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Empathizing with basic emotions: Common and discrete neural substrates

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Empathizing is a quantitative trait involving understanding another's mental state (including their emotion) and responding to this with an appropriate emotion. A reliable, behaviorally validated self-report questionnaire measure of this is the Empathy Quotient (EQ), which is continuously distributed across the general population. The "discrete emotions" model posits that each "basic" emotion has a relatively independent evolutionary antecedent and social-communicative function and is subserved by a discrete neural system. In this study, we investigate if and how empathy influences the perception of basic emotions. Twenty-five volunteers (13 female, 12 male) selected across EQ space participated in a correlational design 3T fMRI study. The stimuli were presented in a box-car design, where 5 blocks (each containing 4 video clips of any one of *happy*, *sad*, *angry*, *disgust* or *neutral* expressions from different actors) and a low-level baseline were presented in pseudo-random order. Using an exploratory analysis, we found different brain regions correlated with EQ, depending on which emotion was being perceived. In particular, the ventral striatal response to *happy* faces correlated positively with EQ, while the ventral striatal response to *sad* faces was negatively correlated with EQ. The precuneus and lateral prefrontal cortical response to *angry* faces correlated positively with EQ. The response of the insula and the superior temporal gyrus cortex to *disgust* faces were negatively correlated with EQ. These results are discussed in the light of the postulated evolutionary function of each emotion. Using a hypothesis-driven conjunction analysis, we found that a region in the left dorsal inferior frontal gyrus/premotor cortex was positively correlated to the EQ across all four emotions. This region could therefore constitute a biomarker for trait empathy across emotions. We conclude that there are common regions underlying empathy across different emotions, and there are regions that show an emotion-specific correlation with empathy. This pattern of results is interpreted using a modification of Haxby et al.'s model of face perception.

This Special Issue focuses on the neuroscience of "theory of mind" (ToM), and this article examines the neuroscience of a related process, empathy. Empathy is broader than ToM, in that ToM is one factor within empathy. This article tests how empathy influences emotion perception.

Facial expressions function as markers of emotions (Darwin, 1872/1998; Ekman & Keltner,

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2000). In addition to being the output component of emotions, facial expressions serve as significant emotional stimuli in their own right. For example, ''social referencing'' is seen in infants when they consult their primary caregiver's facial expression to either approach or avoid an object (Walden & Ogan, 1988). Beyond infancy, we continue to treat facial expressions as salient emotional stimuli throughout life. This suggests links between the perception, recognition and experience of emotions.

The universality (Ekman & Friesen, 1971) and, to a certain extent, homology across species (Lawrence & Calder, 2003) of the facial, and other bodily (Hejmadi, Davidson, & Rozin, 2000), expressions of emotion suggest the existence of distinct cognitive and neural substrates for individual basic emotions. Even though a consensus on what constitutes a basic emotion is yet to emerge (Prinz, 2004), there is relatively little controversy about the universality of expressions of *happiness*, *sadness*, *anger*, *disgust*, and *fear*. One model identifies these as independent ''affect programs,'' or ''pancultural syndromes enabled by inherited biological capabilities'' (Delancey, 2001). Evidence from lesion, neuroimaging and electrophysiological studies suggest these affect programs have discrete neural bases (Calder, Lawrence, & Young, 2001; Panksepp, 1998).

The most well-known examples include the role of the amygdala in *fear* processing (Adolphs, Tranel, Damasio, & Damasio, 1994; Hariri, Mattay, Tessitore, Fera, & Weinberger, 2003; LeDoux, 2000; Prather et al., 2001), and the insula in *disgust* processing (Phillips et al., 1997; Phillips et al., 1998b; Wicker, Keysers, Plailly, Royet, Gallese, & Rizzolatti, 2003). The idea that the ventral striatum processes reward from different sensory domains, e.g., receiving food rewards (O'Doherty, Deichmann, Critchley, & Dolan, 2002), viewing funny cartoons (Mobbs, Greicius, Abdel-Azim, Menon, & Reiss, 2003), remembering happy events (Damasio et al., 2000), fits with studies that report activation of this region in response to viewing *happy* faces (Lawrence, Chakrabarti, & Calder, 2004; Phillips et al., 1998a), fits with studies that report activation of this region in response to viewing *happy* faces (Lawrence, Chakrabarti, & Calder, 2004; Phillips et al., 1998a). Perception of angry expressions evokes a response in the premotor cortex and the striatum, among other areas (Grosbras & Paus, 2006). Studies of the processing of *sad* expressions are less consistent. Perception of *sad* face and induction of sad mood are known to be associated with a response in the subgenual cingulate cortex (Liotti, Mayberg, Brannan, McGinnis, Jerabek, & Fox, 2000; Mayberg et al., 1999), the hypothalamus in humans (Malhi et al., 2004) and in rats (Shumake, Edwards, Gonzalez-Lima, 2001) as well as in the middle temporal gyrus (Eugene et al., 2003).

The above model holds well for ''simple'' emotions, but dimensional models (Rolls, 2000) become relevant in considering more ''socially complex'' emotions, e.g., *pride*, *shame*, and *guilt*. This is because it would not be economical to have discrete neural substrates for the whole gamut of human emotions, estimated to be at least 412 (Golan & Baron-Cohen, 2006). While the discrete vs. dimensional debate addresses broad questions about emotion experience (e.g., whether there are strict boundaries between emotions, or whether emotions lie on a continuum that is best represented by a circumplex model), research on emotion perception per se is comparatively recent.

Early cognitive theories of emotions used a tripartite model, a variant of the classical ''sandwich'' model used to explain cognition in general. This drew distinctions between the perception of and response to (''action tendency'') emotional stimuli (see Figure 1). The middle of this

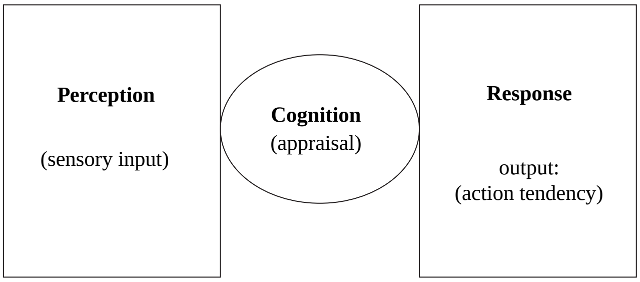

Figure 1. The classical tripartite model of emotion. Recent evidence challenges such models.

sandwich is the cognitive or appraisal/interpretative processing of the stimulus (Power & Dalgleish, 1997). However, there is increasing evidence that "perception" and "action" (levels 1 and 3) are not completely distinct in emotion processing (Hurley, 2005).

The ability to perceive (and hence recognize) other people's emotions and mental states is one element of "empathizing" (Baron-Cohen, 2002), the other element being the appropriate affective response to the other person's mental state. Research on empathy has followed two streams of enquiry. The first is research into "theory of mind" (ToM), defined as the "ability to infer the full range of mental states that cause action ... Having a ToM is to be able to reflect on one's own and other's minds" (Baron-Cohen, 2001). Several neuroimaging studies, using tasks that involve attribution of intentions/emotions (tasks that recruit ToM), have shown a consistent set of brain regions are involved (Frith & Frith, 2003) that include the medial prefrontal cortex (MPFC), the superior temporal sulcus (STS) and the temporo-parietal junction (TPJ).

The other stream of empathy research has focused on action perception. This has attracted considerable attention in the light of the discovery of mirror neurons in monkeys (Gallese, Fadiga, Fogassi, & Rizzolatti, 1996, 2002; Rizzolatti, Fadiga, Gallese, & Fogassi, 1996). Most experiments that suggest the involvement of "mirror areas" in humans have focused on action perception (Rizzolatti & Craighero, 2004), with the exception of one study that looked at disgust perception and experience (Wicker et al., 2003). In the light of these findings from action perception, a "mirror circuit" for empathy has been proposed (Keysers & Perrett, 2004; Rizzolatti & Craighero, 2004).

