

Neurodevelopmental changes of reading the mind in the eyes

Bregtje Gunther Moor,^{1,2,3} Zdeňka A. Op de Macks,^{2,3} Berna Güroğlu,^{2,3} Serge A. R. B. Rombouts,^{2,3,4} Maurits W. Van der Molen,¹ and Eveline A. Crone^{1,2,3}

¹Department of Psychology, University of Amsterdam, Roetersstraat 15, 1018 WB Amsterdam, ²Institute of Psychology, Leiden University, Wassenaarseweg 52, 2333 AK Leiden, ³Leiden Institute for Brain and Cognition (LIBC), P.O. Box 9600, 2300 RC Leiden and ⁴Department of Radiology, Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, the Netherlands

The eyes provide important information for decoding the mental states of others. In this fMRI study we examined how reading the mind in the eyes develops across adolescence and we tested the developmental trajectories of brain regions involved in this basic perceptual mind-reading ability. Participants from three age groups (early adolescents, mid adolescents and young adults) participated in the study and performed an adapted version of the ‘Reading the Mind in the Eyes task’, in which photographs of the eye region of faces were presented. Behavioral results show that the ability to decode the feelings and thoughts of others from the eyes develops before early adolescence. For all ages, brain activity was found in the posterior superior temporal sulcus during reading the mind in the eyes relative to a control condition requiring age and gender judgments using the same eyes stimuli. Only early adolescents showed additional involvement of the medial prefrontal cortex, the inferior frontal gyrus and the temporal pole. The results are discussed in the light of recent findings on the development of the social brain network.

Keywords: fMRI; mind-reading; mentalizing; adolescence; brain development

INTRODUCTION

A key component of human social interactions is mentalizing, which refers to the ability to read and understand the mental states of others (Premack and Woodruff, 1978). The eyes are believed to play a key role in social interactions. Indeed, the eyes automatically capture attention and therefore convey a wealth of information important for social exchange (Langton *et al.*, 2000). Humans are well able to read the mental states of others solely from the eyes (Baron-Cohen *et al.*, 1997). In this study, we examine how mind-reading from the eyes develops across adolescence and we test the developmental changes in the neural correlates associated with this basic perceptual mind-reading ability.

Mind-reading from the eyes has previously been assessed with the ‘Reading the Mind in the Eyes task’, which requires participants to attribute the mental state of others from photographs of the eye region of faces (Baron-Cohen *et al.*, 1997). This task has been used mainly to distinguish between mind-reading skills of autistic and healthy developing individuals (e.g. Baron-Cohen *et al.*, 1997, 2001a; Kaland *et al.*, 2008), but has also been used to examine the neural correlates of mind-reading. Neuroimaging studies using this task

in adults reported that reading the mind in the eyes results in activation in the posterior superior temporal sulcus (pSTS) and the inferior frontal gyrus (IFG) (see Baron-Cohen *et al.*, 1999, 2006; Russell *et al.*, 2000; Adams *et al.*, 2009). The pSTS is believed to play an important role in extracting information about goals and intentions from the eyes and faces (e.g. Allison *et al.*, 2000; Gallagher and Frith, 2003; Carrington and Bailey, 2009), and in the detection of social stimuli (Nelson *et al.*, 2005). The IFG has previously been associated with the mirror neuron system and the assessment of facial expression of emotions (e.g. Frith and Frith, 1999; Rizzolatti and Craighero, 2004; Van Overwalle, 2009).

Developmental models on social information processing have proposed that brain regions involved in the basic perceptual processing of social stimuli develop early in childhood (i.e. the detection node, which involves the pSTS) (see SIPN model Nelson *et al.*, 2005). Indeed, young infants already display a sensitivity to social cues, such as the eyes and faces (e.g. Grossman *et al.*, 2008). These early signs of intention understanding are followed by an increase in explicit understanding of false beliefs which emerges around the ages 4–6 years (e.g. Wellman *et al.*, 2001; Miller, 2009). Recent studies show that mentalizing abilities continue to develop during adolescence (Blakemore, 2008; Güroğlu *et al.*, 2009; Dumontheil *et al.*, 2010). Evidence in support of protracted development of mentalizing comes largely from neuroimaging studies, which show that brain regions involved in more abstract reasoning about the mental states of others, such as the medial prefrontal cortex (mPFC),

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Correspondence should be addressed to Bregtje Gunther Moor, Department of Psychology, University of Amsterdam, Roetersstraat 15, 1018 WB, Amsterdam, the Netherlands. E-mail: b.gunthermoor@uva.nl.

undergo structural and functional changes during adolescence (Nelson *et al.*, 2005; Blakemore, 2008). It has been argued that basic social perceptual processes involved in mental state attribution, such as decoding intentions from the eyes and faces, lie at the foundation of subsequent mentalizing operations (e.g. Nelson *et al.*, 2005; Wellman and Brandone, 2009). To date, it is largely unknown whether these basic perceptual processes involved in mentalizing continue to develop across adolescence.

