Longitudinal changes in functional brain connectivity between childhood and early adolescence during social appraisals

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manuscript in preparation
Abstract

During the transition from childhood to adolescence, there is considerable development of social brain regions, including cortical midline areas and the temporoparietal junction (TPJ). Previous longitudinal research demonstrated that at age 10 as well as age 13, the medial prefrontal cortex (mPFC) was activated more for self-appraisals while the medial posterior parietal cortex (mPPC) was activated more for other-appraisals. The current follow-up study investigated coupling of these regions during social appraisals, specifically how this changed over time. Twenty-seven children judged descriptions of self and a fictional other in the fMRI scanner at the age of 10 and the age of 13. Psychophysiological interaction (PPI) analyses were conducted using the rostral mPFC and mPPC as seed regions. Both regions showed stable task-dependent functional connectivity with several areas but only the mPPC showed changes in functional connectivity over time. Particularly, increased mPPC coupling with bilateral TPJ and the left thalamus was observed during other-appraisals. This pattern might be related to development of social behavior, such as a heightened focus on peers, between late childhood and early adolescence.
Introduction

From late childhood to early adolescence, appraisals of self and others develop considerably. Identities are shaped and the influence of peers increases during this life phase (Steinberg & Morris, 2001). Meanwhile, changes occur in brain regions underlying social processes, including the medial prefrontal cortex (mPFC), medial posterior parietal cortex (mPPC) and temporoparietal junction (TPJ; Pfeifer & Peake, 2012). The next step for developmental neuroscience is to examine how these areas work together in service of social understanding. By complementing localization approaches with network analyses, we can gain more insight into the neural bases of cognition and behavior across age (Stevens, 2009). Functional connectivity methods allow researchers to investigate if activity in one brain area is correlated with activity of other regions, during rest or under specific task conditions (O’Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012; Smith et al., 2012). In the current longitudinal study, we explore functional connectivity during self- and other-appraisals, especially how this changes over time as children transition into adolescence.

Development of neural mechanisms for social appraisals

Functional magnetic resonance imaging (fMRI) studies in adults have demonstrated that cortical midline structures – the mPFC and mPPC – are important for understanding self and others (Northoff, Qin, & Feinberg, 2011; Uddin, Iacoboni, Lange, & Keenan, 2007). The rostral mPFC, including the anterior cingulate cortex (ACC), tends to be relatively more engaged during self understanding while the mPPC might be preferentially engaged for understanding others (Lombardo et al., 2010; Qin et al., 2012). Another region that plays a prominent role in thinking about someone else is the TPJ (Van Overwalle, 2009; Saxe, 2006). The involvement of these areas during social evaluative processing has been confirmed in children and adolescents. For children aged 7 to 10, it was found that activation of the rostral mPFC correlated positively with the extent of the self-reference effect, whereby trait words encoded for self are better recognized than trait words encoded for another social target, in this case participants’ mothers (Ray et al., 2009). This region was
also more active in 9 to 11 year olds when making social and academic self-appraisals versus other-appraisals, especially in comparison to adults (Pfeifer, Lieberman & Dapretto, 2007). Likewise, adolescents aged 11 to 14 showed stronger mPFC recruitment during self-appraisals than adults (Pfeifer et al., 2009). Longitudinal research of children measured at age 10 and age 13 indicated that, at both time points, activation of the mPFC, including ACC, and ventral striatum was stronger for self-appraisals. Concurrently, the mPPC, dorsal mPFC, lateral PFC and the TPJ were recruited more for other-appraisals (Pfeifer et al., 2013).

