Neural connections foster social connections: a diffusion-weighted imaging study of social networks

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Abstract

Although we know the transition from childhood to adulthood is marked by important social and neural development, little is known about how social network size might affect neurocognitive development or vice versa. Neuroimaging research has identified several brain regions, such as the amygdala, as key to this affiliative behavior. However, white matter connectivity among these regions, and its behavioral correlates, remain unclear. Here we tested two hypotheses: that an amygdalocentric structural white matter network governs social affiliative behavior and that this network changes during adolescence and young adulthood. We measured social network size behaviorally, and white matter microstructure using probabilistic diffusion tensor imaging in a sample of neurologically normal adolescents and young adults. Our results suggest amygdala white matter microstructure is key to understanding individual differences in social network size, with connectivity to other social brain regions such as the orbitofrontal cortex and anterior temporal lobe predicting much variation. In addition, participant age correlated with both network size and white matter variation in this network. These findings suggest the transition to adulthood may constitute a critical period for the optimization of structural brain networks underlying affiliative behavior.

Key words: social network; diffusion imaging; white matter; friendship; adolescence

Introduction

Humans are unusual in our propensity to build a network of relationships with unrelated individuals—a network of friends. Our friendships become increasingly important during adolescence when we become more sensitive to the social cues of our peer group and place less importance on familial relationships (Steinberg and Morris, 2001). This epoch is also marked by substantial synaptic pruning and white matter reorganization in the brain (Blakemore, 2008), which continues into young adulthood and typically stabilizes around age 30 (Lebel et al., 2012). Although we know this social and neural development occurs simultaneously, little is known about how the size of adolescent and young adult social network size might affect neurocognitive development or vice versa.

Research has shown, however, that our health depends partly on the size of our social network. For example, Pressman et al. (2005) found that college freshman with smaller social network sizes exhibited a blunted antibody immune response to influenza vaccination. Other studies have shown that social connectedness correlates with decreased rates of heart attack mortality (Seeman, 1996), improved breast cancer prognosis (Spiegel, 1989) and even extended lifespan (Giles et al., 2005). Concordantly, having too few friends can lead to loneliness, which has been associated with negative mental and neurological health outcomes such as personality disorders and Alzheimer’s (reviewed in Hawkley and Cacioppo, 2010). In adolescents in particular, those with smaller social networks often have a lower perception of support by friends and diminished sense of belonging, which can lead to higher levels of depression and suicide (Falci and McNeely, 2009).

Recent research has linked the social affiliative behaviors required to build social networks to an extended system of brain...
regions centered on a small brain region deep within the medial temporal lobe, the amygdala (reviewed in Bickart et al., 2014). Studies of rare lesion patients with bilateral damage to the amygdala exhibit changes in social behavior including diminished social apprehension, increased trust of strangers and inappropriate levels of interpersonal familiarity (reviewed in Bickart et al., 2014). Consistent with these findings, amygdala gray matter volume correlates with social network size in neurologically normal individuals (Kanai et al., 2012; Von Der Heide et al., 2014). Two fMRI studies have also shown that the amygdala is more active in individuals with larger social network sizes when viewing social cues such as other’s faces or biological motion (Dziura and Thompson, 2014; Von Der Heide et al., 2014). Collectively these studies suggest the amygdala may be integral for understanding individual variability in social network size.

Although there has been much research on amygdala gray matter, there has been substantially less study of amygdala white matter connectivity to other brain regions, and its potential implications. In non-human primates, the amygdala communicates with dispersed neural loci via a structural communication system defined by monosynaptic white matter connections (Freese and Amaral, 2005). Specifically, the amygdala has strong white matter connections with the orbitofrontal cortex (OFC) and anterior temporal lobes (ATLs) (Klingler and Gloor, 1960; Craig et al., 2009). We hypothesize that the structural connectivity of the amygdala, OFC and ATL contributes to individual variation underlying social affiliative behavior. This conjecture is based on two findings. First, previous research has shown that variation in the gray matter volume of the amygdala, OFC and ATL correlates with social network size (Kanai et al., 2012; Von Der Heide et al., 2014). Second, lesion studies of non-human primates have shown that bilateral lesions to any of these three regions precipitates a constellation of social deficits including inappropriate production and recognition of social signals, blunted fear and aggression and lack of social interest and affiliative behavior (Myers and Swett, 1970; Von Der Heide et al., 2014). Although these findings are critical for identifying the key neural regions involved with affiliative behavior, they fail to address if these areas form a network and how the connectivity among these regions might influence behavior.