The goal of the current study was to chart the developmental trajectories of brain regions involved in perceptual mind-reading, by using a modified version of the 'Reading the Mind in the Eyes task' (Baron-Cohen *et al.*, 2001b). We obtained behavioral and fMRI data in participants of three age groups: 10- to 12-year-olds (early adolescents), 14- to 16-year-olds (mid adolescents) and 19- to 23-year-olds (young adults). The selection of these age groups enabled us to gain insights in the neural correlates in distinct phases across adolescent development. Besides the mental state condition in which participants were asked to select which of four words best described what the person in the photograph was feeling or thinking, the task included a control condition requiring age and gender judgments using the same eyes stimuli.

Based on previous behavioral studies showing that mentalizing abilities develop during early childhood (e.g. Wellman *et al.*, 2001), we predicted that children aged 10–12 year old would already perform well on the task (Baron-Cohen *et al.*, 2001b). In the fMRI analyses, we tested whether activation in the pSTS and the IFG, the two regions most consistently found using the 'Reading the Mind in the Eyes' task (Adams *et al.*, 2009), were sensitive to developmental changes. Findings from brain imaging allow us to test for differences between age groups which may not be observed at the behavioral level. Previous neuroimaging studies on social perception (i.e. biological motion, eye gaze) or mentalizing reported inconsistent results for developmental changes in the pSTS. Whereas some studies showed comparable activation patterns between children and adults (Mosconi *et al.*, 2005; Moriguchi *et al.*, 2007), others have found increased activity in the pSTS in adults (Blakemore *et al.*, 2007). In addition to the pSTS and the IFG, we tested for developmental changes in activity in other regions of the social brain network, including the mPFC and the temporal poles (Amodio and Frith, 2006; Blakemore, 2008). These regions were of special interest because prior studies have demonstrated protracted development of social brain regions during adolescence, especially in regions important for mentalizing (e.g. Blakemore, 2008; Pfeifer *et al.*, 2009; Saxe *et al.*, 2009).

METHODS

Participants

Fifty-five healthy right-handed volunteers were included in the study. Data of one additional participant (11-year-old

girl) was excluded from the analyses due to excessive head movement (>3 mm). To examine developmental changes in distinct phases of development, we recruited participants from three age groups: Nineteen 10- to 12-year-olds (early adolescence/pubertal; 11 female; mean age = 11.57, s.d. = 0.95), 16 14–16 year olds (mid adolescence/post-pubertal; 8 female; mean age = 15.74, s.d. = 0.75) and 20 19- to 23-year-olds (young adults; 11 female; mean age = 20.51, s.d. = 0.90). A chi-squared analysis showed no significant differences in gender distribution. For participants younger than 18 years a caregiver was asked to fill out the Child Behavior Checklist (CBCL; Achenbach, 1991) to confirm the absence of behavioral problems. All participants scored below clinical levels on all subscales. Participants and primary caregivers (for minors) gave informed consent for the study and received fixed payment for participation. All procedures were approved by the Medical Ethics Committee of the University Medical Center.

To assess pubertal development, a picture-based interview about puberty was administered in participants in the two youngest age groups (PBIP; Shirtcliff *et al.*, 2009). Results revealed a significant difference in puberty levels between participants aged 10–12 years ($M = 2.11$, s.d. = 0.81) and participants aged 14–16 year old [$M = 4.18$, s.d. = 0.62; $t(1, 33) = 70.1$, $P < 0.001$]. All participants completed the WAIS or WISC intelligence subscales similarities and block design (Wechsler, 1991, 1997). There were no significant differences in IQ between the different age groups, $F(2, 52) = 2.24$, $P > 0.1$.

Experimental task

All participants performed an adapted version of the child-version of the 'Reading the Mind in the Eyes task' (Baron-Cohen *et al.*, 2001b) in an event-related fMRI session. In this task, participants were presented with photographs of the eye region of faces. The task had two conditions, a mental state condition and an age/gender condition, which were presented in four blocks of 14 trials in an ABAB or BABA design (counterbalanced across participants). Twenty-eight different black-and-white photographs were used. Each photograph was used once in both task conditions, resulting in the presentation of 56 trials in total (2×28).