Both lines of research treat empathy as a categorical system, for which neural correlates are investigated. In the current study, we treated empathy as a personality trait instead, continuously distributed across the population. We measured this using the Empathy Quotient (EQ), a behaviorally validated 60–item self-report questionnaire (Baron-Cohen & Wheelwright, 2004). EQ is quasinormally distributed in the general population and people with autism spectrum conditions (ASC) score significantly lower than controls on this measure. ASCs are marked by a difficulty in interpreting emotions across sensory modalities (Baron-Cohen, Spitz, & Cross, 1993; Baron-Cohen, Wheelwright, & Jolliffe, 1997; Celani, Battacchi, & Arcidiacono, 1999; Deruelle, Rondan, Gepner, & Tardiff, 2004; Golan, Baron-Cohen, & Hill, 2006; Hobson, 1986; Macdonald et al., 1989; Yirmiya, Sigman, Kasari, & Mundy, 1992). Several neuroimaging studies have also reported altered neural responses in the autistic brain to certain emotions (Baron-Cohen, Ring, Bullmore, Wheelwright, Ashwin, & Williams, 2000; Hall, Szechtman, & Nahmias, 2003). The fact that in people with ASC there is both lower EQ and altered emotion-processing in the brain suggests there may be a link between these, but this possible relationship between trait empathy and perception of basic emotions has not been directly tested.

AIMS

The aim of the current study was to investigate how empathy influences the perception of facial expressions of different basic emotions (*happy*, *sad*, *angry*, and *disgusted*).

The first part of the study was hypothesis-driven, where we searched for common brain regions that correlated with EQ, independent of which emotion was being perceived. We expected that regions implicated in ToM and/or mirror-systems would show a positive correlation with EQ. In particular, we focused on the inferior frontal gyrus (IFG), medial prefrontal cortex (MPFC), premotor cortex (PM), inferior parietal lobule (IPL), posterior superior temporal sulcus (post-STS) and temporo-parietal junction (TPJ) since these have all been shown to be active in ToM/action perception-imitation tasks (Buccino et al., 2001; Chaminade, Meltzoff, & Decety, 2002; Decety, Chaminade, Grezes, & Meltzoff, 2002; Fletcher et al., 1995; Gusnard, Akbudak, Shulman, & Raichle, 2001; Hynes, Baird, & Grafton, 2006; Iacoboni et al., 2001; Johnson-Frey, Maloof, Newman-Norlund, Farrer, Inati, & Grafton, 2003; Leslie, Johnson-Frey, & Grafton, 2004; Saxe & Kanwisher, 2003). We used a functional region of interest (fROI) based analysis (Worsley, Marrett, Neelin, Vandal, Friston, & Evans, 1996) to address this question.

The second part of the study asked which brain regions correlated positively with EQ while perceiving each different emotion. According to the discrete emotions model, different emotions have different evolutionary antecedents and social-communicative functions (Izard & Ackerman, 2000). It follows that there could be

Figure 2. Example stills from stimuli clips used, showing happy, angry, sad, and disgusted expressions.

differences among basic emotions in how much ''mentalizing'' is required to recognize/respond to them. For example, a *disgust* expression arguably requires less ToM or self–other distinction than an angry expression. A *happy* expression might involve a greater degree of covert mimicking than an *angry* expression. Consequently, we predicted that EQ would interact differently during the perception of discrete basic emotions. We did not have a hypothesis regarding candidate regions since we were not aware of any studies that had specifically investigated this question. Hence, we used a permutation-based method of statistical inference to identify regions that were significantly correlated with EQ at a whole brain level.

METHODS AND MATERIALS

Twenty-six student volunteers (13 males, 13 females, mean age = 23.4 years, *SD* = 4.23 years) from the local universities were recruited through advertisement. All participants were matched for age, IQ and educational background. Four participants had a diagnosis of high-functioning autism/Asperger syndrome (HFA/AS) but were nevertheless included since the correlational design of the study ignored clinical diagnosis and instead focused solely on EQ as a dimensional trait. Of these 4 participants, 3 had below average EQ scores, while the final one did not complete the EQ. Participants with a history of head injury/operation or regular drug abuse were excluded since we were interested in EQ as a trait rather than as an index of traumatic or psychopharmacological state. All other participants completed the EQ ($n = 25$, mean = 41.88, median = 42, $SD =$ 17.15, range = 13 to 66).

Stimuli were back-projected onto a translucent screen positioned in the bore of the magnet behind the head of the participant, visible via an angled mirror placed above the participant's head. Four blocks each of *happy*, *sad*, *angry*, *disgusted*, and *neutral* expressions of different actors (each block containing four 3 s video clips, 1 s inter-stimulus interval) and a low-level baseline (a fixation cross) were presented in a pseudo-random order in a box-car design using DMDX (Forster & Forster, 2003). These stimuli were developed and validated in our lab (www.jkp.com/mindreading), and are more realistic than the static photographs of facial expressions of emotion that have been used widely (see Figure 2 for examples). The subjects were instructed to look at the faces and to press a button to every stimulus.

Participants were scanned in a 3T MRI scanner (21 inter-leaved, 4 mm thick axial oblique slices, allowing whole brain coverage, with an in-plane resolution of 2.2 × 2.2 mm, repetition time (TR) = 1093 ms; echo time (TE) = 30 ms, flip angle = 65.5 degrees). BOLD contrast functional images were acquired with an echo-planar T2* weighted echo-planar imaging protocol using a 3T Bruker medspec scanner. The data was preprocessed using a standard preprocessing pipeline (Cusack, 2004) that involved slice-timing correction, realignment, undistortion, spatial normalization (using an affine transformation with 9 parameters and 16 nonlinear iterations of 6 × 8 × 6 basis functions) and smoothing (with a 7 mm kernel). The functional images were normalized to a template brain (Colin27) in standard MNI space.

Parametric methods of statistical inference were used for within-subject analysis (http://www.fil.ion.ucl.ac.uk/spm/software/spm2). A general linear model was used to compute beta values for each regressor (*happy*, *sad*, *disgust*, *anger*, *neutral* and *baseline*), multiplied by the appropriate contrast vector to generate the test statistic. Each (emotion–neutral) contrast was orthogonal to every other contrast. One-sample *t*-tests on these test statistics were used to identify regions significantly active for each (emotion–neutral) contrast.

Two sets of group-level analyses were performed to determine the influence of EQ on emotion perception:

1. For fROI analysis, individual test statistics from each (emotion–neutral) contrast were taken to the second level and analyzed parametrically using a simple regression model with EQ as a covariate in SPM2. The t-statistic maps so generated were thresholded at 1-tailed $p < .005$ (uncorrected). A conjunction of four t-statistic maps, one for each (emotion > neutral) vs. EQ correlation, thresholded at 1-tailed $p < .005$ was used to identify voxels that showed an overlap. This "conjunction map" was then analyzed for effects in regions of interest derived from other studies mentioned before (see Appendix 1 for voxel co-ordinates used).
2. Non-parametric / distribution-free methods of inference have been suggested to be superior to the standard parametric approach because of the elimination of the multiple spatial comparisons problem as well as employing a smoothed variance estimate to determine group-level effects (Nichols & Holmes, 2002). We used permutation-based methods on individual contrast statistics for correlation analysis (http://www-bmu.psychiatry.cam.ac.uk/software/docs/xbamm). This generates maps of suprathreshold voxels that are spatially contiguous in three dimensions (i.e., they constitute clusters) and have been shown to be more sensitive than voxel-based tests (Rabe-Hesketh, Bullmore, & Brammer, 1997; Suckling & Bullmore, 2004). All trait scores were regressed against individual contrast values to generate the group maps, all thresholded with clusterwise two-tailed $p < .01$ by permutation test; equivalent to less than 1 false positive error per map, using the procedure as described in (Bullmore, Suckling, Overmeyer, Rabe-Hesketh, Taylor, & Brammer, 1999).

RESULTS

Perception of basic emotions

The significant responses at the group level to each basic emotion compared to neutral faces are reported in Table 1. Perception of *happy* faces was associated with an increased activation in the ventral striatal region as well as the pre-supplementary motor area (pre-SM(A). For *sad* faces, significantly activated regions included the middle occipital gyrus, the subcallosal cingulate and the hypothalamus. For *angry* faces, significant activations included the supplementary motor area as well as the dorsal striatum. For *disgust* faces, the anterior insula/left inferior frontal gyrus was significantly activated among other regions. Perception of *neutral* faces when compared to the low level baseline (crosshair) yielded characteristic activation patterns in the fusiform gyri and the middle occipital gyri and the amygdala, in addition to other regions.

