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Neural substrates underlying intentional empathy

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Although empathic responses to stimuli with emotional contents may occur automatically, humans are capable to intentionally empathize with other individuals. Intentional empathy for others is even possible when they do not show emotional expressions. However, little is known about the neuronal mechanisms of this intentionally controlled empathic process. To investigate the neuronal substrates underlying intentional empathy, we scanned 20 healthy Chinese subjects, using fMRI, when they tried to feel inside the emotional states of neutral or angry faces of familiar (Asian) and unfamiliar (Caucasian) models. Skin color evaluation of the same stimuli served as a control task. Compared to a baseline condition, the empathy task revealed a network of established empathy regions, including the anterior cingulate cortex, bilateral inferior frontal cortex and bilateral anterior insula. The contrast of intentional empathy *vs* skin color evaluation, however, revealed three regions: the bilateral inferior frontal cortex, whose hemodynamic responses were independent of perceived emotion and familiarity and the right-middle temporal gyrus, whose activity was modulated by emotion but not by familiarity. These findings extend our understanding of the role of the inferior frontal cortex and the middle temporal gyrus in empathy by demonstrating their involvement in intentional empathy.

Keywords: fMRI; brain imaging; empathy

INTRODUCTION

Empathy describes our ability to understand and share the emotional states of others (Batson *et al.*, 1987; Decety and Jackson, 2004; Blair, 2005). This ability is of striking importance for our survival and success in social environments (Blair, 2003; Gallese *et al.*, 2004). Empathy consists of various mechanisms, which can be dissociated psychologically and neuroscientifically (Preston and de Waal, 2002; Blair, 2005). At this, most empathic responses to emotional cues in perceived stimuli, such as facial expressions, occur automatically (Dimberg and Thunberg, 1998; Chartrand and Bargh, 1999; Dimberg *et al.*, 2000; Han *et al.*, 2008; Kramer *et al.*, 2010). Humans, however, are capable to voluntarily focus their empathy on others (Nummenmaa *et al.*, 2008). This intentionally controlled empathy may even occur when no salient emotional cues are available in the perceived stimuli and is dissociated from the automatic empathy processes in time course (Fan and Han, 2008).

Most of the previous studies identified neural substrates underlying emotional empathy by comparing stimuli with different emotional intensities (Breiter *et al.*, 1996; Morris, *et al.*, 1996; Phillips *et al.*, 1997; Sprengelmeyer *et al.*, 1998; Blair *et al.*, 1999), by comparing the perception of emotions and the observation of others experiencing the same emotions (Wicker *et al.*, 2003; Jabbi *et al.*, 2007; Jabbi and Keysers, 2008), or by comparing the perception of emotions with the imitation of the same emotions (Carr *et al.*, 2003).While these studies found neural activity in brain areas such as the anterior cingulate (ACC), anterior insula, superior temporal cortex, amygdala and inferior frontal cortex (Breiter *et al.*, 1996; Morris *et al.*, 1996; Phillips *et al.*, 1997; Sprengelmeyer *et al.*, 1998; Blair *et al.*, 1999; Carr *et al.*, 2003; Wicker *et al.*, 2003; Jabbi *et al.*, 2007), the designs employed in the previous work did not allow to isolate intentionally controlled processes from automatically generated processes of empathy. In addition, although a number of studies investigated the modulation of 'empathy for pain' by cognitive mechanisms (Lamm *et al.*, 2007a, b; Hein and Singer, 2008) or experience to painful practices (Cheng *et al.*, 2007), the neuronal basis underlying the cognitive modulation of 'emotional empathy' has, to our knowledge, not been investigated so far.

The first aim of our study was to uncover the neural mechanisms underlying intentionally controlled processes involved in emotional empathy. To differentiate between intentional empathy and automatic empathic responses, we applied a visual fMRI paradigm that included two tasks. An intentional empathy task asked subjects to actively

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share the emotional state of perceived faces with angry and neutral expressions. Automatic emotional responses may particularly be triggered by the presence of emotional cues in the presented stimuli. It may hence be difficult to completely disentangle intentionally generated and automatic empathic processes in emotional stimuli. The application of facial stimuli showing neutral emotional expressions (Nomi *et al.*, 2008; Nummenmaa *et al.*, 2008) reduces the automatic empathic responses and thus may help to uncover the intentional empathy. A second task asked subjects to evaluate the skin color of the same face stimuli. The first task required understanding and sharing the emotion of faces and thus tackled the intentional process involved in empathy. The second task created a control condition in which subjects concentrated on the facial stimuli alike the first task and were able to generate an automatic emotional response, however, without an intentional empathy component. In addition, the skin color evaluation task controlled for the processing of perceptual features of face stimuli and motor responses.