Both task conditions required participants to select one of the four simultaneously presented words that best described the photograph. In the mental state condition, participants were asked to select the word that best described what the person in the photograph was thinking or feeling. The mental state words included both basic emotions terms (i.e. angry) and other mental state terms (i.e. thinking about something) which were translated to Dutch by the help of native Dutch speakers (see Supplementary Data). The control condition involved age and gender judgments about the person depicted in the photograph. Participants were instructed to judge faces of 60-year olds or above as

'older', resulting in the following four response options: 'younger male', 'younger female', 'older male' or 'older female'. Since the age/gender condition always made use of the same four response options, the location of these phrases differed across trials. This was done to ensure that participants would read the phrases on each trial to increase comparability with the mental state condition in terms of reading requirements. An independent sample of 10 adults judged the age and gender of the faces using the same four response options. High levels of overlap between raters were reported for the gender judgments (25 faces 100%; 2 faces 88%; 1 face 67%). These judgments were comparable to the information provided in the manual of the original task (Baron-Cohen *et al.*, 2001b). For the age judgments, however, three faces obtained a more mixed pattern of judgments concerning the age of the person (overlap between raters approached 50%), while for the remaining 25 faces high overlap was found (22 faces 100%; 2 faces 88%; 1 face 78%). To obtain a sensitive index about the performance of the participants in the fMRI experiment, it was decided to qualify the three items with mixed scores as 'correct' in case participants correctly judged the gender of the faces, independent of their judgment about age.

Each trial started with a jittered fixation cross (between 600 and 8000 ms), followed by the presentation of the facial stimulus accompanied by four simultaneously presented words (Figure 1). The facial stimulus was presented for 9 s, but participants were required to give a response within an 8 s time window. Responses could be made by pressing a button with the index and middle fingers of both hands. The position of the response buttons mapped to the location of the four response options on the screen. Following the response, the word that was selected by the participant was underlined for the remaining length of the trial. If no response was observed within the specified time window, the text 'too slow' was presented for 1 s. This occurred on 1.29% and 0.39% of the trials of the mental state and the age/gender condition, respectively. During scanning, participants completed two runs of 28 trials and switched between conditions once during the run (e.g. AB-short break-AB). Both runs started with a short instruction display explaining

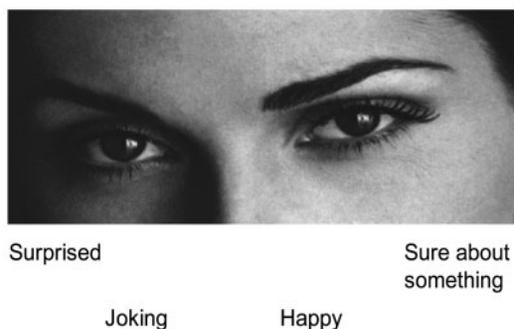


Fig. 1 Example trial of the Mental state condition of the 'Reading the Mind in the Eyes Task' (adopted from Baron-Cohen *et al.*, 2001b).

participants whether they would start with condition A or B. After 14 trials a display with the text 'SWITCH' was presented for 5 s to indicate the switch between task conditions.

Procedure

Prior to scanning, participants received eight practice trials and were asked to read a list of words containing the mental state terms used in the experiment to check whether they understood each word. Six 10- to 12-year olds did not understand one or two words, ensuring that the words were overall well known across participants. The unknown words were explained to the participants and trials containing these words were included in the analysis, except for those trials where participants gave an incorrect judgment. Therefore, incorrect judgments on trials during the fMRI experiment could not be due to a misunderstanding of words. Incorrect judgments on trials containing words previously rated as unknown occurred only in five trials for four 10- to 12-year olds (3 participants: 1 trial; 1 participant: 2 trials), resulting in the exclusion of a total of five trials across participants in the behavioral analyses.

Data acquisition

Prior to scanning, participants were familiarized with the scanner environment using a mock scanner. Scanning was performed using a 3.0-Tesla Philips Achieva scanner at the University Medical Center. Head motion was restricted using foam inserts that surrounded the head. Functional data were acquired using T2*-weighted Echo-Planar Images (EPI) (TR = 2.2 s, TE = 30 ms, slice-matrix = 80 × 80, FOV = 220, 35 2.75 mm transverse slices with 0.28 mm gap) during two functional runs of 156 volumes each. The first two volumes of each run were discarded to allow for equilibration of T1 saturation effects. After the functional scanning, high-resolution T2*-weighted images and high resolution T1 anatomical images were obtained.

fMRI data analysis

Data were analyzed using SPM5 (Wellcome Department of Cognitive Neurology, London, UK). Translational movement parameters never exceeded 1 voxel (<3 mm) in any direction for any subject or scan. Mean and maximum head movement was 0.11 and 2.52 mm for 10- to 12-year-olds, 0.08 and 2.25 mm for 14- to 16-year-olds and 0.08 and 2.11 mm for 19- to 23-year-olds. There were no group differences in average movement, $F(2, 52) = 1.34$, $P = 0.27$. Images were corrected for differences in timing of slice acquisition, followed by rigid body motion correction. Preprocessing further included normalization to EPI templates and spatial smoothing with an 8-mm full-width half-maximum Gaussian kernel. The normalization algorithm used a 12-parameter affine transformation together with a non-linear transformation involving cosine basic functions, and resampled the volumes to 3 mm cubic voxels.