**Functional connectivity in the social brain**

The TPJ and cortical midline structures that play a role in social processing are part of the default mode network (DMN), which shows increased activation during rest (Gusnard & Raichle, 2001). Regions of the DMN are sparsely functionally connected in children but highly integrated during adulthood (Power, Fair, Schlaggar, & Petersen, 2010). Kelly and colleagues (2009) reported stronger functional connectivity between rostral ACC and mPPC from age 9 until age 24. In adults, it has been demonstrated that these regions are not only functionally connected in the resting state, but also during judgments about traits of self and others (Grigg & Grady, 2010). Coupling within the DMN was reduced when participants made trait evaluations of self compared to trait evaluations of others, while connectivity between the DMN and areas outside of the network was increased (Van Buuren, Gladwin, Zandbelt, Kahn, & Vink, 2010). Another study found similar functional connectivity of the mPFC, mPPC and TPJ with lower-level regions, including the insula and motor-related areas, when judging mental states of self as well as others (Lombardo et al., 2010). As of yet, little is known about coupling between brain areas during social appraisals in developmental samples.

**Development of task-related functional connectivity**

The few studies that have examined changes in task-related functional connectivity with age utilized emotional paradigms. For example, adolescents showed more interaction between mPFC and TPJ/superior temporal sulcus (STS) than adults.
during understanding of social emotions compared to basic emotions (Burnett & Blakemore, 2009). The mPFC was less connected to the left thalamus in adolescents than in adults when processing faces with emotional expressions that were congruent with prior expectations (Barbalat, Bazargani, & Blakemore, 2013). In longitudinal research with 10 to 13 year olds, connectivity of the TPJ was assessed during the observation of angry and neutral hand actions (Shaw, Grosbras, Leonard, Pike, & Paus, 2011). It was found that coupling between the TPJ and the insula, lateral PFC as well as the temporal poles was increased for angry versus neutral stimuli, particularly in boys at age 13. Together, these findings suggest that social-emotional brain networks develop throughout adolescence.

**Rationale for the current study**

This longitudinal study investigates functional connectivity during understanding of self and others between late childhood and early adolescence. To our knowledge, we are the first to focus on the interaction between brain regions during social appraisals in this developmental period. Children performed a task involving appraisals of self and a fictional other, Harry Potter, at age 10 as well as age 13. The current research follows up on previous results that indicated stable activation over time in mPFC, particularly during self-appraisals, and mPPC, especially for other-appraisals (Pfeifer et al., 2013). Our hypothesis was that these regions would work in parallel with other social brain areas, such as the TPJ, on this task. Furthermore, we expected that the mPFC might show increased functional connectivity with DMN areas for self-appraisals over time, while the mPPC might show increased connectivity with nodes of the DMN during other-appraisals.

**Methods**

**Participants**

Twenty-seven children (18 girls, 9 boys) participated in this longitudinal fMRI study. They were on average 10.1 years old (SD = 0.35, range = 9.5 – 10.6 years)
Connectivity changes during early adolescence
during the first measurement (T1) and 13.1 years old (SD = 0.33, range = 12.6 – 13.9 years) during the second measurement (T2). Participants had no history of medical, psychiatric or neurological disorders. Written informed consent was obtained from the parents according to guidelines of the UCLA Institutional Review Board.

Procedure

In the fMRI scanner, participants heard short phrases from the social domain (e.g., ‘I have many friends’) or the academic domain (e.g., ‘I like going to the library’). The task was to indicate by button press whether the phrases described the Self (Yes or No) and a familiar fictional Other, Harry Potter (for a complete description, see Pfeifer et al., 2007). There were four blocks which were counterbalanced across participants. Each block contained 20 phrases from either the social or academic domain. Target (Self or Other) was alternated, such that the first block was followed by a block with the same phrases applied to a different target. The last two blocks included the phrases from a different domain applied to Self and Other in the same order as the first blocks. Phrases were presented every 3 seconds. Each block also contained five null events. Between blocks, there was a rest period of 21 seconds. The phrases were preceded by task instructions.

Data acquisition

fMRI images were acquired on a Siemens Allegra 3-Tesla scanner using a T2*-weighted gradient-echo sequence (TR = 3000 ms, TE = 25 ms, flip angle = 90°, matrix size 64 x 64, FOV = 20 cm, 3.125-mm in-plane resolution, 3-mm thick). Coplanar with the functional scans, a high-resolution structural echo-planar imaging volume was acquired (TR = 5000 ms, TE = 33 ms, matrix size 128 x 128, FOV = 20 cm, 1.56-mm in-plane resolution, 3-mm thick).

