The effect of perspective and content on brain activation during mentalizing in young females

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Abstract

In the present fMRI study, we investigated the role of different brain regions in separate aspects of mentalizing. Young females aged 18-19 were asked to imagine a social situation and answer a question. Perspective, self and other, as well as content, emotion and behavior, were varied. Activation was observed in the left precuneus, left temporoparietal junction, left medial prefrontal cortex and left middle temporal gyrus. Left precuneus and left temporoparietal junction were recruited more when taking the perspective of other compared to self. Medial prefrontal areas might be more involved during mentalizing about emotion versus baseline than behavior versus baseline.
Introduction

A core aspect of social cognition is the ability to predict emotional and behavioral responses to a situation, either from one’s own or another person’s perspective. This requires ‘theory of mind’, originally defined as the attribution of mental states to oneself and to others (Premack & Woodruff, 1978), also referred to as ‘mentalizing’ (Frith & Frith, 1999). The capacity to internally represent situations already starts to develop during the second year of life, when infants engage in pretend play (Leslie, 1987). Pioneer work of Wimmer and Perner (1983) suggested that children between the ages 4 and 6 learn that another person can have a ‘false belief’, which is often illustrated by the following example. ‘Maxi puts chocolate in the blue cupboard and leaves the room. His mother replaces the chocolate to the green cupboard. Where will Maxi search for the chocolate when he returns?’ Children age 3.5 – 4 years give the correct answer that Maxi will look in the blue cupboard. Recent research, using a visual detection task instead of verbal responses, indicates that even 7-month-olds are able to encode others’ beliefs (Kovács, Téglás, & Endress, 2010). Despite the elementary presence of belief understanding in young children, mentalizing continues to improve until the age of 18. This was shown by increased accuracy between adolescence and adulthood on a task requiring online mentalizing processes (Dumontheil, Apperly, & Blakemore, 2010). Adolescents between 14 and 18 made more errors than adults when moving objects, taking less often into account the perspective of a director who could not see all the objects.

Different neuroimaging paradigms, such as understanding characters in stories or cartoons, have been used to identify brain regions which are important for mentalizing (Fletcher et al., 1995; Gallagher et al., 2000). A meta-analysis revealed the precuneus, the temporoparietal junction and medial prefrontal cortex as areas involved in making inferences about goals, beliefs or moral issues (Van Overwalle & Baetens, 2009). However, mentalizing is a complex process and regions might be differentially activated depending on specific aspects of mentalizing. A crucial distinction may be ‘perspective’, e.g., one can attribute mental states to self or other. In addition, mentalizing can vary according to ‘content’, an important distinction likely being whether one attributes mental states to make predictions about emotion or behavior (Atique, Erb, Gharabaghi, Grodd & Anders, 2011).
Previous research, aimed at elucidating the role of different brain areas in these separate aspects of mentalizing, has provided inconsistent results. Vogeley and colleagues (2001) compared neural activation during mentalizing from the perspective of self and other. Both conditions activated the medial prefrontal cortex. Stronger activation during mentalizing of self was observed in the right temporoparietal junction and bilateral precuneus. In contrast, Ruby and Decety (2004) demonstrated more activation in temporoparietal junction and precuneus as well as the medial prefrontal cortex and left temporal pole during mentalizing of other compared to self. A comparison between mentalizing of self and other in individual participants showed overlapping and non-overlapping areas (Saxe, Moran, Scholz, & Gabrieli, 2006). During the ‘theory of mind’ condition, stories including false beliefs were presented and participants had to answer questions about the situations. In the ‘self reflection’ condition, participants read trait adjectives and indicated whether the words applied to themselves. Both conditions activated the medial prefrontal cortex and the precuneus, while the temporoparietal junction was only activated during theory of mind. On the other hand, there is evidence that the medial prefrontal cortex is selective for making trait adjective judgments about self compared to a close other (Heatherton et al., 2006). Lombardo and colleagues (2010) asked participants to judge ‘mentalizing’ or ‘physical’ statements about self and a familiar other. The researchers observed overlapping neural representations and functional connectivity patterns in medial prefrontal cortex, precuneus and temporoparietal junction. Thus, although the same regions have been found consistently during mentalizing, the effect of perspective on activation in these areas remains unclear.