Statistical analyses were performed on individual participants' data using the general linear model in SPM5. The fMRI time series data were modeled by a series of events convolved with a canonical hemodynamic response function (HRF). The onset of each facial stimulus was modeled as a separate event and were divided into two task conditions: mental state and age/gender condition. Participants' reaction times (RT) on each trial were used to fit the duration of the events. Both incorrect trials and trials on which the participants did not respond within the 8-s timeframe were not included in the contrasts of interest. The modeled events were used as covariates in a general linear model along with a basic set of cosine functions that high-pass filtered the data and a covariate for run effects. The least-squares parameter estimates of height of the best-fitting canonical HRF for each condition were used in pair-wise contrasts. At the group level, contrasts between conditions were computed by performing one-tailed *t*-tests, treating participants as a random effect.

We further performed voxelwise ANOVAs to identify regions that showed age-related differences in activation in relation to reading the mind in the eyes. A specific set of contrasts was used to test whether activation differed specifically in one age group relative to the other two groups (groups modeled as [2 -1 -1], [-1 2 -1], [-1 -1 2] and their inverse) in the mental state *vs* the age/gender comparison. In addition, we tested for linear age-related trends by performing regression analyses with age per individual as predictor. The MARSBAR toolbox for SPM5 (Brett *et al.*, 2002) was used to extract BOLD activity in functional regions of interest (ROIs) to visualize patterns of activation for different age groups in more detail. To ensure comparability with other developmental neuroimaging studies, task-related responses and age-related differences were considered significant if they consisted of at least 10 contiguous voxels that exceeded an uncorrected threshold of $P < 0.001$. We also examined whether results remained significant using FDR correction ($P < 0.05$, > 10 voxels) for multiple comparisons. All brain coordinates are reported in MNI atlas space.

RESULTS

Behavioral results

Performance was examined in terms of accuracy (quantified as the percentage of correct responses) and response time (RT) on correct trials. In Figure 2, mean percentages of correct responses and averaged RTs for each age group are presented (see also Supplementary Table 1). As can be seen in the figure, accuracy was generally lower and response times were longer for the mental state condition compared to the age/gender condition. In addition, it can be seen that all age groups performed above the chance level of accuracy (25%), showing that the ability to decode the feelings and thoughts of others from the eyes develops at a young age.

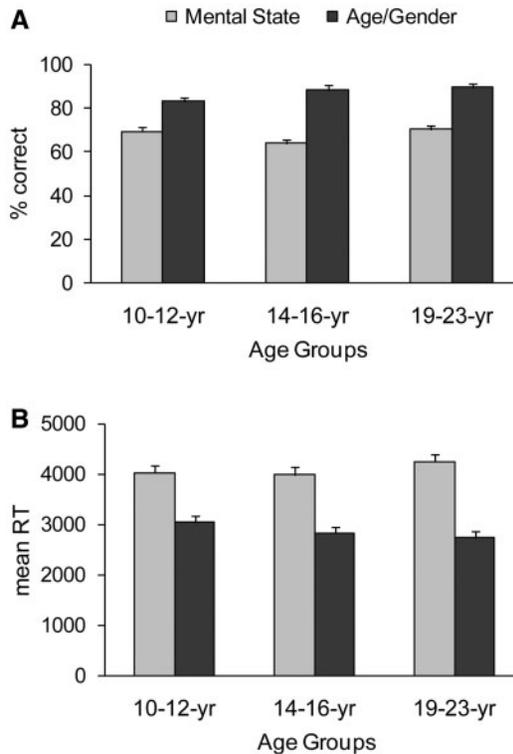


Fig. 2 Accuracy as indicated by the percentage of correct trials (A) and averaged response times for correct trials (B) for the Mental state and the Age/gender condition for each age group.