Data analysis
Dicom files were converted to fMRI data in nifti format with MRIClonevert (http://lcni.uoregon.edu/~jolinda/MRIClonevert/). The images were skull-stripped using the Brain Extraction Tool of FSL (http://www.fmrib.ox.ac.uk/analysis/research/bet). Next, bad slices were detected and fixed in ARTrepair (http://cibs r.stanford.edu/tools/human-brain-project/artrepair-software.html). The structural images were reoriented to the AC-PC line.

Preprocessing was carried out in NeuroElf (http://neuroelf.net). First, structural images were coregistered to the SPM T1 template. Functional images were realigned to correct for head motion after which these were coregistered to the structural images. Then, structural images were segmented based on the SPM template tissue probability maps and the segmentation parameters were used to normalize functional images into a Talairach-compatible atlas. Finally, the functional images were spatially smoothed using a 6-mm full-width, half-maximum (FWHM) isotropic Gaussian kernel.

Statistical Parametric Mapping (SPM8; Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK; www.fil.ion.ucl.ac.uk/spm) was used to analyze the fMRI data. For each participant, the General Linear Model (GLM) was applied to estimate condition effects. The conditions (Self Social, Other Social, Self Academic and Other Academic) were convolved with a canonical hemodynamic response function. Global scaling was used to remove low-frequency drifts and motion parameters were included as regressors of no interest. T1 and T2 were defined as two separate runs. Resulting contrast images were entered into group-level analyses. A 2 x 2 x 2 Analysis of Variance (ANOVA), with factors Target (Self and Other), Domain (Social and Academic) and Age (T1 and T2), as well as paired t-tests were performed.

The main effect of Target ($p < 0.001$) was calculated to determine areas that were differentially active for Self and Other, independent of domain and stable over time. As described by Pfeifer and colleagues (2013), the mPFC (MNI coordinates: -3 36 6, $k = 259$) was more active during Self compared to Other, while the mPPC (MNI coordinates: 9 -51 15, $k = 368$) showed stronger activation for Other than Self. These clusters were used as seed regions for psychophysiological interaction (PPI) analyses (Friston et al., 1997). PPI analyses were conducted to investigate functional
connectivity that was stable over time as well as connectivity changes from T1 to T2 for Self- and Other-appraisals.

The mean timecourses of the mPFC and mPPC were extracted at T1 and T2 for each participant. Timecourses were multiplied with the variable Self and the variable Other (collapsed across the Social and Academic domain). This resulted in two PPI variables for each seed region: the interaction between a physiological variable, which is the region’s timecourse, and a psychological variable, Self or Other. For the mPFC as well as the mPPC, a first-level model was created containing the timecourse, the variable Self, the variable Other, the PPI variable for Self and the PPI variable for Other as regressors. Motion parameters were included as nuisance variables and T1 and T2 were modeled as two separate runs. Contrast images were entered into second-level analyses to examine the main effect of Target (Self and Other) and the interaction effect between Target and Age (T1 and T2). T-tests were performed to find areas that showed connectivity with the seed regions for Self > Other and Other > Self. Stable connectivity as well as changes over time were explored. To interrogate the interaction effects, mean parameter estimates were extracted for Self and Other at T1 and T2 using MarsBaR (http://marsbar.sourceforge.net). The analyses were thresholded at $p < 0.005$, uncorrected with a cluster size of 20 (Lieberman & Cunningham, 2009).