Region-of-interest analysis (hypothesis-driven, parametric)

Conjunction of all (emotion > neutral) vs. EQ correlation t-maps. Functional regions of interest (fROIs) were identified from previous neuroimaging studies that showed activation in areas known to be involved in ToM processes (Fletcher et al., 1995; Gusnard et al., 2001; Hynes et al., 2006; Saxe & Kanwisher, 2003) and mirror systems (Buccino et al., 2001; Chaminade et al., 2002; Decety et al., 2002; Iacoboni et al., 2001; Johnson-Frey et al., 2003; Leslie et al., 2004). Specifically, the following regions were analyzed for MPFC, IFG, IPL, TPJ/post-STS, PM (see Appendix 2). A sphere of 12 mm radius was used for small-volume correction (Worsley et al., 1996).

A conjunction analysis of the four group maps generated by the correlation of EQ with the (emotion > neutral) contrast, thresholded at 1-tailed $p < .005$ and a minimum cluster size of 10 voxels, revealed a significant overlap in a cluster that includes the left dorsal inferior frontal gyrus (Talairach co-ordinates of local maxima: −48 18 24, Z-score = 2.22) and adjacent premotor cortex (Talairach co-ordinates of local maxima: −46 20 24, Z-score = 2.48), see Figure 3e. The cluster response in this region for individual (emotion > neutral) vs. EQ correlations is shown in Figure 3 parts a–d.

Whole-brain analysis (exploratory, non-parametric)

Correlation of EQ with each (emotion > neutral) contrast. Table 2 shows a list of areas that showed significant correlations at a whole-

TABLE 1

Block contrast analyses of emotion > neutral conditions. Significant activations for each emotion > neutral condition, with the relevant Brodmann's area (BA) and maximally active voxel co-ordinates in Talairach space. Talairach co-ordinates were calculated from MNI co-ordinates using a non-linear transformation (mni2tal, available at http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach). All activations significant at $p < .005$ (uncorrected), minimum cluster size $k = 10$ voxels

Emotion contrast	*BA*	*Brain regions*	*x*	*y*	*z*
Happy > neutral					
		Putamen	−28	−4	−7
			−42	0	4
	13	Lateral sulcus	32	20	14
	44	Inferior frontal gyrus	46	8	0
	22	Superior temporal gyrus	−48	6	0
	10	Middle frontal gyrus	−30	40	20
	31	Paracentral lobule	6	−21	45
	40	Inferior parietal lobule	−61	−33	40
		Postcentral gyrus	−61	−41	37
		Sulcus callosomarginalis	−50	−34	55
			−57	−25	40
	19	Lingual gyrus	−12	−25	38
			59	−19	45
	19	Precuneus	−20	−70	0
			−26	−60	3
			−34	−78	35
Sad > neutral					
	37	Middle occipital gyrus	48	−70	3
	37	Middle temporal gyrus	50	−64	9
	22	Superior temporal gyrus	50	−38	11
	22		−59	−42	9
	39		−53	−59	20
	38		−44	15	−14
		Hypothalamus	−8	−6	−6
			10	−6	−5
		Pulvinar nucleus	−8	−29	1
		Claustrum	32	2	−7
	34	Subcallosal gyrus	−18	5	−15
	47	Inferior frontal gyrus	−46	19	−6
	13		32	13	−14
Angry > neutral					
	6	Precentral gyrus	50	−4	41
		Putamen	20	8	7
			−22	8	7
		Caudate body	12	7	20
			−12	12	10
		Claustrum	−34	−13	4
	31	Precuneus	14	−72	28
	39	Angular gyrus	50	−68	31
	7	Superior parietal lobule	22	−65	55
	40	Inferior parietal lobule	16	−63	60
			−51	−35	42
Disgust > neutral					
	47	Inferior frontal gyrus	−42	18	−14
	38	Superior temporal gyrus	50	8	−10
	18	Middle occipital gyrus	34	−81	1
Neutral > baseline					
	37	Middle occipital gyrus	44	−68	5
	18	Lingual gyrus	−6	−60	5
	37	Fusiform gyrus	−38	−43	−10
	22	Superior temporal gyrus	51	−58	14
	38		−34	5	−19
	3	Postcentral gyrus	−46	−17	−56
	6	Superior frontal gyrus	−8	12	53

Table 1 (*Continued*)

Emotion contrast	*BA*	*Brain regions*	*x*	*y*	*z*
	6		8	17	58
	32	Cingulate gyrus	−12	23	36
	6	Precentral gyrus	50	0	35
	6		−57	−12	41
	6	Middle frontal gyrus	48	2	42
		Amygdala	20	−10	−8
			−20	−6	−10

brain level with EQ for each emotion >neutral contrast. For *happy* faces, the EQ correlated positively with a cluster centered on the parahippocampal gyrus that includes the ventral striatum and substantia nigra (see Figure 4a for group map). A very similar cluster showed a negative correlation to the EQ in response to *sad* faces (see Figure 4b for group). In response to *angry* faces, clusters showing a positive correlation with EQ included the posterior cingulate cortex (BA23), the inferior parietal lobule (BA40), the precuneus (BA31) and the dorsolateral prefrontal cortex (BA9), see Figure 4c. In response to *disgust* faces, the EQ was negatively correlated to a cluster centered on the brainstem that includes the insula (see Figure 4d).

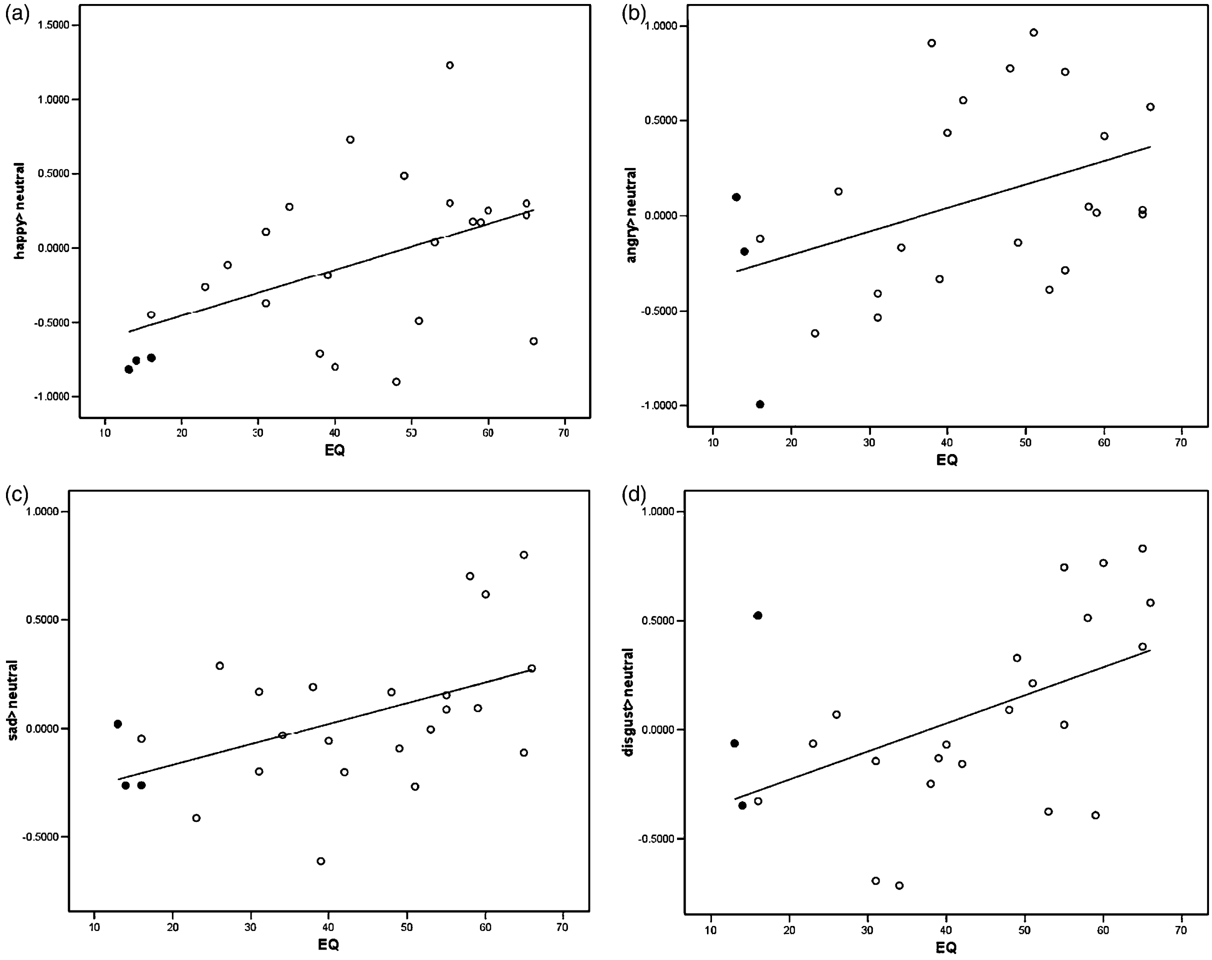

Figure 3 (a–d). The left dorsal IFG-premotor cortex cluster response for the four (emotion >neutral) contrasts plotted against EQ, for (a) happy (b) sad (c) angry, and (d) disgust, respectively. The three participants with HFA/AS are marked with filled dots.