We submitted the percentages of correct responses to a repeated measures ANOVA with age group (10–12, 14–16, 19–23 years) as between subjects factor and condition (mental state, age/gender) as within subjects factor. This ANOVA confirmed that accuracy was higher for the age/gender condition, $F(1, 52) = 150.31$, $P < 0.001$. In addition, there was a significant interaction between condition \times age group, $F(2, 52) = 3.97$, $P < 0.05$, showing that the difference in accuracy between task conditions was less pronounced in 10- to 12-year-olds (Figure 2A). When comparing the age groups in each task condition separately, age-effects at trend level were found [mental state; $F(2, 52) = 3.03$, $P = 0.057$; age/gender; $F(2, 52) = 2.81$, $P = 0.069$]. *Post hoc* independent sample *t*-tests demonstrated that accuracy in the mental state condition was lower in 14- to 16-year-olds relative to adults ($P = 0.024$), whereas the other groups did not differ from each other. For the age/gender condition, a difference was found between 10- and 12-year-olds and adults ($P = 0.048$), suggesting an increase in accuracy with age.

A similar condition (mental state, age/gender) \times age group (10–12, 14–16, 19–23 years) ANOVA was performed for mean RTs on correct trials. There was no main effect of age ($P = 0.78$), but a main effect of condition [$F(1, 52) = 429.13$, $P < 0.001$], confirming that response times were longer for the mental state condition. In addition, there was a significant interaction between age group \times condition, $F(2, 52) = 7.64$,

$P=0.001$, showing that the difference in response times between both task conditions was most pronounced in 19- to 23-year-olds (Figure 2B). *Post hoc* analyses for each task condition separately revealed no significant differences in response times between age groups.

fMRI results

Brain regions involved in mental state attribution

First, brain regions were identified underlying reading the mind in the eyes across all participants. We performed a GLM analysis on the functional data modeled at the onset of each facial stimulus with individual RTs as durations of each trial, and computed a voxelwise contrast for the contrast mental state > age/gender condition. Replicating previous studies using this task, this analysis revealed robust activation in the bilateral pSTS, extending into the middle and superior temporal gyrus, and in the left IFG, extending into the anterior insula (Figure 3A) (Adams et al., 2009). In addition, activation was found in the right middle cingulate cortex, right insula, supplementary motor area (SMA) and left precentral gyrus ($P<0.001$, uncorrected). Activation in the bilateral pSTS, IFG, insula and SMA remained significant after FDR correction ($P<0.05$). The reversed contrast of age/gender > mental state condition resulted in activation in the right middle orbital gyrus, left superior frontal gyrus, right superior occipital gyrus and superior parietal lobe ($P<0.001$, uncorrected and $P<0.05$ FDR corrected). The significant clusters and corresponding MNI coordinates are reported in Supplementary Table 2.

Neural correlates of age-related differences in mental state attribution

The next question concerned the test of age-related differences in neural activation associated with reading the mind in the eyes. In Figure 3B, whole-brain results for the contrast

mental state > age/gender for each age group are presented. As can be seen in the figure, all age groups showed activity in the pSTS at the statistical threshold of $P<0.001$ (uncorrected). In addition, both the oldest and youngest age groups showed activity in the left IFG. For 10- to 12-year-olds these regions were also significant after FDR correction ($P<0.05$).

Age-related changes in brain activation were tested by ANOVAs with age group as between subjects factor on the contrast mental state > age/gender. No regions were found that showed a peak activity in 14- to 16-year-olds or adults. In contrast, the ANOVA testing for a peak in 10- to 12-year-olds [2 -1 -1] resulted in several clusters of activation including the ventral mPFC (peak at: 15, 54, 12, $z=4.12$; also significant after FDR correction, $P<0.05$), right ACC (peak at: 15, 39, -3, $z=3.67$), right temporal pole (peak at: 33, 12, -30, $z=3.96$; also significant after FDR correction, $P<0.05$), left IFG (peak at: -27, 33, -15, $z=3.72$), right IFG (peak at: 57, 21, 0, $z=3.71$) and right posterior insula (peak at: 39, -15, -6, $z=3.69$) (Figure 4A). All regions are listed in Supplementary Table 3. We created functional ROIs for the left IFG, vmPFC and right temporal pole to further visualize patterns of activation. Figure 4B shows that these brain regions were more engaged in the mental state condition compared to the age/gender condition in 10- to 12-year-olds. It should be noted that none of the comparisons resulted in significant age effects on pSTS activation.