Contradicting findings of previous studies might be due to heterogeneity of participants with regard to age and sex. It has been shown that the role of brain regions in mentalizing changes with development. Dosch and colleagues (2010) showed that adults activated the precuneus and left temporoparietal junction during the perspective of other compared to self. Children aged 8 to 10 also activated the right temporoparietal junction and dorsolateral prefrontal cortex. Adolescents between 12 and 18 years activated the medial prefrontal cortex more while adults activated temporal areas more when thinking about intentions (Blakemore, den Ouden, Choudhury, & Frith, 2007). This indicates that the recruitment of brain
regions used for mentalizing depends on age. In most research, all participants above 18 years old are grouped together as adults. However, structural maturation of the cortex continues until the early 20s (Giedd, 2004; Gogtay et al., 2004), so there might be individual differences within this group. Therefore, in the present study we used a homogeneous sample of 18 and 19 year olds. An effect of sex on brain activation during mentalizing has also been observed. Males compared to females showed stronger involvement of the medial prefrontal cortex in taking the perspective of a human game partner during a ‘prisoner’s dilemma’ (Krach et al., 2009). In addition, brain development during childhood and adolescence is delayed in males compared to females (De Bellis et al., 2001; Giedd, 2008), thus it is difficult to compare an 18-year-old male with an 18-year-old female. To control for this type of variation between participants, we included females only, while others have used males (Lombardo et al., 2010; Ruby & Decety, 2004; Vogeley et al., 2001). Furthermore, our sample consisted solely of first-year students in Medical School.

A variety of tasks have been applied to investigate mentalizing. Some studies focus on traits (Heatherton et al., 2006; Saxe et al., 2006) while we look at responses to a situation. We also distinguish between different content of mentalizing, e.g., whether inferences are made about what one would feel in a situation or what one would do. Research has demonstrated that the ventromedial prefrontal cortex is especially important for mentalizing about emotion (Hynes, Baird, & Grafton, 2006; Sebastian et al., 2012). The dorsolateral prefrontal cortex appears to be necessary for mentalizing about cognition, e.g., attributing beliefs and knowledge (Kalbe et al., 2010; Shamay-Tsoory & Aharon-Peretz, 2007). Little is known about which brain regions are specialized for predicting upcoming behavior. Atique and colleagues (2011) found activation in different subparts of the temporoparietal junction when comparing mentalizing about emotion and behavior. However, they considered only the perspective of other and not the perspective of self.

The present study aimed to further investigate brain activation during separate aspects of mentalizing by varying perspective as well as content. Participants were presented with real-life scenarios and asked to imagine the situation and answer a corresponding question. The questions were formulated from the perspective of self or other and pertained to either an emotional or behavioral response to the situations. Based on previous research, we expected...
involvement of the precuneus, temporoparietal junction and the medial prefrontal cortex. Our main goal was to test whether activation in these areas differed based on perspective. In addition, we explored the effect of content.

**Methods**

*Participants and procedure*

A total of 25 right-handed female first-year students (Mean age = 19.06, Age range = 18.17-19.93) from Maastricht University Medical School participated in this study. The participants completed three sessions of 4.5 hours in total. A training session served to practice the experimental tasks using a mock scanner. In addition, questionnaires and neuropsychological tests were administered. In the second session, a mentalizing task was performed in the fMRI scanner. An fMRI gambling paradigm was carried out in the third session, the results of which will be described in another paper.

All volunteers had normal or corrected-to-normal vision and no hearing problems. None had any history of neurological or psychiatric disorders. No clinical behavioral problems were present as indicated by scores below 63 (Mean score = 43.96, Score range = 31-62) on the total scale of the Adult Self Report (Achenbach & Rescorla, 2003). Mean estimation of verbal IQ was 110.12 (SD = 4.54) measured by the Peabody Picture Vocabulary Test-III-NL (Schlichting, 2005). Mean estimation of non-verbal IQ was 120.56 (SD = 3.40) on the Raven Progressive Matrices (Raven, Raven, & Court, 1998). The volunteers gave written informed consent prior to the study and received an exchange voucher for their participation. This research was approved by the Ethical Committee Psychology of Maastricht University.

*Experimental paradigm*

The mentalizing task required participants to think about a social situation and a following question. There were 20 positive situations, e.g., ‘Next week the summer break starts’ and 20 negative situations, e.g., ‘A man is noisy in the cinema’. For each
situation, five questions were formulated, corresponding to four experimental conditions and the baseline. Each situation was presented five times followed by a different question.

The conditions included Emotion Self, e.g., ‘A man is noisy in the cinema. Do you feel uncomfortable?’, Emotion Other, e.g., ‘A man is noisy in the cinema. Does your friend feel uncomfortable?’, Behavior Self, e.g., ‘A man is noisy in the cinema. Do you therefore change seats?’ and Behavior Other, e.g., ‘A man is noisy in the cinema. Does your friend change seats?’ In conditions involving other, several persons were used, e.g., friend, mother, neighbor or saleslady. Yes or no answers were provided by button press. The average number of syllables per question did not significantly differ between the experimental conditions. The baseline condition consisted of a situation and a question asking to press left or right, to control for reading processes and motor responses. In addition, 66 situations without a question as well as 50 dummy events showing only a fixation cross were used as filler items.