Which brain regions did we expect to be involved in intentional empathy? Considering the different empathy concepts, the paradigm used in the current study is similar to the tasks previously applied to investigate emotional mentalizing a]TJhsn

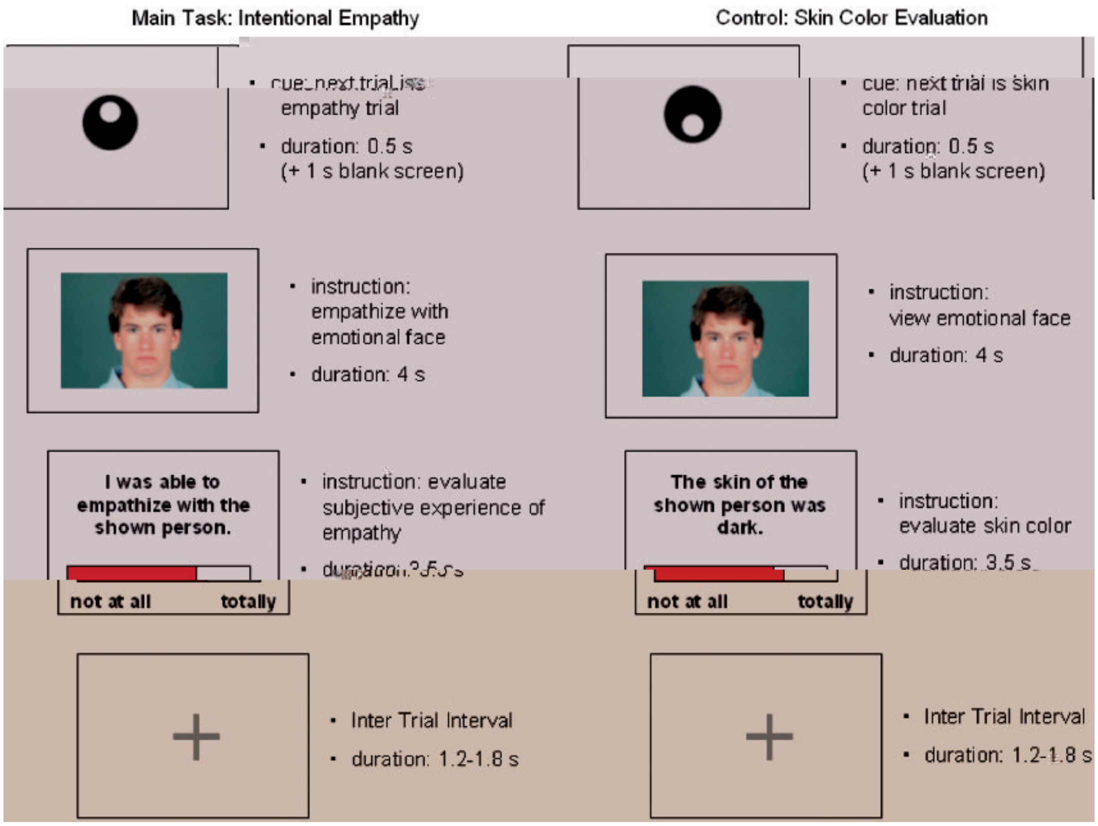

Fig. 1 Paradigm. A black circle with a small white circle in the 'North'- or 'South'-position cued the task of the next trial. The white circle in the 'North' position indexed an intentional empathy trial; the white circle in the 'South' position cued a skin color evaluation trial. In 'intentional empathy trials' subjects were instructed to empathize with perceived emotional or neutral faces. After a 4-s lasting viewing period, subjects were supposed to rate their subjective impression of empathy capability in the evaluation period, which lasted for 3.5 s. By virtually moving a red bar, they were instructed to make a statement on a visual analogue scale. In 'control trials', subjects were instructed to concentrate on the skin color of the presented faces. Analogue to the intentional empathy task, a 4-s lasting viewing period was followed by a 3.5-s-lasting evaluation period. After every trial a short inter trial interval of 1.2–1.8-s duration was presented. The face stimuli consisted of familiar (Chinese) neutral and angry faces as well as unfamiliar (Caucasian) neutral faces.

IRI uses four subscales related to perspective taking, empathic fantasy, empathic concern and empathic personal distress.

