance behavior, with connections to areas of the brain involved in decision-making, motivation, and motor planning (Devinsky *et al.*, 1995; Shackman *et al.*, 2011). Possibly, the intensity of dACC activation is one of a series of conditions that determines goal directed behavior. Within an unsafe context one might expect avoidance in the face of social ambiguity as the norm.

Neighborhood quality, executive function and emotion regulation

Prefrontal activations in response to exclusion as a function of lower neighborhood quality, however, may lend some support for a 'social pain' interpretation of our findings. Given previous reports of prefrontally mediated suppression and reappraisal strategies for affective regulation (Ochsner and Gross, 2005; Ohira *et al.*, 2006; Goldin *et al.*, 2008), it is plausible that participants from lower-SES neighborhoods exerted greater regulatory effort during exclusion, but other factors lead to lower self-reports of distress. For example, lower neighborhood SES is associated with greater social isolation and social exclusion (Tigges *et al.*, 1998). Over time, as with physical pain, humans may subjectively habituate even as the infraction continues to confer biological stress and encourage vigilance for that stressor. For example, self-reports on witnessing violence can decrease as a child ages and yet violence-exposure related social cognitions and behaviors will increase (Guerra *et al.*, 2003). That said, SES disparities in executive function (Farah *et al.*, 2006) could also explain the observed difference. It is plausible that increased prefrontal activation/ regulatory effort may be due to lower executive function capacity afforded to participants from lower quality neighborhoods. These are conjectures, however, as we neither measured executive function nor attention control in any of our participants.

Limitation and future directions

A particular limitation of the current study concerns our inability to clearly distinguish current state-based effects from true developmental context effects. For example, we were not able to account for current neighborhood quality. And, while the data do express an association between neighborhood-level subjective SES and adult neural activation, it is possible that a third variable better explains this association. Extra analyses on ethnic identity and household income (see Supplementary Material) did fail to disentangle the direct association in our findings. However, income is a limited measure of SES and more questions remain. Nevertheless, it is possible that neighborhood quality, as measured here, is a latent variable capturing various factors that independently only weakly impact neural development.

Moreover, the Cyberball procedure includes the use of ambiguous descriptions about the other players as a means of deception. One potential explanation for our results may be that these ambiguous descriptions encourage participants to assume relatively high status co-participants, especially given the scanning environment, and the university context (Devos and Banaji, 2005). It is possible that lower adolescent neighborhood quality may confer an internalized sense of lower status, particularly within a high-status context as is our scanning environment. Therefore, participants from lower-quality neighborhoods may believe that they are playing with much higher status members in comparison to their peers from higher-quality neighborhoods.

If results are about experimental context and relative social status, then results may better reflect the effects of social exclusion by individuals of higher status. We know that middle to upper-middle class individuals will experience some of the negative cognitive and emotional outcomes associated with lower status when placed in a relatively higher status context (Johnson *et al.*, 2011). Muscatell and colleagues (2012) observed that lower SES students exhibited greater DMPFC, MPFC, and precuneous/PCC activity in response to social threat (angry faces). Although they used current individual SES as the predictor, their findings somewhat align with our own neighborhood-level findings. It may be that social threat is more salient for lower SES individuals in general. However, it remains to be seen were the 'true effects' lie. Subjective status differences at the individual or contextual level, current objective SES at individual and contextual levels, and developmental SES context provide good avenues for further research on status-based neural processing of social uncertainty or threat.

Finally, future research needs contextualized neurodevelopment theories of neural variability for clearer hypothesis testing regarding developmental context and the adult brain. Although many questions remain, results reported here suggest that individuals from lower-quality neighborhoods are responding more intensely at the neural level than their higher neighborhood quality counterparts to social exclusion.

SUPPLEMENTARY DATA

Supplementary data are available at *SCAN* online.

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