The task consisted of two runs, both including 158 randomly presented items in an event-related design. One run lasted approximately 20 minutes depending on individual reaction times. In each run, the first situation was presented after 6000 ms (TR = 3) and the first question after 8000 ms (TR = 4). The next situation appeared when the subject had pressed a button with an interstimulus interval varying between 500 – 3500 ms, in steps of 500 ms. Maximum response time was set to 7000 ms, after which the task continued.

Data acquisition

Data acquisition was performed on a 3T head-only Allegra scanner (Siemens, Erlangen, Germany) with a T2*-weighted EPI sequence (TR = 2000 ms, TE = 30 ms, flip angle = 90°, FOV = 224 mm, number of slices = 32, voxel size = 3.5 x 3.5 x 4 mm). A T1-weighted anatomical scan was acquired to aid with spatial normalization (TR = 2250 ms, TE = 2.6 ms, flip angle = 9°, FOV = 256 mm, number of slices = 192, voxel size = 1 x 1 x 1 mm).
**Behavioral data analysis**

Yes or no responses and reaction times were recorded. There were no correct answers, therefore yes or no responses were not analyzed. Reaction times of the experimental conditions were normally distributed. To test if the average reaction times over all four experimental conditions differed from baseline, a t-test was carried out (threshold $p < 0.05$).

Repeated measures Analysis of Variance (ANOVA) including reaction times as a dependent variable and within-subject factors Perspective (Self versus Other) and Content (Emotion versus Behavior) was conducted to test for main effects and an interaction effect (threshold $p < 0.05$).

**fMRI data analysis**

Statistical Parametric Mapping (SPM8, www.fil.ion.ucl.ac.uk/spm) was used for analyzing the fMRI data. Preprocessing of the data consisted of the following steps. The images were corrected for slice timing and then realigned to correct for head motion using a six-parameter rigid body transformation. The images were coregistered with the anatomical scan and normalized to a T1 template. Spatial smoothing was carried out using a 7-mm full width at half maximum (FWHM) isotropic Gaussian kernel.

At the first-level, a General Linear Model (GLM) was applied for statistical analyses. A design matrix was specified and onsets of all situations as well as onsets of questions for Emotion Self, Emotion Other, Behavior Self, Behavior Other and baseline were entered. The events were convolved with a canonical hemodynamic response function. Motion parameters were included as covariates of no interest.

For each participant, the experimental conditions (Emotion Self, Emotion Other, Behavior Self, Behavior Other) were pooled together and contrasted with baseline to test which brain regions were activated during mentalizing. Additionally, main effects of Perspective (Self versus Other) and Content (Emotion versus Behavior) as well as the interaction effect between Perspective and Content were calculated. The resulting contrast images were entered into second-level analyses. One tailed t-tests, with participants as random effects, were conducted.
Comparisons were thresholded at $p < 0.05$, Family Wise Error rate (FWE) corrected with a minimum cluster of 3 voxels. If no significant results were found, a less conservative threshold of False Discovery Rate (FDR), $p < 0.05$ was applied. For significant effects, a voxel-wise multiple regression analysis (FWE corrected, $p < 0.05$, $k = 3$) was performed to see if differences in brain activation could be explained by differences in reaction times.

**Results**

**Behavioral results**

A t-test comparing the average reaction times pooled across the four experimental conditions (Mean = 2905.89 ms, SD = 795.26 ms) versus baseline (Mean = 1177.35 ms, SD = 344.84 ms) showed a significant result ($t(24) = 12.12$, $SE = 142.64$, $p < 0.001$). This indicates that answering a yes or no question about a social situation took more time than only pressing a left or right button.

In the 2 x 2 ANOVA, there was a significant main effect of Perspective, $F(1, 24) = 44.57$, $MSE = 21275.90$, $p < 0.001$, involving longer reaction times for questions about Other (Mean = 3003.26 ms, SD = 163.38 ms) compared to Self (Mean = 2808.51 ms, SD = 155.97 ms). In addition, there was a significant main effect of Content, $F(1, 24) = 25.69$, $MSE = 15691.55$, $p < 0.001$, with longer reaction times for Behavior questions (Mean = 2969.37 ms, SD = 158.22 ms) than Emotion questions (Mean = 2842.40 ms, SD = 160.86 ms). No interaction effect between Perspective and Content was found, $F(1, 24) = 0.01$, $MSE = 15099.03$.