Behavioural data analysis

The subjects' performance and reaction times for intentional empathy and skin color evaluation trials were compared using paired *t*-tests.

fMRI data acquisition

The study was conducted using a General Electrics 3 Tesla Magnetic Resonance Imaging Scanner (24 slices parallel to the AC-PC plane, slice thickness 5 mm, TR 2000 ms, TE 30 ms, flip angle $\alpha = 90^\circ$, 64×64 voxels per slice with $3.75 \times 3.75 \times 5$ mm). Functional data were acquired in seven scanning sessions containing 156 volumes per session for each subject.

fMRI data analysis

The statistical analysis of the fMRI data was performed using the SPM2 software package (SPM2, http://www.fil.ion.ucl.ac.uk) and Matlab 6.5.1 (The Mathworks Inc., Natick, MA, USA). fMRI data were slice time corrected with regard to the first slice acquired and movement corrected by realignment to the first volume. Subjects' T1-weighted anatomical images were coregistered to their first functional image. All functional images were normalized to a standard T1-weighted SPM template (Ashburner and Friston, 1999). The normalization was generated by warping the subject's coregistered anatomical image to the T1-weighted SPM template followed by the application of the same normalization parameters to the functional images. Smoothing was performed using an $8 \times 8 \times 8$ mm full-width half-maximum Gaussian kernel.

A statistical model for each subject was computed by applying a canonical response function (Friston *et al.*, 1998). All relevant periods (namely the viewing and evaluation periods for all emotions and both tasks, as well as viewing and evaluation periods for trials without confirmed responses, and the baseline event) were included in the SPM model. Regionally, specific condition effects were tested by employing linear contrasts for each subject and different conditions. The resulting contrast images were submitted to a second-level random-effects analysis. Here, one-sample *t*-tests were used on images obtained for each subject's volume set and different conditions. To control for the multiple testing problem, we performed a false discovery rate correction (Nichols and Hayasaka, 2003). The anatomical localization of significant activations was assessed with reference to the standard stereotactic atlas and by superimposition of the SPM maps on a mean brain generated by averaging of each subject's T1-weighted image.

In a second step, we analysed the fMRI raw data using the Marseille Region of Interest Toolbox software package [(Brett *et al.*, 2002), MarsBaR 1.86, http://www.sourceforge.net/projects/marsbar]. Using a sphere-shaped 'region of interest' (ROI, radius 5 mm), we extracted the raw data from activations found in the second-level analysis. fMRI raw data timecourses were processed using the software package PERL (http://www.perl.org). The timecourses were linearly interpolated and normalized with respect to a time window ranging from −6 to 30 s before and after the onset of each event. fMRI signal changes of every event were calculated with regard to the fMRI signal value of 0 s. Mean normalized fMRI signal values from two following time steps (6 and 8 s after onset of the viewing period) were included in the statistical analysis. We used paired *t*-tests to analyse the effect of the different emotion conditions on the fMRI raw data.

RESULTS

Behavioural results

Intra-scanner ratings

We did not find any significant differences between intentional empathy trials and skin color evaluation trials with regard to performance (Figure 2A) and reaction times of the first response (Figure 2B). However, we detected significant faster confirmation responses during intentional empathy when compared to skin color evaluation trials (Figure 2B). In addition, we found significant differences with regard to the subjective impression of empathy capability for the different conditions (Figure 2C).

Results of the IRI

Mean scores of our subjects for the different IRI subcategories were: empathic fantasy: 18.0 (95% CI: 15.6–20.4), empathic concern: 18.5 (95% CI: 17.2–19.8), perspective taking: 18.5 (95% CI: 17.2–19.8) and empathic distress 12.6 (95% CI: 11.3–13.9).

fMRI results

SPM contrast [intentional empathy] > [baseline]

This contrast revealed a number of brain regions commonly associated to the empathy network, including the inferior frontal cortex, anterior cingulate cortex, the supplementary motor area, the anterior insula and others (see Table 1 for details).