Further age-related differences were tested by conducting regression analyses testing for linear effects with age on the contrast mental state > age/gender. Negative correlations between BOLD activity and age were found in the left IFG (peak at: -30, 30, -12, $z=3.52$), and the right temporal pole (peak at: 36, 9, -33, $z=3.47$). These regions overlap with the regions reported in the ANOVA testing for a peak in activity in 10- to 12-year-olds. All regions are listed in

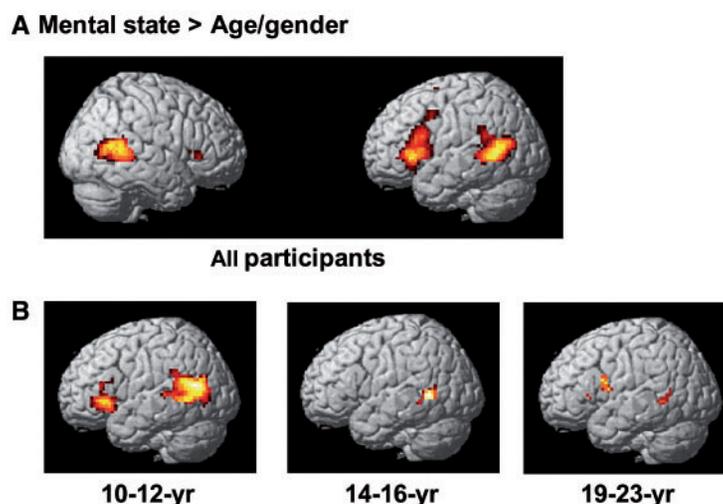


Fig. 3 Whole-brain results for the contrast Mental state > Age/gender at $P<0.001$ (uncorrected). Results averaged across all participants are presented in **A**. Results for 10- to 12-year-olds, 14- to 16-year-olds and 19- to 23-year-olds are presented in **B**.

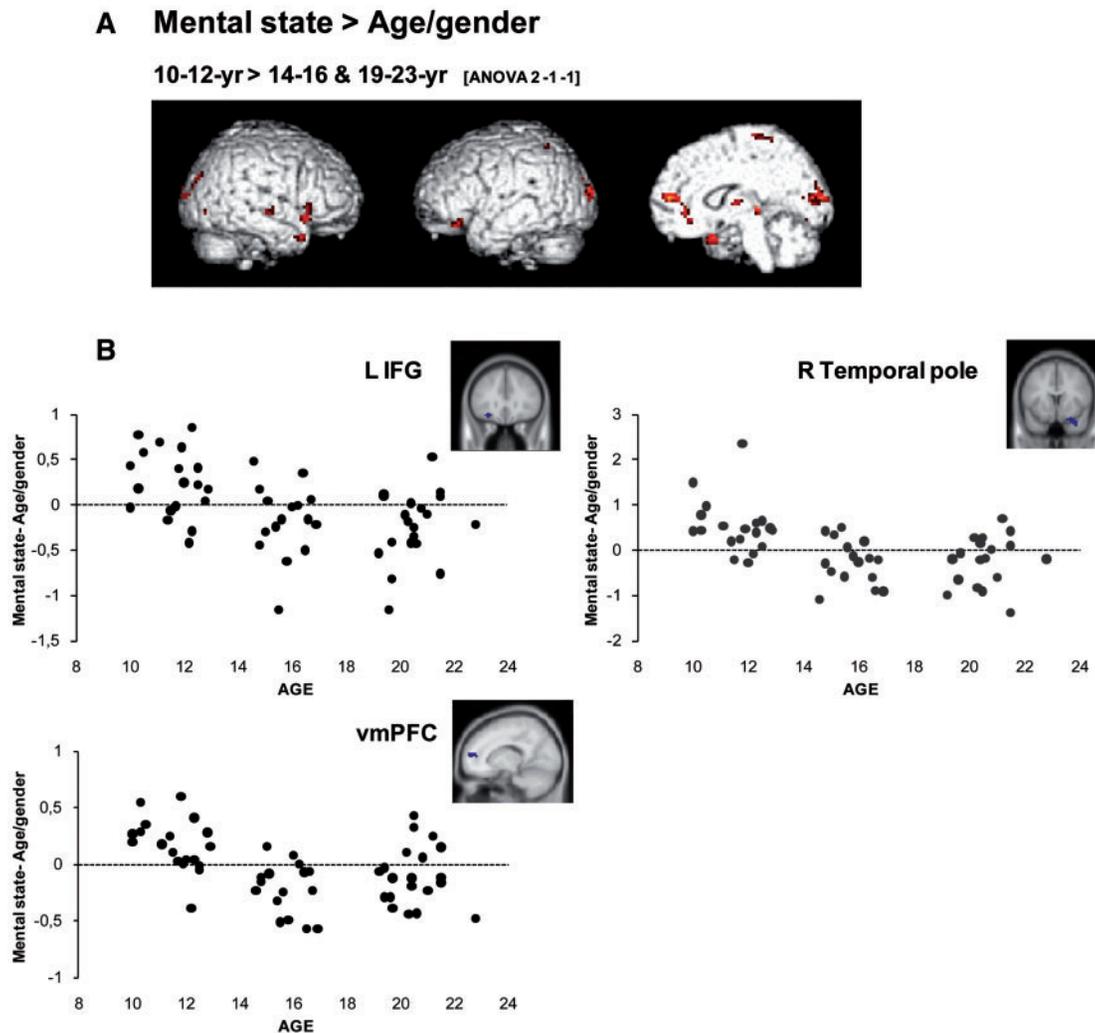


Fig. 4 Whole-brain results for the contrast Mental state > Age/gender which show a peak in activity for 10- to 12-year-olds (A) at $P < 0.001$ (uncorrected). In (B) scatterplots of contrast values for age and activity in the left IFG ($-27\ 33\ -15$), right temporal pole ($33\ 12\ -30$) and vmPFC ($15\ 54\ 12$) are presented.