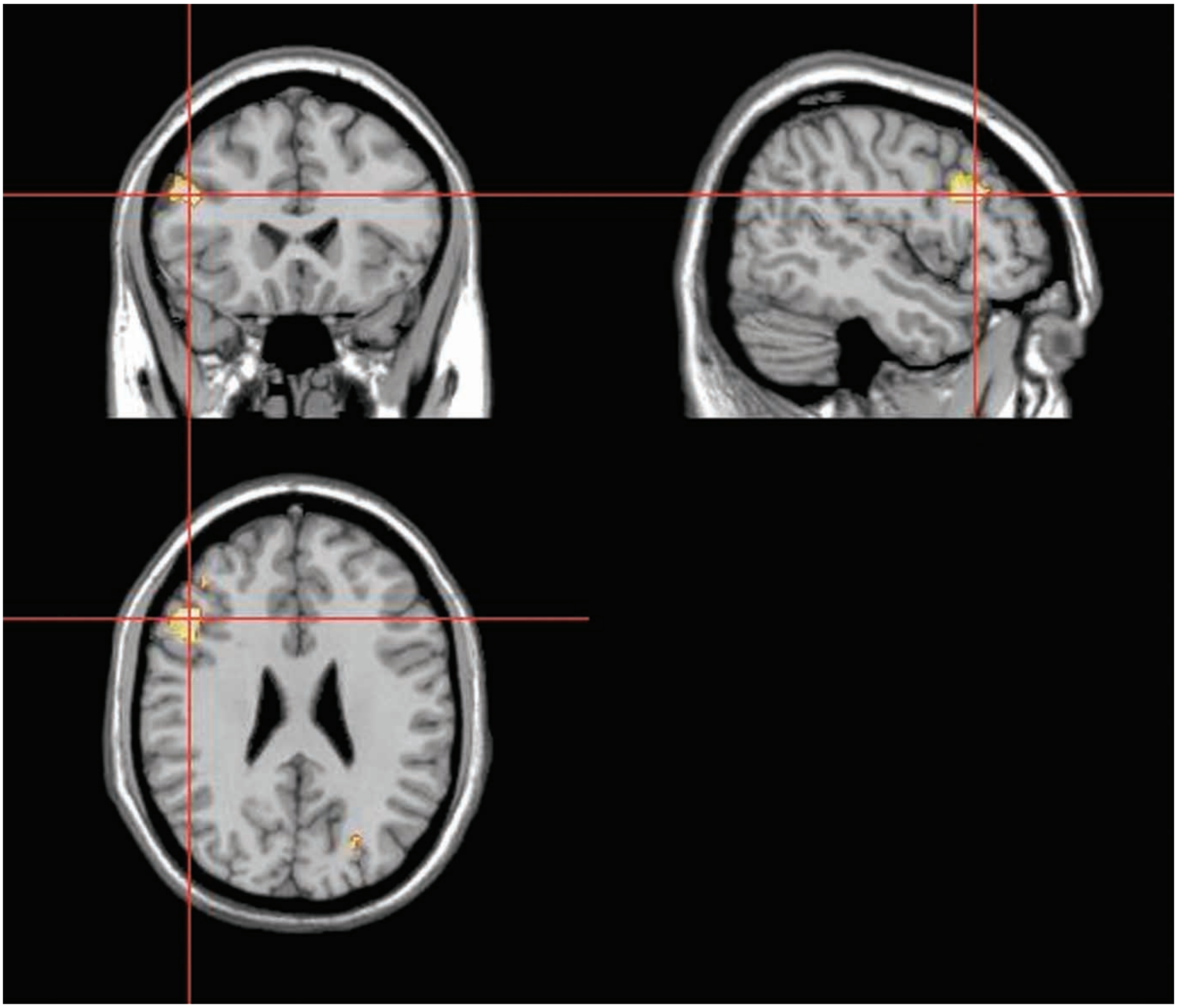

Figure 3. (e) The left dorsal IFG-premotor cortex cluster that shows a common activation in all four (emotion >neutral) vs. EQ correlation maps (cross-hair indicates a local maxima at the following Talairach co-ordinate: −46 20 24).

DISCUSSION

In this study we tested how empathy influences the perception of facial expressions of basic emotions (*happy*, *sad*, *angry*, and *disgusted*). We used two approaches. The first was to test if there was a common brain region, or regions, correlated positively with empathy (EQ), across different

TABLE 2

Correlation of each emotion >neutral contrast with EQ. Number of voxels in each suprathreshold cluster and the Talairach co-ordinates of the centroid of the cluster are indicated. See Appendices 1 and 2 for constitutent voxel co-ordinates for each cluster

	EQ					
Emotion	*Brain area*	*BA*	*Voxels*	*x*	*y*	*z*
Happy >neutral	Parahippocampal gyrus	28	578	−23.3	−16.4	−9.2
Sad >neutral	Parahippocampal gyrus*	28	802	−23.4	−13.0	−6.9
Angry >neutral	Precuneus	31	4039	7.0	−71.8	21.7
	Mid frontal gyrus	9	784	34.8	23.6	32.3
Disgust >neutral	Brain stem*	–	4925	−0.6	−9.9	−2.0

Note: *Indicates a negatively correlated cluster. All clusters significant at $p < .01$, with less than one false positive cluster per map.