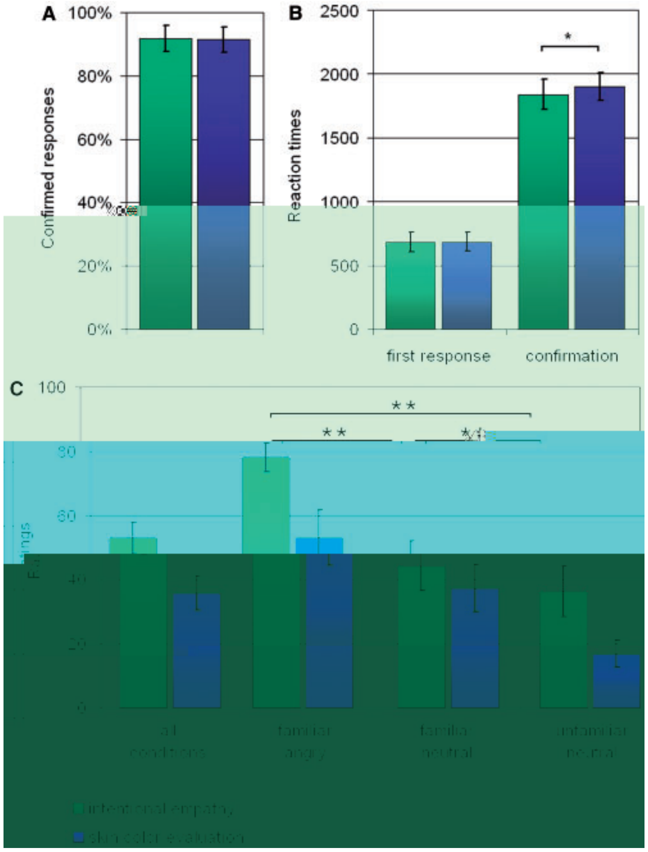

Fig. 2 Behavioural results. (**A**) Confirmed responses. Confirmed responses required the press of the confirmation button after the right score on the visual analogue scale was chosen. The percentage of confirmed responses did not differ significantly between intentional empathy and skin color evaluation trials [$t(19) = 0.326$; $P_{[\text{two-tailed}]} = 0.748$]. (**B**) Reaction times. Reaction times for first responses (when the left or right button was pressed for the first time to move the bar of the visual analogue scale) and for confirmation responses (when the confirmation button was pressed to indicate the right position of the bar). There were no significant differences between the first responses of intentional empathy trials and skin color evaluation trials. However, comparing the confirmation responses showed significantly faster reaction times during intentional empathy trials compared to the skin color evaluation trials [$t(19) = -3.172$; $P_{[\text{two-tailed}]} = 0.005$**]. (**C**) Ratings. Intra-scanner empathy ratings for familiar neutral faces were significantly smaller relative to empathy ratings for familiar angry faces [$t(19) = 7.297$; $P_{[\text{two-tailed}]} < 0.001$**]. Ratings for familiar neutral faces where nevertheless larger compared to empathy rating for unfamiliar neutral faces [$t(19) = 4.914$; $P_{[\text{two-tailed}]} < 0.001$**]. Skin color ratings for familiar neutral faces were greater when compared to unfamiliar neutral faces [$t(19) = 5.183$; $P_{[\text{two-tailed}]} < 0.001$**] and smaller when compared to skincolor ratings of familiar angry faces [$t(19) = 9.713$; $P_{[\text{two-tailed}]} < 0.001$**]. In addition, skin color estimations of unfamiliar neutral faces were smaller than skin color scores of familiar angry faces [$t(19) = 7.926$; $P_{[\text{two-tailed}]} < 0.001$**]. (Error bars indicate the 95% CI. Not all significant differences are indexed in the diagram.)

SPM contrast [intentional empathy] > [skin color evaluation]

This contrast revealed three regions associated with intentional empathy: the left and right inferior frontal cortex and the right middle temporal gyrus (Table 2 and Figure 3).

Table 1 Significant regions of the contrast [intentional empathy] > [baseline]

Region	x, y, z (mm)^a	T	$P_{[FDR]}$
Left Inferior frontal cortex	−48, 2, 43	5.88	0.001
Right Inferior frontal cortex	50, 6, 24	5.18	0.002
	48, 6, 32	5.11	0.002
	40, 30, 14	3.67	0.020
Left Prefrontal cortex	−36, 50, 16	3.40	0.030
	−35, 40, 10	3.39	0.030
Left Anterior cingulate cortex	−6, 0, 54	6.35	<0.001
Right Anterior cingulate cortex	10, 8, 48	6.50	<0.001
Left Supplementary motor area	−26, −10, 54	7.04	<0.001
Right Supplementary motor area	26, −4, 60	4.38	0.007
	38, −14, 56	3.52	0.025
Left Anterior insula	−30, 22, 4	4.90	0.003
Right Anterior insula	32, 22, 6	4.08	0.010
Left Putamen	−22, 4, 4	4.89	0.003
Right Putamen	22, 6, 6	4.10	0.010
Left Posterior parietal cortex	−10, −76, 50	4.17	0.009
	−22, −72, 40	3.16	0.042
	−32, −50, 36	3.81	0.016
	−28, −66, 52	3.14	0.044
Left Occipital cortex	−14, −96, −8	10.47	<0.001
	−40, −70, −28	9.17	<0.001
	−34, −76, −28	8.44	<0.001
Right Occipital cortex	28, −88, −8	11.62	<0.001
	24, −84, −15	11.08	<0.001
	36, −62, −24	8.93	<0.001

The contrast was calculated using an FDR correction for multiple comparisons. The table contains all clusters with $P_{[FDR]} < 0.05$ and a minimum cluster size of 10 voxels ($n = 20$).

[a] Coordinates refer to the MNI stereotactic space.