Here we tested the hypothesis that variability in the structural white matter connectivity between the amygdala and other socially implicated brain regions would predict individual variation in social network size. Given that adolescence is a time of both immense social and neural development, we sampled a group of neurologically normal adolescents and young adults. We also sought to investigate whether social network size and white matter varied with age. To measure white matter tract variation, we employed probabilistic tractography of diffusion tensor imaging (DTI) data.

Methods

Participants

Thirty-five participants, aged 12–30 (M = 21.17; SD = 6.06) were recruited from the greater Philadelphia area via local advertisements. Our sample size was comparable to previous studies examining the relationship between white matter connectivity and behavior (e.g. Sigmundsson et al., 2001; Barnea-Goraly et al., 2004; Scholz et al., 2009). We sampled individuals from an extended age range because research has shown that, unlike gray matter, white matter continues to develop into young adulthood, with some limbic white matter tracts peaking around 30 (Lebel et al., 2012). We restricted our sample to female participants to decrease gender-related variance in social cognition (Killgore and Yurgelun-Todd, 2001). All participants received monetary compensation for their participation, were right-handed, native English speakers, had normal or corrected-to-normal vision, normal hearing and had no history of psychological, developmental or neurological disorders. Informed consent was obtained according to the guidelines of the Institutional Review Board of the Temple University.

Materials

The Norbeck Social Support Questionnaire (NSSQ) was used to measure social network size. The NSSQ is a self-administered questionnaire that provides a reliable measurement of several dimensions of social support including the size of a person’s real-world social network (Norbeck, 1984). The NSSQ has been widely used for social science research, including in adolescent populations (Nichols et al., 1995). Its widespread use can be attributed to its comprehensive approach to measuring social support and its ongoing psychometric evaluation (Gigliotti and Samuels, 2011). In this study, participants were asked to list one significant person in their life and to include all persons who ‘provide personal support… or are important to [them] now’. In the adjacent column participants indicated the category of each relationship from a list of choices. Responses were binarily coded as either a family member or a friend. The number of friends in a person’s network, i.e. social network size, has been shown to be associated with individual differences in social cognitive ability (Stiller and Dunbar, 2007), gray matter volume (Von Der Heide et al., 2014) and neural activation (Lewis et al., 2011). Given that relationships with family members are not as freely chosen or ‘built’ by individuals (Bukowski et al., 1998), we used the number of family members as a control measure.

MR data acquisition and preprocessing

Neuroimaging sessions were conducted at Temple University Department of Radiology on a 3.0 T Siemens Trio (Erlangen, Germany) using a 12-channel multiple-array Nova Medical (Wilmington, MA) head coil using parallel imaging (GRAPPA). The T1-weighted images were acquired using a three-dimensional magnetization-prepared rapid acquisition gradient echo pulse sequence (TR = 8.67 ms, TE = 3.47 ms, flip angle = 12°.). Diffusion-weighted imaging (DWI) was performed at a resolution of 2.5 × 2.5 × 2.5 mm³, with 3 repeats of the b0 (no diffusion weighting image) and 2 repeats of each of 20 gradient directions at b1000 (TR = 9900 ms, TE = 95 ms) with a 1.2-mm gap between slices. The FMRIB Diffusion Toolbox (FDT, http://www.fmrib.ox.ac.uk/fsl/fdt/) was used to correct the DTI data for head movement and eddy currents and least squares tensor model fitting. Data from the two acquisitions of each diffusion direction were averaged to improve the signal-to-noise ratio.