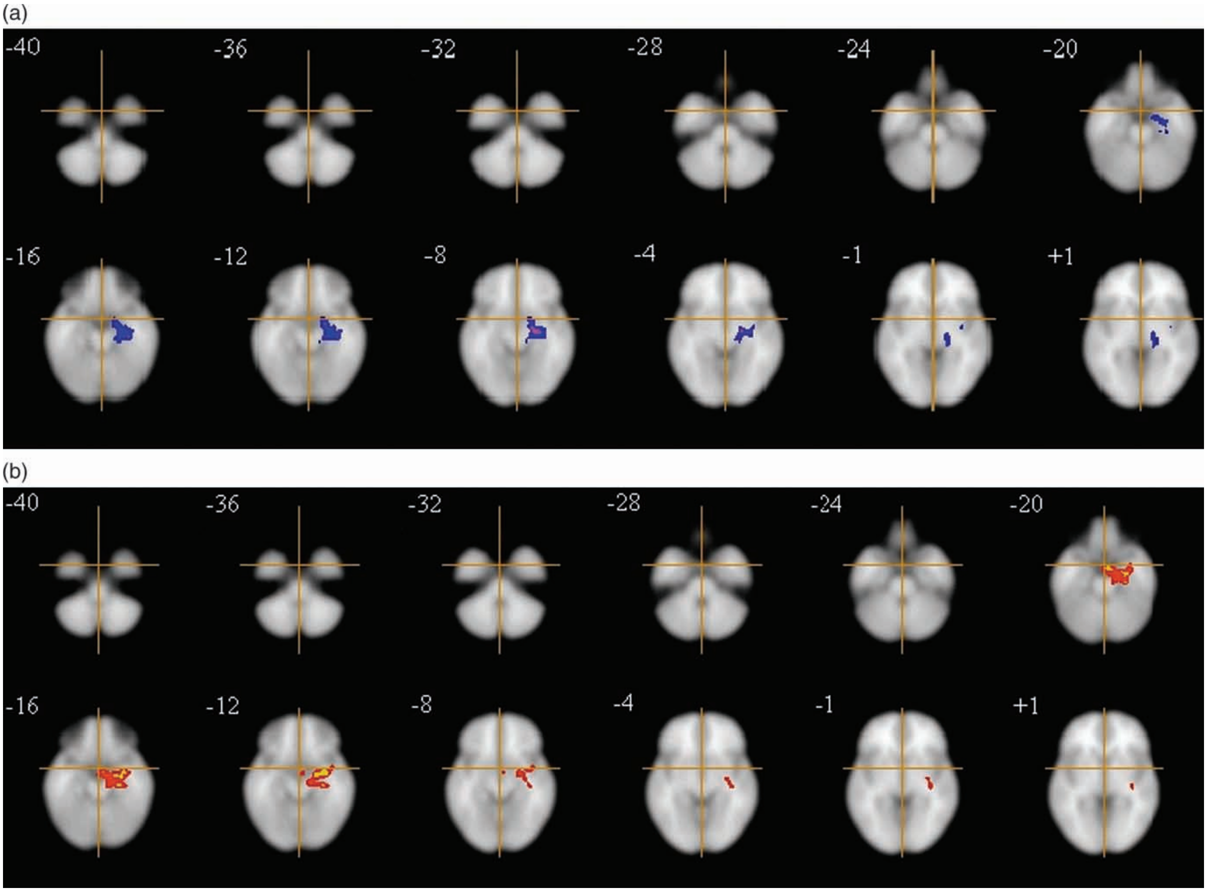

Figure 4 (a–b). Correlation of individual (emotion >neutral) contrasts with EQ. All maps are in standard Talairach space and are thresholded at clusterwise $p < .01$, with less than one false positive cluster per map. Color change indicates regions where the magnitude changes by more than 25% of the maximum value. Image orientation is radiological. (a) Group map of the (happy–neutral) contrast showing clusters that show significant correlation with EQ. (b) Group map of the (sad–neutral) contrast showing clusters that show significant correlation with EQ. (c) Group map of the (angry–neutral) contrast showing clusters that show significant correlation with EQ. (d) Group map of the (disgust–neutral) contrast showing clusters that show significant correlation with EQ.

emotions. We focused our search on certain regions of interest (ROI) derived from earlier studies on ToM and action perception, as possible candidate neural substrates of empathy. This revealed that a cluster including the inferior frontal gyrus and the ventral premotor cortex was positively correlated to EQ across all emotions, confirming earlier reports suggesting a fundamental role of this region in action perception (Hamzei, Rijntjes, Dettmers, Glauche, Weiller, & Buchel, 2003; Johnson-Frey et al., 2003; Rizzolatti et al., 1996). The second aim was to test which brain regions correlated significantly with EQ for each of the four emotions when compared to neutral expressions. A whole-brain cluster-based non-parametric analysis revealed varying spatial patterns of correlation of EQ with the different emotions. These results are discussed in light of the evolutionary function of each emotion and how empathy differently influences the perception of each.

Response to basic emotions

The significant response of the fusiform gyrus and the amygdala to neutral faces compared to the low-level baseline was a landmark activation to suggest that our experiment was working (Chakrabarti & Lawrence, 2004; Kanwisher, McDermott, & Chun, 1997). Individual brain areas responding significantly to each emotion corroborate the previous literature on brain areas involved in discrete emotion perception (Calder

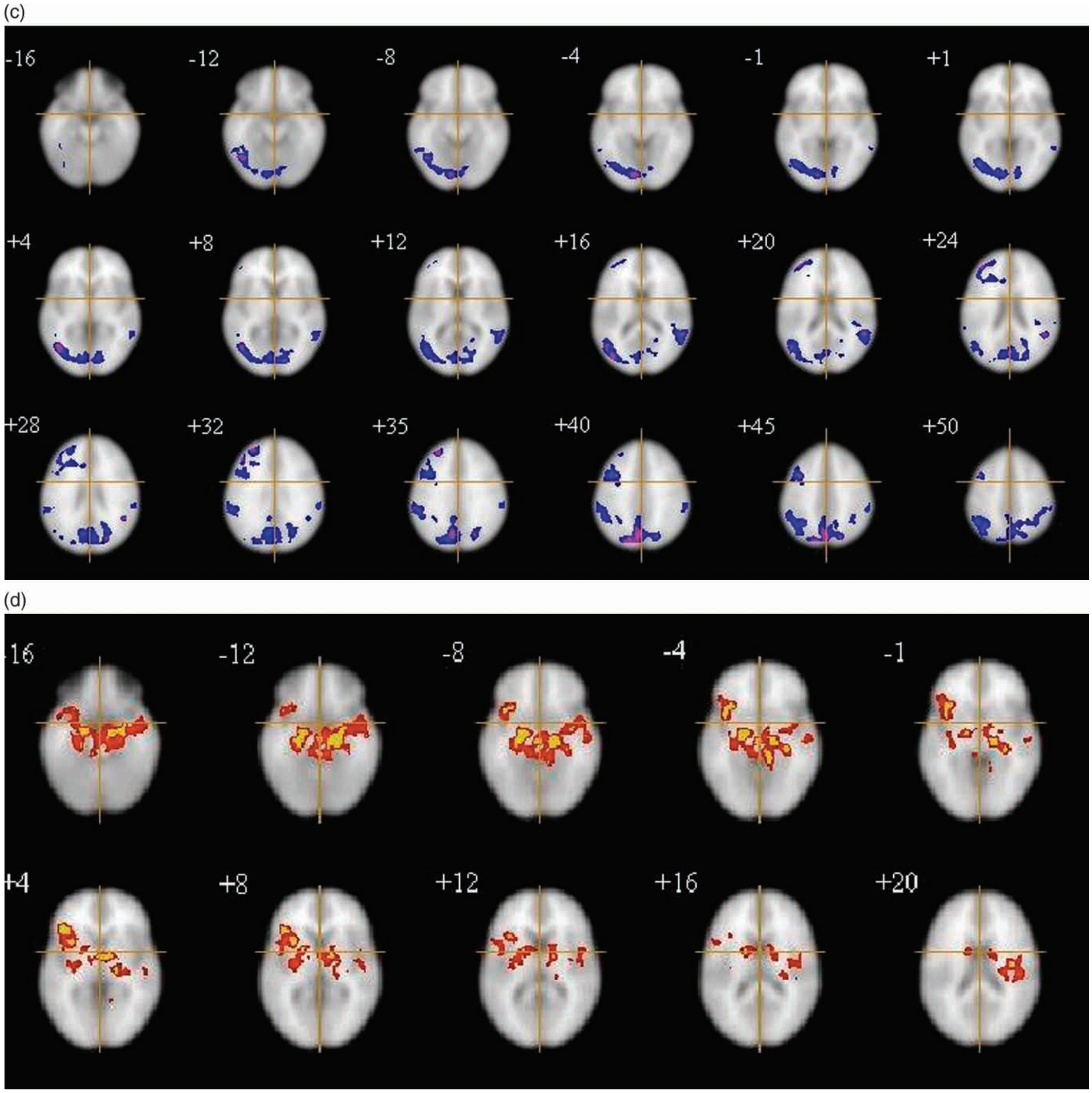

Figure 4 (c–d). (c) Group map of the (angry–neutral) contrast showing clusters that show significant correlation with EQ. (d) Group map of the (disgust–neutral) contrast showing clusters that show significant correlation with EQ.

et al., 2001; Murphy, Nimmo-Smith, & Lawrence, 2003; Phan, Wager, Taylor, & Liberzon, 2002). In particular, for the perception of *happy* faces, the role of the ventral striatal region in reward processing is well established (O'Doherty, 2004; Schultz, Tremblay, & Hollerman, 2000), supporting the hypothesis that *happy* faces are perceived as social rewards in themselves. Recent electrophysiological evidence from humans suggest a significant role for the pre-SMA both in the experience and recognition of happiness (Krolak-Salmon et al., 2006).

A strong activation cluster in the visual areas immediately adjacent to the face processing areas in BA37 in response to *sad* faces suggests that this area may subserve increased attention to *sad* faces, which clearly carries socially important information. The ventromedial prefrontal activation (subcallosal cingulate, inferior frontal gyri) replicates several previous results (Phan et al., 2002). This area has been a prime candidate for being one of the neural substrates of ToM (Frith, 2001). These results support the idea that people engage areas involved in ToM processing to make sense of *sad* faces. Hyperactivity of the hypothalamus occurs in depression (Swaab, Bao, & Lucassen, 2005) in both human and animal studies (Shumake et al., 2001). In the light of this, the observed increased activity in the hypothalamus in response to sad faces points toward a link between the observation and experience of sadness.