Table 2 Significant regions of the contrast [intentional empathy] > [skin color evaluation]

Region	x, y, z (mm)^a	T	$P_{[uncorrected]}$
Left Inferior frontal cortex	−48, 22, −2	4.66	<0.001
Right Inferior frontal cortex	48, 28, 4	4.66	<0.001
Right Middle temporal gyrus	62, −54, 0	3.98	<0.001

This contrast ($n = 20$, uncorrected threshold 0.001, minimum cluster size 10 voxels) revealed three regions with stronger hemodynamic responses during intentional empathy: the bilateral inferior frontal cortex and the right middle temporal gyrus. The opposite contrast [skin color evaluation] > [intentional empathy] did not reveal any significant regions under the sa(bila-302.9([skin)-3y)-DR](The)-25.9768534.3873678.3746Tm5

The opposite contrast [skin color evaluation] > [intentional empathy] showed no regions activated above the threshold of $P_{[\text{uncorrected}]} \leq 0.001$.

Analyses of fMRI raw data

The results of the fMRI raw data analysis are presented in Figure 3.

SPM contrasts for the different emotion conditions

Using SPM one sample *t*-tests, we looked for regions with different hemodynamic responses during the intentional empathy subconditions (namely familiar angry, familiar neutral and unfamiliar neutral). Applying a threshold of $P_{[\text{uncorrected}]} < 0.001$ and a minimum cluster size of 10 voxels, we did not find regions with differences in hemodynamic responses during the presentation of familiar angry and familiar neutral faces. Using the same threshold, we did not find any areas with different hemodynamic responses during familiar neutral faces and unfamiliar neutral faces.

SPM contrast [familiar neutral] > [unfamiliar neutral]

In addition, we used an SPM one sample *t*-test, to look for regions with different hemodynamic responses during the perception (intentional empathy + skin color evaluation) of familiar neutral and unfamiliar neutral faces. Applying a threshold of $P_{[\text{uncorrected}]} < 0.001$ and a minimum cluster size of 10 voxels, we did not find any cluster for the contrast [familiar neutral] > [unfamiliar neutral]. In addition, we did not find any activations in the opposite contrast [unfamiliar neutral] > [familiar neutral] using the same threshold criteria.

SPM correlations using mean empathy ratings and IRI scores

We performed a supplementary SPM analysis, in which we introduced behavioural variables into simple SPM correlations using the images of the contrast [intentional empathy] > [skin color evaluation]. Looking for regions in which each subject's mean intra-scanner empathy rating predicted their contrast value of the contrast [intentional empathy] > [skin color evaluation], the SPM correlation revealed only one region, the left-posterior fusiform gyrus [−34, −82, −20, $t(18) = 3.87$, $P_{[\text{uncorrected}]} < 0.001$, minimum cluster size 10 voxels, Figure 4].

Correlating the same contrast images with each subjects mean IRI score for empathic fantasy, empathic concern, perspective taking and empathic distress, we found no significant voxels above the rational threshold of $P_{[\text{uncorrected}]} < 0.001$ and a minimum cluster size of 10 voxels.

DISCUSSION

Relative to the baseline condition, the intentional empathy task increased activity in a neural circuit consisting of the inferior frontal cortex, anterior cingulate cortex, the supplementary motor area and the anterior insula. This is consistent with the observation of previous studies of empathy (Breiter *et al.*, 1996; Morris *et al.*, 1996; Phillips *et al.*, 1997; Sprengelmeyer *et al.*, 1998; Blair *et al.*, 1999; Carr *et al.*, 2003; Wicker *et al.*, 2003; Jabbi *et al.*, 2007). However, compared to the control condition that required skin color evaluation, the intentional empathy task induced significant stronger hemodynamic responses in the bilateral inferior frontal cortex and the right middle temporal gyrus, revealing brain regions specifically involved in intentional