**fMRI results**

**Experimental conditions versus baseline**

To find the areas involved in mentalizing, a contrast of all four experimental conditions (Emotion Self, Emotion Other, Behavior Self, Behavior Other) versus baseline was calculated. This revealed activation in regions reported previously
Mentalizing in young females using comparable tasks. The largest cluster was found in the left precuneus. In addition, the left middle temporal gyrus, the left dorsomedial prefrontal cortex, left ventromedial prefrontal lobe and the left temporoparietal junction were activated (see Table 1).

**Table 1.** MNI coordinates for regions significantly activated in the experimental conditions versus Baseline (FWE corrected, \( p < 0.05, k = 3 \)).

<table>
<thead>
<tr>
<th>Peak of activation</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Z</th>
<th>k</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left precuneus</td>
<td>-7</td>
<td>-56</td>
<td>21</td>
<td>5.49</td>
<td>54</td>
</tr>
<tr>
<td>Left middle temporal gyrus</td>
<td>-63</td>
<td>-18</td>
<td>-18</td>
<td>5.12</td>
<td>10</td>
</tr>
<tr>
<td>Left dorsomedial prefrontal cortex</td>
<td>-4</td>
<td>60</td>
<td>35</td>
<td>5.05</td>
<td>7</td>
</tr>
<tr>
<td>Left ventromedial prefrontal cortex</td>
<td>-4</td>
<td>42</td>
<td>-18</td>
<td>4.92</td>
<td>13</td>
</tr>
<tr>
<td>Left temporoparietal junction</td>
<td>-49</td>
<td>-70</td>
<td>35</td>
<td>4.76</td>
<td>12</td>
</tr>
</tbody>
</table>

**Main effects and interaction effect**

A main effect of Perspective was found (see Figure 1). During Other versus Self, increased activation was observed in the left precuneus and the left temporoparietal junction. No regions were activated more during Self versus Other. To investigate if the stronger brain activation in the left precuneus and left temporoparietal junction was related to the longer reaction times for Other than Self, a voxel-wise multiple regression analysis was performed. This analysis showed that reaction times did not correlate with brain activation.

There was no main effect of Content and no interaction effect between Perspective and Content at both the FWE and FDR corrected level. Since Emotion versus Behavior and Behavior versus Emotion did not reveal any significant results and to make sure no effects were missed, we explored the contrasts Emotion versus Baseline as well as Behavior versus Baseline (FWE corrected, \( p < 0.05, k = 3 \)). During Emotion versus Baseline, activation was found in the left dorsomedial prefrontal cortex, the left precuneus, left ventromedial prefrontal cortex, the left middle temporal gyrus and the left temporoparietal junction. During Behavior versus Baseline, the left precuneus, left middle temporal gyrus and the left temporoparietal junction were activated (see Figure 2). Thus, it appears that left dorsomedial and ventromedial prefrontal regions are more involved in mentalizing.
about emotion than behavior, although this effect did not reach significance in the direct contrast.

**Figure 1.** Main effect of Perspective: increased activation during Other vs. Self in the precuneus (MNI coordinates: 0 -60 39, Z = 5.01) and left temporoparietal junction (MNI coordinates: -46 -70 35, Z = 4.34).

**Figure 2.** (A) Activation during Emotion versus Baseline in the left dorsomedial prefrontal cortex (MNI coordinates: -7 56 35, Z = 5.43), the left precuneus (MNI coordinates: -7 -56 25, Z = 5.38), the left ventromedial prefrontal cortex (MNI coordinates: -4 42 -18, Z = 5.25), the left middle temporal gyrus (MNI coordinates: -63 -18 -14, Z = 4.89) and left temporoparietal junction (MNI coordinates: -49 -70 35, Z = 4.48). (B) Activation during Behavior versus Baseline in the left precuneus (MNI coordinates: -7 -56 21, Z = 5.46), left middle temporal gyrus (MNI coordinates: -63 -18 -18, Z = 4.97) and left temporoparietal junction (MNI coordinates: -49 -70 35, Z = 4.89).
Discussion

Previous research has uncovered brain regions that are activated during mentalizing (Van Overwalle & Baetens, 2009). Nonetheless, the precise role of these areas remains unclear, which might be related to the fact that mentalizing includes several aspects. In addition, discrepancies between experiments may result from differences in age or sex of the participants. Our study adds to the existing literature by varying perspective, self and other, as well as content, emotion and behavior, in one task. This task was administered to a homogeneous group consisting of 18 and 19 year old female students in Medical School.