Supplementary Table 3. No regions were found that showed a linear increase in activation with age.

DISCUSSION

The goal of this study was to examine how basic perceptual mind-reading processes develop during adolescence and to test the developmental trajectories of brain regions involved in mental state attribution. All age groups performed well above chance level on the 'Reading the Mind in the Eyes task', showing that the general ability to decode the feelings and thoughts of others from the eyes develops at a young age. These findings are consistent with other studies which reported that children aged 8–10 years perform well on this task compared to younger participants (Baron-Cohen *et al.*, 2001b). *Post hoc* analyses, however, revealed a slight dip in accurate performance in this mind-reading ability in 14- to 16-year-olds compared to adults, whereas the other groups did not differ from each other. This effect was only present

in follow-up comparisons and therefore should be replicated in future studies.

Consistent with previous neuroimaging studies, reading the mind in the eyes resulted in activation in the pSTS and the IFG, which are the two areas most consistently reported using the 'Reading the Mind in the Eyes task' (Adams *et al.*, 2009). Importantly, pSTS activation was found for all age groups supporting the model of Nelson *et al.* (2005) suggesting that brain regions involved in social perception (i.e. the detection node) develop early in life. The pSTS has often been implicated in the processing of signals of biological motion, such as information provided by the body and the eyes (e.g. Hoffman and Haxby, 2000; Carrington and Bailey, 2009), as well as in the visual analysis of other people's mental states and intentions (Pelphrey *et al.*, 2003, 2004). Prior studies on development of mentalizing and eye gaze perception also reported activity in the pSTS in both children and adults (Mosconi *et al.*, 2005; Carter and Pelphrey, 2006; Moriguchi *et al.*, 2007). Possibly, the human system for

social perception is already tuned to read the intentions of others from the eyes at a young age. Indeed, the eyes have been found to have a privileged status in attracting attention early in life (Langton *et al.*, 2000).

Besides activation in the pSTS, 10- to 12-year-old adolescents additionally activated bilateral IFG, vmPFC and the right temporal pole when reading the mind in the eyes. The question then arises: why are these brain regions additionally recruited in 10- to 12-year-olds despite adult-level activity in the pSTS and the lack of strong age-related differences in performance? To our knowledge the current study is the first examining age-related differences in neural activation associated with the 'Reading the Mind in the Eyes task'. Interestingly, results of this study fit well with previous fMRI studies on mentalizing and face processing showing increased activity in the mPFC and the IFG in adolescents and children relative to adults (e.g. Kobayashi *et al.*, 2007; Blakemore, 2008, 2010; Johnson *et al.*, 2009). The current findings add to this literature by extending it to basic social-perceptual processes involved in mentalizing. Together, this pattern of developmental changes may suggest that while brain regions involved in social perception develop early in life, the fine-tuning or functional specialization of other regions of the social brain network may continue during adolescence.

There are several plausible explanations for the observed age-related differences in functional activity in the current study. At a general level, prior studies have suggested that the age-related decrease in activation in frontal regions could reflect maturational processes (e.g. synaptic pruning) involved in the fine-tuning of neural systems (Blakemore, 2008; Burnett and Blakemore, 2009a). Indeed, brain regions such as the IFG and the mPFC show protracted structural development with a peak in gray matter around the onset of puberty followed by gray matter thinning (e.g. Gogtay *et al.*, 2004; Sowell *et al.*, 2004). Further, there is increasing evidence that pubertal hormones could have an impact on structural and functional brain maturation, as well as on behavior (Sisk and Foster, 2004; Blakemore *et al.*, 2010). It is possible that these biological events around the onset of puberty may contribute to the current results showing age-related differences in functional activity between 10 and 12-year-olds (mean Tanner stage 2.11) and older participants when reading the mind in the eyes. Interestingly, activity in the vmPFC showed a more categorical or non-linear change between 10- to 12 and 14- to 16-year-olds, suggesting that this region was specifically engaged in adolescents around the onset of puberty, in contrast to their older counterparts. In future research, it would be of considerable interest to test in more detail how pubertal hormones could shape brain activity and performance on the 'Reading the Mind in the Eyes task'. Further, there is a need of studies trying to relate structural and functional brain maturation across adolescent development, for instance by tracking these changes longitudinally over time.