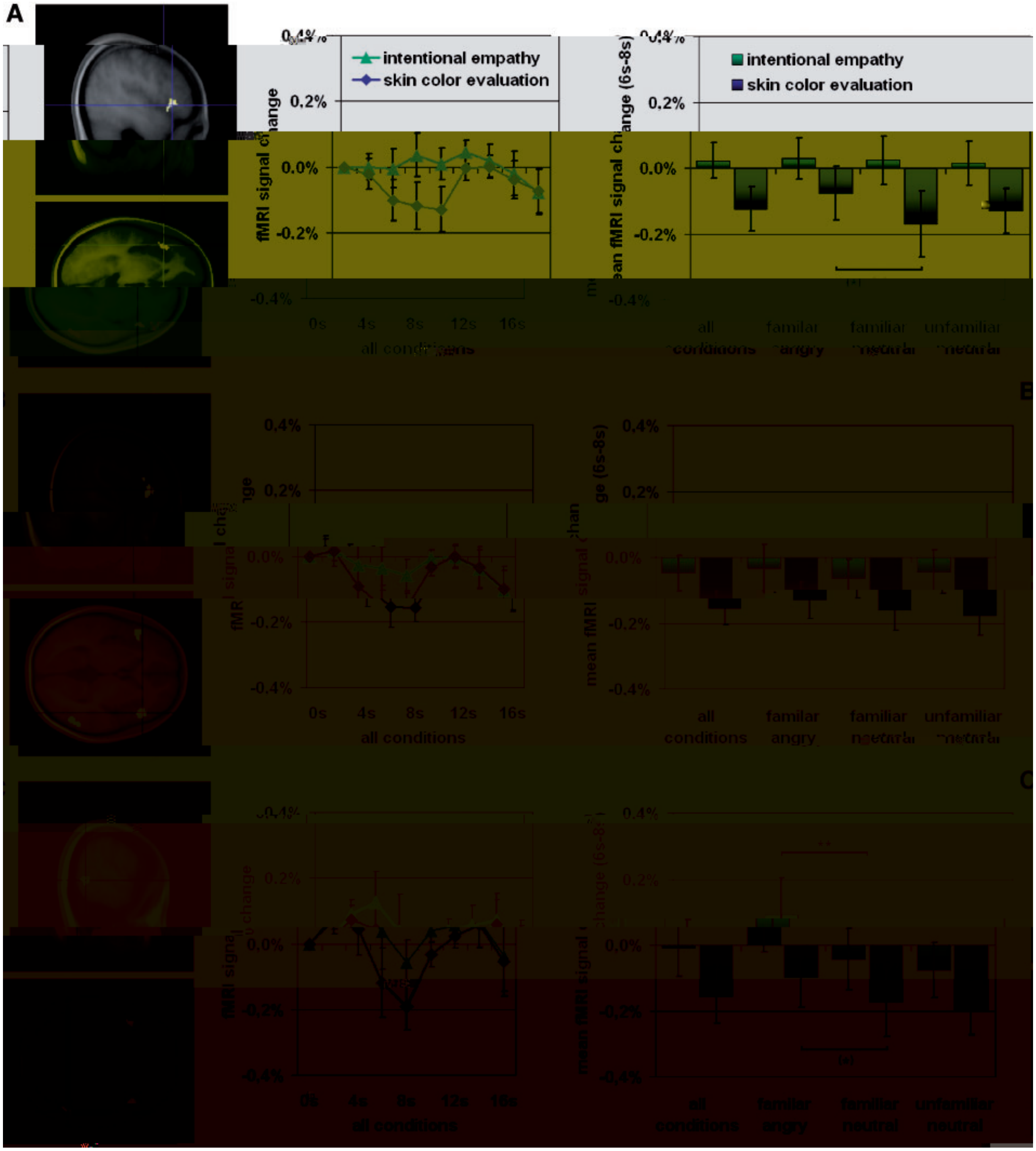

Fig. 3 Significant regions of the contrast [intentional empathy] > [skin color evaluation]. Three regions showed stronger hemodynamic responses during the intentional empathy task when compared to the skin color task: the left inferior frontal cortex [−48, 22, −2] (**A**), the right inferior frontal cortex [48, 28, 4] (**B**) and the right middle temporal gyrus [62, −54, 0] (**C**). SPM analysis was supplemented by an analysis of the raw fMRI signal data. The diagrams in the center of each line show the averaged time courses of the fMRI signal during intentional empathy and skin color evaluation for all conditions. The bar diagrams on the right depict the mean fMRI signal values (6–8 s after onset) for the average of all conditions as well as for the single conditions separately. Looking for modulations by emotion, we only found the right middle temporal gyrus with significant stronger hemodynamic responses during the empathic perception of familiar angry faces compared to familiar neutral faces [$t(19) = 4.277$, $P_{[\text{two-tailed}]} = 0.001$**, C]. The left and right inferior frontal cortex did not show any modulation by emotion during intentional empathy (A and B). In addition, none of the regions showed a significant difference between the neutral familiar and neutral unfamiliar condition. Surprisingly, we found a statistical trend for a modulation of hemodynamic responses during skin color evaluation caused by emotion in two regions: the left inferior frontal cortex (A) and right middle temporal gyrus (C) showed the tendency to respond stronger during skin color evaluation of familiar angry faces compared to familiar neutral faces [$t(19) = 1.855$, $P_{[\text{two-tailed}]} = 0.079$* and $t(19) = 2.011$, $P_{[\text{two-tailed}]} = 0.059$*]. Interestingly, we found significant deactivations in all three regions during all skin color evaluation conditions (all $P_{[\text{two-tailed}]} \leq 0.061$*). (Error bars indicate the 95% CI).