Selection of regions of interest

The neural regions of interest (ROIs) in this study were the amygdala, the OFC, the ATL and the temporoparietal junction (TPJ). We selected our left/right lateralized amygdala ROI using the Harvard-Oxford Atlas available through FSL tools (http://www.fmrib.ox.ac.uk/fsl/). As an OFC mask was not available in the FSL atlas, our left/right lateralized OFC ROI was derived
from the Wake Forest Pick Atlas (http://fmri.wfubmc.edu/soft ware/pickatlas) and included the entire ventral surface of the frontal lobe extending to the frontal pole and up to the genu of the corpus callosum. Last, because the ATL has ambiguous anatomical boundaries and several distinct functional subregions, we defined the social subregion of the ATL empirically. Twenty individuals were asked to complete a one-back working memory task in the scanner as they viewed famous and non-famous faces, and famous and non-famous places. Using the contrast all faces > all places, a 9-mm sphere was drawn around the peak voxel of activation of the group map. We included the TPJ as a control region because it has been implicated in Theory of Mind abilities which could plausibly be linked to variation in social network size. One study in non-human primates suggested that gray matter increases in the TPJ could reflect an increasing social network size. One study in non-human primates suggested that gray matter increases in the TPJ could reflect an increasing network size. One study in non-human primates suggested that gray matter increases in the TPJ could reflect an increasing social network size. One study in non-human primates suggested that gray matter increases in the TPJ could reflect an increasing social network size. One study in non-human primates suggested that gray matter increases in the TPJ could reflect an increasing social network size.

DWI preprocessing and analysis

DWIs were preprocessed to correct for eddy currents and participant motion using an affine registration model. The b-vector matrix was adjusted based on rigid body registration, ensuring a valid computation of the tensor variables. Non-brain tissue was removed using an automated brain extraction tool, and a least squares diffusion tensor fitting model was then applied to the data. All preprocessing was performed using FSL (Smith et al., 2004).

DTI tractography models the anisotropic movement of water molecules in restricted compartments, such as axons, to investigate white matter connectivity. Virtual reconstruction of the underlying tracts can be obtained from diffusion data, allowing for the assessment of specific WM fasciculi, and their associated diffusion properties. Fractional anisotropy (FA) is a measure commonly used in DTI studies to relate anatomical differences in white matter to behavior. FA depends on several biologic factors, such as axonal thickness, membrane thickness, myelination and crossing fibers (Jones et al., 2013). In this study we were particularly interested in specific white matter pathways. As such, we employed ‘seeded’ tractography, with the amygdala as the seed region—the starting location for subsequent white matter tractography.

Tractography analyses were performed in the subjects’ native anatomical space and the results were output in Montreal Neurological Institute (MNI) standard space according to transformation parameters. Each FA image was registered to each subject’s high-resolution T1-weighted image using six degrees of freedom and a mutual information cost function. The T1-weighted image was registered to an MNI template via a nonlinear warping algorithm. These transformation parameters were then used as a conversion matrix to transform from DWI to MNI space. We then conducted probabilistic tractography using the FDT Toolbox with a partial volume model, and up to two fiber directions in each voxel. Probabilistic tractography has been shown to more accurately trace fibers than deterministic tractography, and dual-fiber models better account for crossing fibers and therefore yield more reliable results compared with single-fiber models (Behrens et al., 2007).

Five thousand sample tracts were generated from each voxel in the seed mask, the amygdala. We visually inspected tractography maps to ensure tractography was successful and acceptable for further analysis. All tractography was performed separately for the left and right amygdala and to respective lateralized target ROIs. An exclusion mask was placed for the contralateral brain hemisphere to ensure modeled tracts were fully lateralized. Finally, FA values were extracted for each individual for each amygdala-ROI tract from the probabilistic tractography and thresholded such that voxels with higher tractography probability were weighted proportionally more.

Statistical analyses

Statistical analyses were performed using SPSS (Version 21.0). Regression analyses were used to examine the relationship between FA of amygdala white matter tracts and data from the surveys described earlier.

Results

First, we examined the relationship between white matter microstructure and social network size. Norbeck Friends (M = 7.63, SD = 4.87) scores ranged from 1 to 23 friends; Norbeck family scores (M = 3.91, SD = 2.04) ranged from 0 to 9. The variables included in our statistical analyses were normally distributed and were not significantly collinear. A Pearson correlation revealed a positive correlation between age and Norbeck Friends scores, r = 0.51, P = 0.002. Therefore, age was included in subsequent regression models (Figure 1).

Together, age and white matter tract FA values significantly predicted social network size F(6,28) = 11.96, P < 0.001, R² = 0.72. In order to better understand the relative predictive power of age and the white matter tracts, we performed a stepwise hierarchical linear regression. Findings are summarized in Table 1 and visually depicted in Figure 2.