The lateral aspects of the precentral gyrus are thought to represent facial muscle movement in macaques, primarily the zygomaticus, in expressions of *anger* and *fear* (McGuinness, Silversten, & Allman, 1980). The activation in this region might point toward the existence of "mirror neurons" (Koski, Iacoboni, Dubeau, Woods, & Mazziotta, 2003). Additionally, bilateral striatal activation was observed. A recent lesion study has suggested a role for the striatum in *angry* face recognition (Calder, Keane, Lawrence, & Manes, 2004). The idea that acts of "appetitive aggression" are motivated by pursuit of rewards (Blanchard & Blanchard, 1989) may explain this apparent overlap between areas involved in *angry* face perception and reward processing.

We restrict our discussion to the regions reported in previous studies of discrete emotion perception and experience, since this part of our experiment aimed to verify that the stimuli used elicited activation in known regions for each emotion. Additional brain regions that survive the threshold are included in Table 1 for completeness, but have not been discussed further since this was not central to our experimental aims.

A common substrate for empathy across emotions

The conjunction analysis for all four (emotion > neutral) vs. EQ correlation plots revealed a significant overlap in the left IFG-premotor cortex. This region is a fundamental part of the "mirror systems" discussed earlier (Keysers & Perrett, 2004; Rizzolatti & Craighero, 2004). Several studies have shown involvement of "mirror systems" during perception of facial expressions (Buccino et al., 2001; Carr, Iacoboni, Dubeau, Mazziotta, & Lenzi, 2003; Dapretto et al., 2006) and actions (Johnson-Frey et al., 2003; Molnar-Szakacs, Iacoboni, Koski, & Mazziotta, 2004) in humans. This fits well with predictions from heuristic models that integrate perception and action (Hurley, 2005). The lower IFG-premotor response to all expressions as a function of trait empathy corroborates similar findings (Dapretto et al., 2006; Nishitani, Avikainen, & Hari, 2004). However, some studies (Carr et al., 2003; Dapretto et al., 2006) have used paradigms involving perception and explicit imitation of facial expressions and did not report any analysis for possible differences between emotions. Our analysis takes these possible differences into account and the IFG-premotor cluster emerges as a candidate region that correlates with empathy, independent of which emotion is being perceived.

This result provides a putative biomarker for empathy, a trait distributed continuously across the general population, with people with ASC clustering toward the low end (Baron-Cohen & Wheelwright, 2004). This suggests that EQ could constitute a useful endophenotypic parameter (Gottesman, Psych, & Gould, 2003) to study ASC. In contrast to the standard quantitative measures used in similar correlational design studies, such as the ADOS-G or the ADI-R (Lord et al., 1989; Lord, Rutter, & Le Couteur, 1994), which are targeted specifically at people with ASC, EQ has a larger range, no known ceiling effects and a quasi-normal distribution of scores in the general population.

Empathy influences the perception of each emotion differently

The whole-brain analysis of correlation for each (emotion > neutral) contrast with EQ revealed different regions that correlated with EQ for different emotions. Specifically, for perception of *happy* faces, a parahippocampal–midbrain–ventral striatal cluster response correlated positively with EQ. The role of this region in reward processing is well known (O'Doherty, 2004). This suggests that the more empathic a person is, the higher their reward response to a *happy* face. Interestingly, the response from the same region correlated negatively with EQ during perception of *sad* faces. This fits with the earlier results, i.e., the more empathic a person is, the lower their reward response to a *sad* face.

For *happy* and *sad* faces, therefore, empathizing seems to involve "mirroring." The higher a person's EQ, the stronger the reward response to *happy* faces and the weaker the reward response for *sad* faces. This is in concordance with earlier studies on *pain* (Singer, Seymour, O'Doherty, Kaube, Dolan, & Frith, 2004) and *disgust* perception (Wicker et al., 2003), where observation and experience were shown to be mediated by an overlapping set of structures. Both these studies focused on negative emotional stimuli and hence might have involved a potential confound with "personal distress." (A negative emotional expression of disgust/pain can be distressing by itself, as can be the experience of a painful stimulus or a disgusting odor.) The novel element in our study is that we specifically tested empathizing in relation to perception of specific emotions including both positive and negative basic emotions.

However, empathizing does not simply involve mirroring. During perception of *angry* faces, EQ correlated positively to clusters centered on the precuneus/inferior parietal lobule and the dorsolateral prefrontal cortex. The posterior cingulate/precuneus is involved in the self–other distinction and judgment of intentions (den Ouden, Frith, Frith, & Blakemore, 2005; Vogt, 2005). This suggests that higher EQ may correspond to higher activation in areas related to the distinction of self vs. other, as well as those recruited to determine another person's intentions. The dorsolateral prefrontal cortex is known for its role in decision making and context evaluation, in addition to response inhibition (Rahm et al., 2006; Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004). Higher EQ should therefore predict better evaluation of threat from an *angry* expression. Since expressions of *anger* are usually more socially urgent than are either *sadness* or *happiness*, it makes evolutionary sense that a highly empathic person does not merely mirror the expression. A high empathizer's perception of an *angry* face will by definition be accompanied by an accurate identification of the person's intentions as well as an evaluation of the posed threat.

In response to *disgust* faces, a cluster including the posterior superior temporal gyrus and medial prefrontal cortices was negatively correlated with EQ, suggesting that the areas involved in attribution of mental states (primarily required for deciphering the "complex" emotions) are selectively recruited less by people of high EQ. This is what might be expected, since *disgust* as an emotion is less interpersonal than *anger* or *sadness*, so resources for decoding complex emotional signals need not be utilized to the same extent. Interestingly, this cluster also includes the insula bilaterally. Given the well-established role of this region in processing *disgust*, this was a surprising result. We expected that an increased ability to empathize would result in an increased response to *disgust* faces. The negative correlation suggests that people with high EQ have a lower insula response to *disgust* expressions. A re-examination of the literature on *disgust* sensitivity reveals a similar result (Haidt, McCauley, & Rozin, 1994) where it was reported that increased socialization leads to lower *disgust* sensitivity. It might be that individuals with high EQ socialize more than those with low EQ, and are therefore able to regulate their true *disgust* response to another person's expression of *disgust*. This result needs to be understood better.

Common and discrete neural substrates of empathy

Comparing the results from the conjunction analysis (showing a common neural substrate of EQ across different emotions) with those from the whole brain analysis (showing varying spatial patterns of correlation of EQ with different emotions) shows that there are both common regions, which underlie empathy across different emotions, and regions specific to certain emotions.

We interpret this using a model of face processing (Haxby, Hoffman, & Gobbini, 2000) applied to a discrete-emotions framework (see Figure 5a). At its simplest, the model proposes a core visual system for face perception. This constitutes the inferior occipital gyrus (for low-level facial feature analysis), the lateral fusiform gyrus (for higher-order invariant aspects of faces such as identity) and the superior temporal sulcus (for variable aspects of faces such as lip movement and speech comprehension). This then interacts with an extended system, which involves different structures for different emotions (Haxby, Hoffman, & Gobbini, 2002). Focusing specifically on perception of dynamic facial expressions of emotion, we propose that an intermediate module for action perception is involved, in line with similar suggestions from others (Gallese, 2003; Keysers & Perrett, 2004; Preston & de Waal, 2000; Rizzolatti & Craighero, 2004), see Figure 5b.