Other explanations for the additional involvement of brain regions in early adolescents focus on the functional role of these regions to perform the task. In particular, regions such as the vmPFC and the temporal pole have been most consistently reported in theory of mind tasks that require more abstract reasoning about mental states (e.g. Gallagher and Frith, 2003; Amodio and Frith, 2006), instead of mental state decoding from limited visual cues, such as the eyes (Adams *et al.*, 2009). As such, early adolescents might engage brain regions important for higher-order cognitive processes for reading the mind in the eyes, as well as regions involved in social perception (i.e. pSTS). Indeed, given the nature of the task requiring an understanding of (lexical) social concepts, it is possible that younger children rely more on social semantic knowledge when performing this task, which may be due to less experience with mental state terms or mental state attribution. Prior studies demonstrated that abstract social semantic information necessary to understand the mental states of others is mainly subserved by the same brain regions involved in theory of mind, including the mPFC and the temporal poles (Mitchell *et al.*, 2005a; Zahn *et al.*, 2007; Ross and Olson, 2010). This interpretation could also account for age-related differences in the IFG which has been associated with language processing and semantic retrieval (e.g. Thompson-Schill, 2003).

Finally, age-related differences in functional activity could hint towards the use of different strategies when performing the task. That is, early adolescents might employ a more explicit mentalizing strategy (Burnett and Blakemore 2009b). Alternatively, it has previously been suggested that children or adolescents may use a more 'self-oriented' strategy for mentalizing (Moriguchi *et al.*, 2007; Burnett *et al.*, 2009). Although the vmPFC is believed to play a key role for understanding the intentions of others (Frith and Frith, 2003), prior studies indeed pointed to a role of this region in self-referential processes and self-evaluation (Amodio and Frith, 2006; Mitchell *et al.*, 2006). In addition, it has been reported that the vmPFC could facilitate the understanding of what another person is thinking or feeling by self-referential processing (Mitchell *et al.*, 2005b; Ames *et al.*, 2008). On a related note, it is possible that developmental differences are related to the way older participants recruited the vmPFC during the age/gender condition. In particular, the mPFC is believed to be a key area of the 'default mode network' that is typically engaged during rest, allowing spontaneous self-reflection (Amodio and Frith, 2006). It seems plausible that the age/gender condition required less cognitive effort in older participants, resulting in higher levels of activity in the mPFC. Nevertheless, this interpretation could not fully account for the results obtained for early adolescents, since activity in this age group was stronger for the mental state condition compared to activity during baseline and the control condition.

An unresolved issue in the current study concerns the question whether the additional involvement of brain

regions that support social-information processing in young adolescents reflects the engagement of a wider network of brain areas which is important for mind-reading, or whether these activations reflect performance-independent engagement. Patient studies and studies with transcranial magnetic stimulation (TMS) could test the functional role of these areas in mental state attribution more directly. In addition, a priority for future work should be to test which brain regions function as a network during the 'Reading the Mind in the Eyes task' by using functional connectivity analyses, and how this changes with age. Second, it should be noted that the conditions in the current study may also differ in terms of cognitive load, instead of exclusively in terms of mental state attribution (see also Baron-Cohen *et al.*, 1999). For instance, whereas the mental state condition involved the presentation of novel mental state terms on each trial, the control condition involved the presentation of the same response options, albeit at different locations. Although care was taken to calibrate both conditions, a difference in cognitive load precludes a straightforward comparison of task conditions in terms of mentalizing. However, it is important to note that this problem is typical in fMRI studies using subtraction designs, requiring a close matching of task conditions. In future studies it will be important to optimize the control condition in terms of task difficulty, for instance by using different choice options on each trial.

A significant next step would be to build a theoretical framework that could account for the emerging evidence showing a protracted functional development across adolescence in a wide range of mentalizing tasks. To achieve this goal, it would be important to test in more detail how biological events (i.e. pubertal hormones) and experience could shape neural activity associated with mentalizing and the social-cognitive strategies that are used. A second priority for future work would be to determine whether the ability to read and understand the mental states of others requires a general level of abstract thinking that may be largely independent of specific task demands which still develops during adolescence, or whether regions of the social brain may be poorly functionally defined during adolescence followed by an increase in functional specialization or task selectivity with age (e.g. 'interactive specialization') (Johnson *et al.*, 2010).

SUPPLEMENTARY DATA

Supplementary Data are available at SCAN online.

Conflict of Interest

None declared.

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