In Step 1, age was entered; there was a significant effect of age, F_change(1,33) = 11.84, P = 0.002, R = 0.27. In Step 2, FA values for lateralized amygdala-ATL white matter tracts were entered; this was also significant, F_change(3,31) = 12.56, P < 0.001, R² = 0.33, indicating that amygdala-ATL white matter microstructure accounted for an additional 33% of the variability in social network size. Overall, model 2 was significant F(3,31) = 15.09, P < 0.001, R² = 0.59, indicating that 59% of the variability in social network size was accounted for by age and amygdala-ATL white matter microstructure. In Step 3, FA values for lateralized amygdala-OFC tracts were entered; this produced a significant model F_change(5,29) = 4.58, P = 0.02, R² = 0.10, showing that amygdala-OFC white matter microstructure accounted for an additional 10% of the variability in social network size. Overall, model 3 was significant F(5,29) = 12.98, P < 0.001, R² = 0.69, indicating that 69% of the variability in social network size was accounted for by age, and amygdala-ATL and amygdala-OFC white matter microstructure. In the final step, Step 4, FA values for the right amygdala-TPJ tract were entered; this addition did not significantly improve the model F_change = 2.80, P = 0.11, R² = 0.03. We rotated the order in which the variables were entered, and the same significance levels were observed.

Norbeck family scores were not correlated with age (P = 0.77). When Norbeck family scores were substituted for Norbeck friends scores in the hierarchical regression above, none of the steps produced significant models (all P > 0.25).
Table 1. Age and white matter connectivity explain social network size variability

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model 1 B</th>
<th>Model 2 B</th>
<th>Model 3 B</th>
<th>Model 4 B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.51**</td>
<td>0.61**</td>
<td>0.60**</td>
<td>0.62**</td>
</tr>
<tr>
<td>[R] amygdala-ATL</td>
<td>0.57**</td>
<td>0.70**</td>
<td></td>
<td>0.72**</td>
</tr>
<tr>
<td>[L] amygdala-ATL</td>
<td>0.45**</td>
<td>0.45**</td>
<td></td>
<td>0.41**</td>
</tr>
<tr>
<td>[R] amygdala-OFC</td>
<td>0.17</td>
<td>0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[L] amygdala-OFC</td>
<td>0.30**</td>
<td>0.36**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>[R] amygdala-TPJ</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.26</td>
<td>0.60</td>
<td>0.70</td>
<td>0.72</td>
</tr>
<tr>
<td>F for change in $R^2$</td>
<td>11.84**</td>
<td>12.56**</td>
<td>4.58*</td>
<td>3.80</td>
</tr>
</tbody>
</table>

*R < 0.05. **P < 0.01.

General discussion

The goal of this study was to test the hypothesis that white matter structural connectivity from the amygdala to other social brain regions predicts individual differences in affiliative behavior as measured by social network size. We used probabilistic tractography of DTI data in neurologically normal adolescents and young adults. Our results showed that individual differences in structural connectivity between the amygdala and two regions, the OFC and ATL, accounted for a surprisingly large amount of the variance in social network size. In contrast, structural connectivity between the amygdala and a brain region implicated in theory of mind, the TPJ, did not predict social network size.

These findings suggest that the amygdala, OFC and ATL form an interconnected structural network, and that variation in the white matter connecting these regions manifests as differences in the quantity of real-world friendships. This finding is consistent with past research in non-human primates: bilateral lesions to these regions cause devastating social deficits including lack of social interest and affiliative behavior (Myers and Swett, 1970; Von Der Heide et al., 2014) with amygdala ablation causing the most persistent deficits (reviewed in Olson et al., 2007). In clinical populations, persons with a disorder called behavioral variant of frontotemporal dementia also have damage to this neural circuitry and present with symptoms of impaired social comportment, empathy, and affiliative behaviors (reviewed in Olson et al., 2007). Our findings also add increased specificity to nascent research implicating white matter connectivity in autism spectrum disorders and schizophrenia (Sigmundsson et al., 2001; Barnea-Goraly et al., 2004). Indeed, it is possible that perturbations to the amygdalocentric structural white matter network proposed in this paper are responsible for the social affiliative deficits observed in such psychiatric disorders.