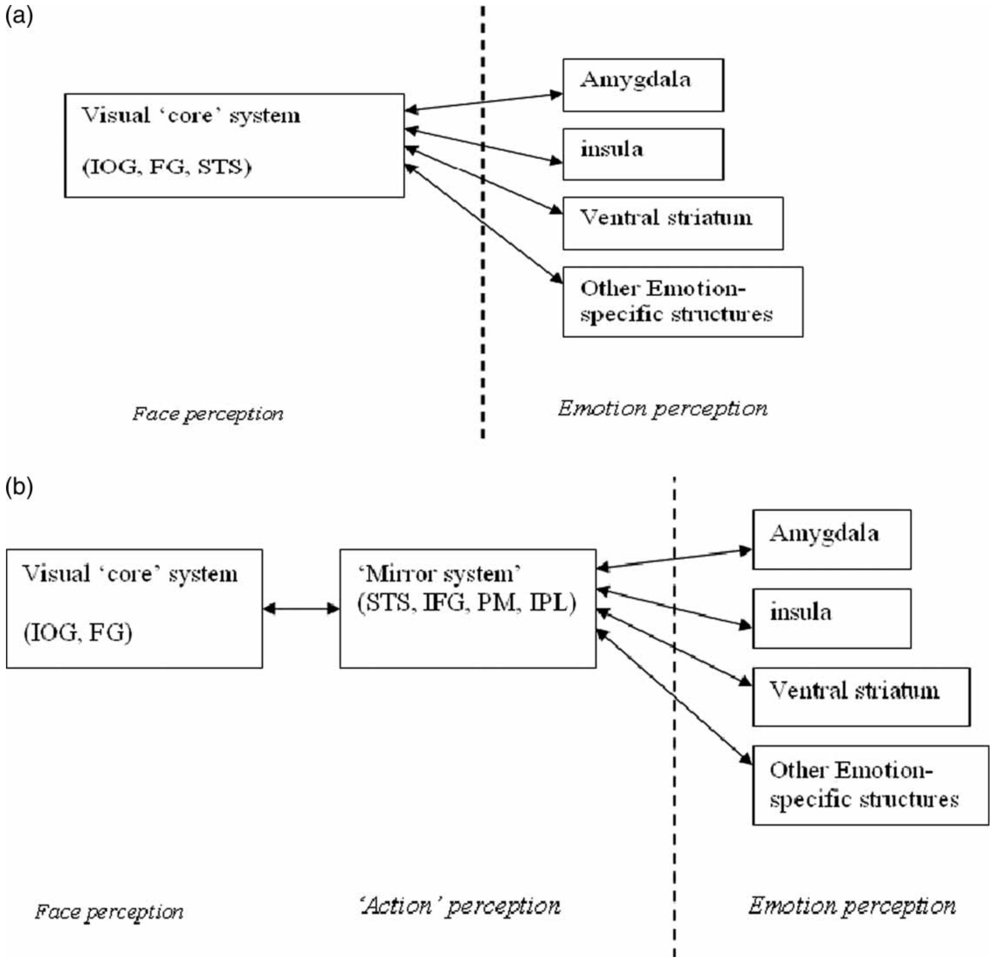

Figure 5. (a) The original model for face perception proposed by Haxby, Hoffman, and Gobbini (2000) applied to a discrete-emotions framework (adapted from Haxby et al., 2000). (b) Suggested modifications to the model, specifically for perception of facial expressions of emotion, incorporating a module for "action perception." See text for discussion.

Focusing on the left of the dotted line in Figure 5b shows the processes that are equally influenced by trait empathy across all emotions. This includes the regions involved in face perception and the fundamental "mirror" systems used for action perception. This is revealed by the conjunction analysis, which shows a cluster that includes the inferior frontal gyrus–premotor cortex. The common element between different facial expressions of emotion is the fact that they involve movement of eyes and mouth, which are possibly coded for by generic "mirror systems" used for action perception. However, on investigating the interaction of each emotion with empathy, we move over to the right hand side of the dotted line, which gives us emotion-specific correlation maps, in accordance with the discrete emotions model. We have interpreted these in light of their evolutionary function. It is worth noting, though, that we do not propose a strict temporal sequence of activation from left to right of this model, neither do we represent subcortical pathways from the visual areas to the emotion-related structures. As in the original model, several of these regions are reciprocally connected and the temporal progression of activation could be mediated through reafferent projections (Iacoboni et al., 2001). These can be investigated through methods that allow better temporal resolution (e.g., MEG) and forward-model-based connectivity analysis (e.g., Dynamic Causal Modeling; Friston, Harrison, & Penny, 2003).

CONCLUSIONS

To our knowledge, this is the first study to investigate the influence of trait empathy on perception of different basic emotion expressions (*happy*, *sad*, *disgusted*, *angry*). Using a whole-brain analysis, we found different brain regions correlated with EQ, depending on which emotion was being perceived. This is in keeping with the suggestion that different basic emotions have relatively independent evolutionary antecedents (Panksepp, 1998) and social-communicative functions (Izard & Ackerman, 2000). Using a hypothesis-driven analysis for ROIs, we showed that a cluster in the left dorsal inferior frontal gyrus–premotor cortex correlated positively with trait empathy (as measured by EQ) independent of which emotion expression is being perceived. This region is an important part of proposed ''mirror-systems'' in the brain that mediate perception and recognition of actions and emotions (Gallese, 2003; Rizzolatti & Craighero, 2004).

This region could therefore constitute an emotion-independent biomarker for trait empathy and hence be an interesting candidate for psychopathological conditions marked by empathy disability (e.g., ASC). The biological basis of individual differences in empathy still remains to be fully determined. We suspect that such individual differences reflect both genetic (Chakrabarti, Kent, Suckling, Bullmore, & Baron-Cohen, 2006), endocrine (Knickmeyer, Baron-Cohen, Raggatt, Taylor, 2005; Chapman, Baron-Cohen, Auyeung, Knickmeyer, Taylor, & Hackett, 2006), and environmental (Bowlby, 1969) influences. The relative contributions from each constitute important questions for future research.

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APPENDIX 1

Voxel co-ordinates in Talairach space for significant clusters in each (emotion > neutral) vs. EQ correlation analysis. Putative Brodmann areas (BA) are indicated where applicable. Co-ordinates are reported with ascending *z* values (along the inferior–superior axis)

		Talairach co-ordinates		
Brain region	*BA*	*x*	*y*	*z*
(a) Happy > neutral vs. EQ: One positively correlated cluster				
Parahippocampal gyrus	34	−23.4	−10.2	−20.0
Parahippocampal gyrus	28	−30.8	−24.4	−20.0
Parahippocampal gyrus	28	−25.6	−15.5	−16.0
Parahippocampal gyrus	28	−24.9	−14.9	−12.0
Parahippocampal gyrus	28	−22.9	−14.1	−8.0
Putamen/Pallidum	–	−24.3	−17.8	−4.0
Claustrum	–	−35.2	−10.4	−1.0
Midbrain	–	−17.1	−24.9	−1.0
Thalamus/midbrain	–	−16.8	−24.7	1.0
Thalamus	–	−16.5	−21.6	4.0
Thalamus	–	−16.8	−21.1	8.0
Putamen	–	−18.7	−21.3	12.0
(b) Sad > neutral vs. EQ: One negatively correlated cluster				
Parahippocampal gyrus	34	−17.9	−11.0	−20.0
Parahippocampal gyrus	28	−20.2	−11.9	−16.0
Hippocampus	–	−26.6	−11.9	−12.0
Cingulate gyrus	25	−3.8	−6.4	−12.0
Insula	–	−32.7	−7.9	−8.0
Brain stem	–	−5.0	−5.0	−8.0
Insula	–	−35.0	−18.0	−4.0
Insula	–	−34.8	−18.9	−1.0
Putamen/Globus pallidus	–	−35.1	−22.6	1.0
Insula	–	−33.0	−22.0	4.0
Putamen	–	−26.0	−7.0	8.0
Thalamus	–	−23.1	−19.9	8.0
Putamen	–	−22.9	−6.2	12.0
Putamen	–	−24.5	−19.8	12.0
Caudate nucleus	–	−23.6	−14.3	16.0
Postcentral gyrus	43	−24.6	−15.6	20.0
Cingulate gyrus	33	−21.0	−8.0	24.0
Cingulate gyrus	23	−26.6	−21.0	24.0
(c) Angry > neutral vs. EQ: Two positively correlated clusters				
Fusiform gyrus	37	41.5	−45.0	−16.0
Cerebellum	–	36.0	−71.0	−16.0
Fusiform gyrus	37	41.1	−61.7	−12.0
Lingual gyrus	18	3.0	−82.	−12.0
Inf temporal gyrus	37	53.7	−50.4	−8.0
Lingual gyrus	18	20.7	−75.7	−8.0
Inf temporal gyrus	37	58.4	−50.8	−4.0
Lingual gyrus	19	21.3	−79.7	−4.0
Mid occipital gyrus	19	50.7	−72.7	−4.0
Lingual gyrus	18	−12.4	−76.0	−4.0
Lingual gyrus	18	27.0	−77.8	−1.0
Lingual gyrus	18	−11.1	−80.1	−1.0
Inf occipital gyrus	18	27.6	−77.7	1.0
Lingual gyrus	18	−11.1	−82.1	1.0
Cuneus	18	16.4	−79.5	4.0
Mid temporal gyrus	21	49.0	−51.0	8.0
Cuneus (Rad Opt)	17	12.6	−80.0	8.0
Mid frontal gyrus	10	32.0	49.3	12.0
Mid occipital gyrus	19	39.5	−74.8	12.0