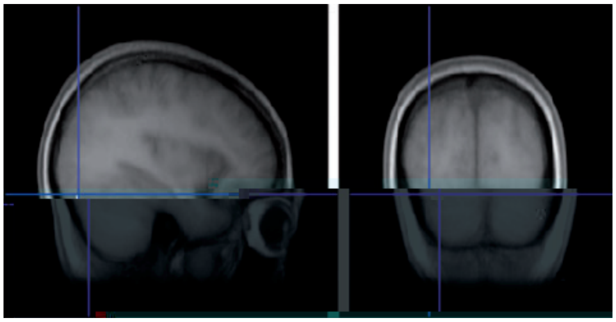

Fig. 4 Correlation in the left posterior fusiform gyrus [−34, −80, −20]. The left posterior fusiform gyrus showed a significant correlation of hemodynamic responses for the contrast [intentional empathy] > [skin color evaluation] and mean empathy ratings (simple SPM correlation analysis, $P_{[\text{uncorrected}]} < 0.001$, minimum cluster size 10 voxels).

empathy. Looking for effects of emotion, we found only the right middle temporal gyrus with stronger hemodynamic responses during intentional empathy for familiar angry faces compared to familiar neutral faces. None of the regions showed evidence for modulations by the race-based familiarity between the observed and target person. Hemodynamic responses during skin color evaluation of the left inferior frontal cortex and the right middle temporal gyrus showed a tendency for an emotional effect, with stronger hemodynamic responses during familiar angry faces, compared to familiar neutral faces. Again, we did not find any modulation of hemodynamic responses caused by race-based familiarity. Differences in hemodynamic responses between intentional empathy and skin color evaluation of the left fusiform gyrus correlated with mean intra-scanner empathy ratings.

The inferior frontal cortex and middle temporal gyrus have been shown to be involved in emotional empathy (Blair *et al.*, 1999; Carr *et al.*, 2003; Decety and Chaminade, 2003; Chakrabarti *et al.*, 2006; Jabbi *et al.*, 2007). Our fMRI results indicate that these brain areas engage in intentional empathy for other individuals even when no perceived emotional cues are available. In other words, the neuronal activity of left and right inferior frontal cortex during intentional empathy was independent of the emotional content of the stimuli. This finding demonstrates that neuronal activity in the bilateral inferior frontal cortex can be exclusively internally generated, without any modulation by the external emotional cues. Hemodynamic responses of the right middle temporal gyrus, however, were modulated by the emotional content of the presented pictures, indicating that neuronal activity of this region is not exclusively internally generated.

Our findings extend our understanding of the role of the inferior frontal cortex in empathy. The inferior frontal cortex is known to be part of the human mirror neuron system, a network of brain regions which are involved in the generation of actions as well as in the perception of actions performed by others (Iacoboni *et al.*, 1999; Carr *et al.*, 2003; Grezes *et al.*, 2003; Iacoboni, 2005; Iacoboni *et al.*, 2005; Iacoboni and Dapretto, 2006; Kaplan and Iacoboni, 2006); at first, it was detected in the monkey (Gallese *et al.*, 1996; Rizzolatti *et al.*, 1996; Buccino *et al.*, 2001; Rizzolatti *et al.*, 2001; Ferrari *et al.*, 2003; Rizzolatti and Craighero, 2004). A number of studies showed the involvement of the mirror neuron system and particularly the inferior frontal cortex in empathic processes such as emotional empathy (Kaplan and Iacoboni, 2006), emotional imitation (Carr *et al.*, 2003; Lee *et al.*, 2006), passive emotion perception (Chakrabarti *et al.*, 2006) and emotion evaluation (Decety and Chaminade, 2003). Since these studies used emotional stimuli, the observed inferior frontal activity may mainly subserve emotion regulation. In our work, however, the observed inferior frontal activity observed mainly reflects intentional control of emotional empathy, since it was detected in a task requiring empathy for neutral faces. This task reduced emotional responses to a minimum degree and thus did not require emotion regulation. Interestingly enough, two studies reported the inferior frontal cortex to be involved in intentional emotion imitation (Carr *et al.*, 2003; Lee *et al.*, 2006). Our study contributes to these findings in showing that the mere intentional emotional sharing of another's state is sufficient to activate the inferior frontal cortex—even without emotions expressed by the target.