<table>
<thead>
<tr>
<th>Region</th>
<th>$x$</th>
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<tbody>
<tr>
<td><strong>Self &gt; Other</strong></td>
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<td>No significant clusters</td>
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<td><strong>Other &gt; Self</strong></td>
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<tr>
<td>Right superior frontal gyrus</td>
<td>21</td>
<td>-3</td>
<td>69</td>
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<td>-15</td>
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</tr>
<tr>
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<td>3</td>
<td>69</td>
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<td>45</td>
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<tr>
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<td>0</td>
<td>3.64</td>
<td>31</td>
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<tr>
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<td>-57</td>
<td>6</td>
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<td>38</td>
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<tr>
<td>Left superior occipital cortex</td>
<td>-12</td>
<td>-69</td>
<td>39</td>
<td>3.31</td>
<td>22</td>
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**Table 1.** Functional connectivity of medial prefrontal cortex that was stable over T1 and T2.

**Results**

**Stable connectivity across age**
The first PPI analyses focused on characterizing patterns of functional connectivity with the mPFC and mPPC during appraisals of Other and Self that were stable over time. For the mPFC seed region, no areas showed stronger connectivity for Self > Other. Meanwhile, stronger connectivity for Other > Self was observed with the ventral mPFC, left superior temporal sulcus as well as frontal and occipital regions outside of the DMN (see Table 1).

The mPPC showed stronger connectivity with several areas for Self > Other (see Table 2). These areas included the mPFC, encompassing rostral ACC, and left TPJ. A cluster in the posterior cingulate cortex (PCC), which was anterior to the seed region, also showed more connectivity with the seed region for Self > Other. There were no areas that showed stronger connectivity with the mPPC for Other > Self at both timepoints.

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<tr>
<th>Region</th>
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<tr>
<td><strong>Self &gt; Other</strong></td>
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<tr>
<td>Medial prefrontal cortex</td>
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<td>Right pallidum</td>
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<td>-3</td>
<td>3.61</td>
<td>27</td>
</tr>
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<td>3.10</td>
<td>28</td>
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<tr>
<td><strong>Other &gt; Self</strong></td>
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<td>No significant clusters</td>
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**Connectivity changes over time**

Next, PPI analyses were carried out to examine whether task-dependent functional connectivity during appraisals changed with age. No increases or decreases in connectivity over time were found for the mPFC seed region. For the mPPC (Figure 1A), there was a significant interaction between Target (Other versus Self) and Age (T2 versus T1) in three clusters: left TPJ (MNI coordinates: -39 -63 42, $t = 3.38$, $k = 56$), right TPJ (MNI coordinates: 48, -63, 33, $t = 3.31$, $k = 30$), and left thalamus (MNI coordinates: -18 -15 15, $t = 3.47$, $k = 28$). These areas are displayed in Figure 1B.
Connectivity changes during early adolescence

Figure 1C illustrates the change in mean parameter estimates from T1 to T2 for the left TPJ. The change was significant for Other \((t = 3.28, p < 0.01, df = 26)\) but not for Self \((t = -0.87, p = 0.40, df = 26)\). A similar pattern was found for the right TPJ (Other: \(t = 2.12, p < 0.05, df = 26\); Self: \(t = -1.00, p = 0.33, df = 26\) and the left thalamus (Other: \(t = 3.12, p < 0.01, df = 26\); Self: \(t = -0.65, p = 0.52, df = 26\)). This indicates that functional connectivity between mPPC and these regions increases from age 10 to age 13 during Other-appraisals.

Discussion

Prior work has demonstrated the involvement of cortical midline structures – mPFC and mPPC – during self- and other-understanding throughout adolescence
(Pfeifer et al., 2009, 2013; Pfeifer, Lieberman, & Dapretto, 2007; Ray et al., 2009; Veroude, Jolles, Croiset, & Krabbendam, 2013). In the current longitudinal fMRI study, we investigated for the first time how these regions work together with the rest of the brain to facilitate social evaluations during the transition from late childhood to early adolescence. The mPFC showed stronger coupling with several areas for other-appraisals compared to self-appraisals at age 10 as well as age 13, while the reverse was true for the mPPC. Moreover, our results suggest that there are important within-subject changes in mPPC connectivity supporting appraisals of a distant other between age 10 and age 13.