APPENDIX (*Continued*)

		Talairach co-ordinates		
Brain region	*BA*	*x*	*y*	*z*
Cingulate gyrus	23	−20.0	−58.0	12.0
Cuneus (Rad Opt)	17	−5.3	−81.1	12.0
Sup frontal gyrus	10	31.7	47.1	16.0
Mid temporal gyrus	19	41.0	−74.0	16.0
Cingulate gyrus	23	−20.0	−58.0	16.0
Cingulate gyrus	31	−14.0	−74.6	16.0
Cuneus	18	5.7	−81.0	16.0
Mid frontal gyrus	10	31.6	45.0	20.0
Mid temporal gyrus	19	42.0	−72.7	20.0
Cingulate gyrus	23	−21.0	−59.0	20.0
Cuneus	18	5.3	−79.0	20.0
Mid occipital gyrus	18	−20.9	−79.3	20.0
Mid frontal gyrus	9	28.9	32.1	24.0
Cuneus	18	−6.7	−75.8	24.0
Med temporal gyrus	39	46.4	−69.0	24.0
Cuneus	19	21.3	−84.7	24.0
Mid frontal gyrus	46	29.9	30.1	28.0
Inf parietal	40	−61.3	−33.4	28.0
Cuneus	18	−6.1	−74.4	28.0
Mid temporal gyrus	39	49.0	−69.0	28.0
Sup occipital gyrus	19	39.8	−77.8	28.0
Sup occipital gyrus	19	23.0	−84.4	28.0
Mid frontal gyrus	9	27.3	42.0	32.0
Mid frontal gyrus	9	42.0	29.7	32.0
Mid frontal gyrus	9	27.5	25.5	32.0
Inf frontal gyrus	44	42.6	12.1	32.0
Supramarginal gyrus	40	−61.3	−33.4	32.0
Precuneus	7	7.5	−51.1	32.0
Cuneus	19	−23.6	−68.9	32.0
Cuneus	19	7.1	−76.1	32.0
Mid frontal gyrus	9	27.0	40.7	35.0
Mid frontal gyrus	9	41.7	13.1	35.0
Precentral gyrus	6	30.7	−3.3	35.0
Inf parietal	40	−61.1	−32.7	35.0
Precuneus	7	10.3	−73.1	35.0
Cuneus	19	−24.4	−72.0	35.0
Mid frontal gyrus	8	28.5	38.0	40.0
Mid frontal gyrus	9	39.9	8.3	40.0
Inf parietal	40	−60.1	−35.5	40.0
Precuneus	7	1.6	−72.7	40.0
Mid frontal gyrus	6	39.5	8.0	45.0
Inf parietal	40	−57.8	−37.3	45.0
Inf parietal	40	−37.0	−52.0	45.0
Precuneus	7	−0.9	−69.6	45.0
Mid frontal gyrus	6	39.8	8.1	50.0
Precuneus	7	−16.3	−60.9	50.0
Sup parietal	7	−32.1	−54.1	55.0
Sup parietal	7	−1.0	−61.3	55.0
Postcentral gyrus	5	−43.8	−41.1	60.0
Postcentral gyrus	7	−1.1	−55.3	60.0
Postcentral gyrus	7	−20.9	−57.8	60.0
(d) Disgust >neutral vs. EQ: One negatively correlated cluster				
Mid temporal gyrus	21	40.3	7.8	−28.0
Sup temporal gyrus	38	39.0	7.8	−24.0
Hippocampus	–	27.8	−3.2	−20.0
Parahippocampal gyrus	34	−16.7	−12.9	−20.0
Parahippocampal gyrus	28	−2.2	−10.7	−16.0
Sup temporal gyrus	38	37.7	15.0	−12.0
Parahippocampal gyrus	28	−20.2	−17.1	−12.0

APPENDIX (*Continued*)

Brain region	*BA*	*Talairach co-ordinates* *x*	*y*	*z*
Parahippocampal gyrus	28	22.9	−17.8	−12.0
Insula	–	37.7	14.1	−8.0
Brain stem	–	−9.8	−20.3	−8.0
Insula	–	38.8	17.3	−4.0
Insula	–	−33.9	−6.5	−4.0
Brain stem	–	0.1	−24.4	−4.0
Mid temporal gyrus	21	−55.9	−17.3	−4.0
Inf frontal gyrus	47	39.4	18.2	−1.0
Parahippocampal gyrus	27	−19.2	−19.9	−1.0
Putamen/Globus pallidus	–	15.8	−11.9	−1.0
Putamen/Globus pallidus	–	−24.0	−9.0	−1.0
Insula	–	33.2	−19.2	−1.0
Sup temporal gyrus	21	−56.0	−18.7	−1.0
Brain stem	–	6.0	−35.4	−1.0
Lingual gyrus	19	−13.0	−52.0	−1.0
Inf frontal gyrus	47	39.3	18.2	1.0
Thalamus	–	−11.5	−15.8	1.0
Putamen/Globus pallidus	–	32.4	−17.4	1.0
Lingual gyrus	19	−13.2	−52.4	1.0
Insula	–	38.2	17.0	4.0
Putamen/Globus pallidus	–	18.9	2.5	4.0
Thalamus	–	−3.8	−6.1	4.0
Insula	–	30.2	−15.4	4.0
Putamen	–	−23.1	−21.5	4.0
Sup temporal gyrus	22	−52.4	−21.8	4.0
Lingual gyrus	18	−12.7	−54.7	4.0
Inf frontal gyrus	44	38.2	14.2	8.0
Putamen	–	25.6	−7.8	8.0
Thalamus	–	−12.6	−9.0	8.0
Thalamus	–	12.7	−6.7	8.0
Sup temporal gyrus	22	−47.4	−13.9	8.0
Insula	–	34.0	16.1	12.0
Precentral gyrus	6	47.0	6.1	12.0
Thalamus	–	−14.5	−2.7	12.0
Putamen	–	21.2	−5.1	12.0
Precentral gyrus	6	−48.2	−5.1	12.0
Insula	43	−36.0	−9.0	12.0
Caudate nucleus	–	−19.4	−28.0	12.0
Insula	–	34.2	17.8	16.0
Insula	–	51.3	10.8	16.0
Thalamus	–	−15.3	−1.8	16.0
Thalamus	–	13.9	0.7	16.0
Postcentral gyrus	33	−41.3	−12.0	16.0
Caudate nucleus	–	−27.7	−26.3	16.0
Cingulate gyrus	33	13.4	−0.3	20.0
Cingulate gyrus	40	−15.4	−4.0	20.0
Postcentral gyrus	2	−38.7	−20.1	20.0
Postcentral gyrus	–	−43.3	−22.3	24.0
Inf parietal	40	−48.5	−23.1	28.0
Postcentral gyrus	2	−52.3	−21.5	32.0
Supramarginal gyrus	40	−41.4	−30.0	32.0
Postcentral gyrus	1	−51.9	−20.4	35.0

APPENDIX 2

Voxel co-ordinates (in standard MNI space) used for fROI analysis. Wherever the original study reported co-ordinates in Talairach space, corresponding MNI co-ordinates were calculated using a non-linear transformation (tal2mni, available at http://imaging.mrc-cbu.cam.ac.uk/imaging/MniTalairach)

MPFC				*IFG*				*IPL*				*TPJ/post-STS*				*PM*			
	x	*y*	*z*		*x*	*y*	*z*		*x*	*y*	*z*		*x*	*y*	*z*		*x*	*y*	*z*
(±)	3	53	29	(±)	52	22	10	(±)	42	−52	24	(±)	51	−54	27	(±)	50	6	52
(±)	4	60	36	(±)	48	2	4	(±)	52	−26	20	(±)	54	−60	21	(±)	48	10	26
(±)	10	60	12	(±)	47	8	6	(±)	50	−47	28	(±)	57	−52	14	(±)	48	−2	34
(±)	8	52	22	(±)	34	36	6	(±)	54	−48	20	(±)	42	−66	14	(±)	56	−2	40
				(±)	56	10	22					(±)	56	−30	18				

Note: MPFC = medial prefrontal cortex, IFG = inferior frontal gyrus, IPL = inferior parietal lobule, post-STS/TPJ = posterior superior temporal sulcus/temporo-parietal junction, PM = premotor cortex.