In addition, the right middle temporal gyrus (as part of the posterior superior temporal sulcus region) showed stronger hemodynamic responses during intentional empathy when compared to the control task. These results complement previous findings which described the involvement of the superior temporal sulcus region in several emotional tasks. Activation of the superior temporal sulcus region was often found together with co-activation of the inferior frontal cortex during the same contrasts (Carr *et al.*, 2003; Grezes *et al.*, 2003; Chakrabarti *et al.*, 2006; Hoekert *et al.*, 2008; Hooker *et al.*, 2008, 2010). Additional papers suggest nevertheless that the superior temporal sulcus region is comparatively more involved in social cognitive tasks, such as the passive perception of social scenes (Kramer *et al.*, 2010) or Theory of Mind (Vollm *et al.*, 2006). In their review paper, Allison and colleagues (Allison *et al.*, 2000) suggest that the superior temporal sulcus region is 'sensitive to stimuli that signal the actions of another individual'. Interestingly, and in contrast to the inferior frontal cortex, the right middle temporal gyrus showed a significant modulation by emotion with stronger hemodynamic responses during familiar angry faces compared to familiar neutral faces. This finding can perhaps be explained by the assumption that angry facial expression are comparatively more salient to neutral ones and imply greater social relevance (Blair, 2005).

None of the three regions involved in intentional empathy observed in our study was affected by familiarity. Recently, a number of studies found race-based familiarity to be an effective modulator of brain activity related to empathy for pain. Regions modulated by race-based familiarity included the anterior cingulate cortex (Xu *et al.*, 2009; Mathur *et al.*, 2010), the insula (Mathur *et al.*, 2010) and the sensorimotor system (Avenanti *et al.*, 2010). In addition, differences in activity of the fusiform gyrus during the memorizing of facial stimuli of the same race (African-American) and another race (Caucasian) were reported (Golby *et al.*, 2001) as well as differences in the activity of the amygdala, the superior temporal cortex and other regions during very short presentations of other race (African-American) and same race (Caucasian) facial stimuli (Cunningham *et al.*, 2004). However, none of these studies reported differences of inferior frontal cortex activity related to race-based differences in familiarity. Moreover, none of these studies investigated intentional emotional empathy. Together these results suggest that the social relation between an observer and a target mainly modulates the automatic processes of empathy. The intentionally controlled process of empathy mediated by the inferior frontal cortex, however, seems to function independently of the social relation between the observer and a target. These findings provide additional evidence for the dissociation between intentionally controlled processes from the automatically generated processes of empathy.

The voxel-based correlation analysis revealed a significant correlation of neuronal activity in the left posterior fusiform gyrus with subjective empathy ratings. This brain area is located posterior to the fusiform face area that is crucially involved in the processing of faces (Kanwisher *et al.*, 1997; Grill-Spector *et al.*, 2004; Iidaka *et al.*, 2006; Fusar-Poli *et al.*, 2009). The posterior fusiform region observed in our study seems nonetheless to overlap with regions observed in the processing of emotional faces (Geday *et al.*, 2003; Etkin *et al.*, 2004; Nomi *et al.*, 2008) and empathy with painful emotional faces (Lamm *et al.*, 2007a). The here observed correlation of hemodynamic modulation in the posterior fusiform gyrus and mean empathy ratings might hence be interpreted as increased processing of the facial stimuli in those subjects, which gave overall higher empathy ratings.

A few limitations of our study should be noted. First, during both tasks we were not able to control on which specific aspect of the facial stimuli our subjects focused. It might be that during the intentional empathy task subjects focused more on the eyes of the facial stimuli, while subjects possibly concentrated on the cheeks and the forehead during the skin color perception task. Second, as demonstrated in Figure 3, the contrast between the intentional empathy task and the skin color evaluation task was mainly shaped by the distinct negative signal changes during the skin color evaluation task, rather than by the positive hemodynamic responses during intentional empathy. We are puzzled by this finding and can only provide a rather speculative explanation that awaits further research. It may be the case that the pronounced negative fMRI signal changes during skin color evaluation reflect the intentionally controlled inhibition of empathy processes. In other words, neuronal activity of the bilateral inferior frontal cortex and superior temporal sulcus region may be not so much affected by the intentionally controlled generation of empathy, but rather by its intentionally controlled inhibition. Third, the variety of emotions applied in our paradigm is rather low (only angry and neutral). Future studies may investigate intentional empathy with other emotions. In addition, it might be interesting for future studies to examine whether the influence of race-based familiarity on empathy is modulated by different emotions of perceived facial expressions.

CONCLUSIONS

Our results underline the important role of the bilateral inferior frontal cortex and the right superior temporal sulcus region in empathy. We were able to show that these regions play a pivotal role in intentional empathy. Hemodynamic responses of bilateral inferior frontal cortex during intentional empathy were only modulated by the task, whereas the right superior temporal sulcus region was affected by the emotional content of the facial stimuli. None of the three regions showed an effect of the race-based familiarity of perceived stimuli. Our findings suggest that the inferior frontal activity underlying intentionally controlled empathic responses is independent of both emotional contents in perceived stimuli and familiarity between the observer and target person.

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