When contrasting all experimental conditions with baseline, we observed activation in regions known to be important for mentalizing, including the left precuneus, left temporoparietal junction and the left medial prefrontal cortex. Widely differing coordinates in the medial prefrontal cortex have been reported (Ochsner et al., 2005). Here we found two clusters, one in the left dorsomedial prefrontal cortex and one in the left ventromedial prefrontal lobe. According to Amodio & Frith (2006), the first area is specialized for mentalizing and knowledge of self and other while the latter is involved in reward processing. Both of these regions are part of the core mentalizing system as defined by Van Overwalle (2011). The left middle temporal gyrus, was also activated, consistent with another study (Brunet, Sarfati, Hardy-Bayle, & Decety, 2000). We did not find activation of the temporal poles, which has been demonstrated in some, but not all, mentalizing tasks (Frith & Frith, 2003). Thus, it appears that our task is relatively consistent with the literature, indicating that this is a valid measure to assess mentalizing.

The left precuneus and left temporoparietal junction were more involved during mentalizing of other compared to self. This is in accordance with several previous findings (Dosch et al., 2010; Ruby & Decety, 2004; Van Overwalle & Baetens, 2009). The temporoparietal junction has been identified as an area that is important for reasoning about the content of someone else’s mind (Saxe & Kanwisher, 2003). Cavanna and Trimble (2006) propose that taking the perspective of self and other both involve internal representation through mental imagery, which is a function of the precuneus. Thus, mentalizing of other results in stronger recruitment of brain regions that are activated during mentalizing of self. The
difference in brain activation could not be explained by differences in reaction times between the two conditions.

No effect of perspective on activation in the medial prefrontal cortex was observed. Heatherton and colleagues (2006) reported selective engagement of this area in making judgments about self compared to a close other. However, they looked at personal traits while our task was focused on responses to situations. There is also evidence for a differential role of the medial prefrontal cortex in mentalizing based on closeness of the other person (Jenkins, Macrae, & Mitchell, 2008; Krienen, Tu, & Buckner, 2010; Mitchell, Macrae, & Banaji, 2006). The ventral medial prefrontal cortex responds more to a similar other and the dorsal medial prefrontal cortex to a dissimilar other (Mitchell et al., 2006). Activation of the ventral medial prefrontal cortex during mentalizing about the self and a similar, but not dissimilar other, shows that people use ‘simulation’ for understanding others to whom they can relate (Jenkins et al., 2008). Krienen and colleagues (2010) showed that the effect in the ventral medial prefrontal cortex is driven by closeness as opposed to similarity. In the present paradigm, no distinction was made between close and non-close others because this was not the focus of our study.

We did not find a difference in brain activation when directly comparing mentalizing about emotion and behavior. Inspection of the contrasts Emotion versus Baseline and Behavior versus Baseline tentatively suggests that medial prefrontal areas are active during mentalizing about emotion but not during mentalizing about behavior. However, this result must be treated with caution since this effect was not significant in the direct contrast. Our finding is in line with previous studies which have demonstrated that specific regions of the prefrontal cortex are involved in different content of mentalizing (Hynes et al., 2006; Kalbe et al., 2010; Sebastian et al., 2012; Shamay-Tsoory & Aharon-Peretz, 2007). An analysis of fine-scale distribution of activity revealed that the anterior part of the temporoparietal junction is more active during mentalizing about emotion and a more posterior area during mentalizing about behavior (Atique et al., 2011), but there was also a large amount of overlap. In the present study we found a similar peak of activation in the temporoparietal junction during mentalizing about emotion and mentalizing about behavior. Imagining a situation and predicting a
behavioral response might automatically evoke feelings as well, which could explain why there was no large effect of content.

A limitation of our task was that we could not control whether participants were actually imagining the situations, since no accuracy data are available for this type of paradigm. However, reaction times were longer for the experimental conditions compared to baseline, which indicates that the participants were thinking about the questions and not merely pressing a button.

To conclude, the present study demonstrates stronger activation of the left precuneus and the left temporoparietal junction for the perspective of other compared to self. The left dorsomedial and ventromedial prefrontal cortex appear to be more involved in mentalizing about emotion than behavior. We have shown this with a task that separates different aspects of mentalizing, which was performed by a homogeneous sample of young females aged 18 and 19. Our findings suggest that the left precuneus and left temporoparietal junction play a role in imagining the perspective of someone else. The left dorsomedial and ventromedial prefrontal cortex might be especially important for predicting an emotional response to a social situation.

References


Mentalizing in young females