**Developmental increases in functional connectivity**

We observed increased functional connectivity between the mPPC and TPJ for other-appraisals over time. Previous research found that the mPPC is crucial for understanding others in adults as well as in children and adolescents (Pfeifer & Peake, 2012; Qin et al., 2012). Meanwhile, the TPJ has been implicated in distinguishing between self and someone else (Decety & Sommerville, 2003) and reasoning about another’s mind (Saxe & Kanwisher, 2003). A recent meta-analysis indicated that activation of TPJ on social-cognitive reasoning tasks either increases with age or shows ‘adolescent transitions’, meaning that the pattern seen in adolescents differs from that in children and adults (Crone & Dahl, 2012). Connectivity between the mPPC and TPJ during social-emotional processing has been observed in 13 year olds (Shaw et al., 2011) and adults (Atique, Erb, Gharabaghi, Grodd, & Anders, 2011). Here, we report a change in functional connectivity from age 10 to age 13 for appraisals of other. This may ultimately be related to the development of more mature responses in TPJ.

**Social changes during early adolescence**

Increased functional connectivity with age for understanding others might be related to changes in the social environment. During the transitional period from childhood to adolescence, relationships with peers become especially important. More time is spent with friends (Larson & Richards, 1991) and the ability to take
another person’s perspective improves (Choudhury, Blakemore, & Charman, 2006). The mPPC and TPJ, which play a prominent role in social understanding (Van Overwalle & Baetens, 2009), seem to increasingly work together during this life stage. Notably, developmental changes in functional connectivity of mPPC were observed in bilateral TPJ and left thalamus only. Another cluster in left TPJ was found to be more connected to mPPC during self-appraisals at both time points. However, the area that showed increased connectivity with mPPC for other-appraisals was slightly posterior to this cluster and extended medially.

Stable functional connectivity for social appraisals

The mPPC was more connected to the mPFC for self- compared to other-appraisals at age 10 as well as age 13. At the same time, the mPFC seed region showed stronger coupling with several areas during other- versus self-appraisals. These areas included the ventral mPFC and STS, which are part of the DMN and are involved in social understanding (Spreng, Mar, & Kim, 2008). Thus, the mPFC is less activated during other- than self-appraisals (Pfeifer et al., 2013), but connected more to the rest of the brain in order to achieve evaluative processes of other. Functional connectivity of the mPFC did not change over time, suggesting this is stable between late childhood and early adolescence.

Limitations and future directions

The transition from childhood to adolescence is marked by biological and social changes (Nelson, Leibenluft, McClure, & Pine, 2005). The reported functional connectivity increases as well as the stable effects might be typical for this transitional phase. However, it could be expected that development of functional connectivity continues over the course of adolescence and into adulthood. The current study did not include a group of older adolescents or adults, therefore it is unclear whether the observed patterns extend after the age of 13. Consequently, it would be interesting to follow children over a longer period to gain more insight into longitudinal functional connectivity changes.
Increases in mPPC connectivity during other-appraisals might be explained by environmental changes, such as the start of middle school which is accompanied by new peer relations. Meanwhile, it is known that the cortex undergoes significant anatomical maturation between childhood and early adolescence (Giedd & Rapoport, 2010; Shaw et al., 2008; Toga, Thompson, & Sowell, 2006). Surface area of the TPJ shows a peak during this time (Mills, Lalonde, Clasen, Giedd, & Blakemore, 2012). Structural brain development may be related to functional changes in coupling between regions. Unfortunately, we cannot distinguish between age-related biological effects or effects of social transitions on task-related connectivity increases. Future neuroimaging research might shed light on this issue by concurrently examining functional and structural maturation.

Conclusions

We demonstrated that the mPPC and bilateral TPJ increasingly work together during other-appraisals from childhood to adolescence. Connectivity of mPPC and mPFC with different areas was stable at age 10 and age 13. Functional changes in these regions may occur before or after the particular age range studied here. In summary, these results indicate that changes in mPPC coupling take place during a developmental phase in which social relations become particularly salient. Our findings underline the value of using a longitudinal design and functional connectivity analyses to advance the field of developmental neuroscience.

References


Connectivity changes during early adolescence