Our results also appear to be neurally selective as connectivity between the amygdala and the TPJ did not predict number of friends in a person’s social network. The TPJ was selected because a large neuroimaging literature has implicated the right TPJ in theory of mind and empathy (reviewed in Lamm and Decety, 2011) and one study has implicated a nearby region, the posterior superior temporal sulcus (STS), in social network complexity (Dziura and Thompson, 2014). However, the role of this region in social behavior remains controversial, as damage to this region does not commonly result in obvious changes in social comportment, personality or emotionality. It is also possible that the TPJ is involved, but not integral, to theory of mind, as some research has suggested (Mitchell et al., 2008).

Why do some people have larger social networks than others? Certain social behaviors confer survival advantages and accordingly have been selected for by evolution. We naturally direct our attention to follow another’s gaze (Frischen et al., 2007), cultivate social networks through ‘social grooming’ behaviors, and generally find social interactions rewarding (Lazarro-Perea et al., 2004; Trezza et al., 2011). Some also actively seek to increase their social network size by gossiping and flattering others (Burt and Knez, 1996) and consciously groom their social reputations (Tennie et al., 2010). Certain social signals, such as a smile, have been shown to not only be sexually attractive to us (Otta et al., 1996), but also to invoke similar neural activity as do basic rewards such as food (Tsukiura and Cabeza, 2008). Despite our deeply social nature, individuals vary in the amount and type of affiliative behavior they engage in, which is borne out in differences in social network size.

The question then is whether intrinsic variation in white matter facilitates social network expansion, or vice versa? Our data do not allow us to ascertain directionality. We speculate, however, that the brain-behavior relationship is best described as a positive feedback loop of cumulative advantage: maintaining larger networks requires more person memory, more theory of mind and more social acumen (Dunbar, 2012), which much like other effortful skills (Scholz et al., 2009), may cause plastic changes in white matter. Once put into place, this altered
structural network promotes the acquisition of more friendships. If correct, this suggests that social experience and friendship building during critical periods of white matter development might be key for the optimization of social affiliation brain networks.

The developmental trajectory of white matter change appears to be more prolonged than that of gray matter. White matter continues to develop throughout adolescence, with some limbic white matter tracts peaking around age 30 (Lebel et al., 2012). Our findings are consistent with this as we found a significant positive relationship between age and white matter microstructure in our sample of 12–30-year olds. We also found that social network size varies with age, an intuitive finding consistent with prior research (Van Tilburg, 1998). Indeed, adolescents and younger adults are extremely sensitive to social signals and are hyper-sensitive to the feelings and decisions of their peers (Steinberg and Morris, 2001). Taken together, these results suggest that the transition from adolescence to young adulthood may constitute a critical period for the optimization of structural brain networks underlying affiliative behavior.

Limitations and Future Research. We found that there was a positive relationship between left ATL FA and Norbeck friends, and a negative relationship between right ATL FA and Norbeck friends. FA is a composite measure of white matter structure, rendering specific interpretation of directionality imprudent. Although we are not aware of any published work examining such differences, this left-right flipped pattern is the subject of ongoing investigation by a number of research groups. These studies, combined with burgeoning research examining the exact neurobiological underpinnings of FA, will likely explain the origin and implication of such lateralized FA differences.

In this study, we built a regression model in which the white matter microstructure of certain amygdalocentric fiber pathways predicted social network size. It is also plausible that there is an interaction between age and white matter on social network size such that as one progresses from adolescence to young adulthood, white matter is more or less predictive. Although we are underpowered in this study to examine these interactions, future studies with larger sample sizes could explore this interesting potential interaction. Our regression models also suggest that different white matter tracts may predict different amounts of variance in social network size. This is an intriguing prospect; future research might be designed to examine the relative contribution of different tracts by, for example, using a more focused collection of ROI exclusion masks, a larger sample size and more imaging gradient directions.

Our findings complement recent research suggesting that amygdala functional neural connectivity predicts social network size in humans (Bickart et al., 2012). The amygdaloid complex is composed of more than 10 nuclei, which can be distinguished based upon cytoarchitecture and relative connectivity (Sah et al., 2003). In this study, we used the entire amygdala as our ROI for two main reasons. First, although...
amygdala subregions are known, these nuclei are highly interconnected, making DTI separation potentially inaccurate (LeDoux 2007). Second, we warped our ROIs from standard to native space, further rendering subdivisional analyses problematic. Future research utilizing functional localization of subregions at the participant level would allow for more precise ROIs and help elucidate the relationship between the structural and functional connectivity of amygdala subdivisions and social network size.

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References


