

## Relating Anatomical and Social Connectivity: White Matter Microstructure Predicts Emotional Empathy

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**Understanding cues to the internal states of others involves a widely distributed network of brain regions. Although white matter (WM) connections are likely crucial for communication between these regions, the role of anatomical connectivity in empathic processing remains unexplored. The present study tested for a relationship between anatomical connectivity and empathy by assessing the WM microstructural correlates of affective empathy, which promotes interpersonal understanding through emotional reactions, and cognitive empathy, which does so via perspective taking. Associations between fractional anisotropy (FA) and the emotional (empathic concern, EC) and cognitive (perspective taking, PT) dimensions of empathy as assessed by the Interpersonal Reactivity Index were examined. EC was positively associated with FA in tracts providing communicative pathways within the limbic system, between perception and action-related regions, and between perception and affect-related regions, independently of individual differences in age, gender, and other dimensions of interpersonal reactivity. These findings provide a neuroanatomical basis for the rapid, privileged processing of emotional sensory information and the automatic elicitation of responses to the affective displays of others.**

**Keywords:** diffusion tensor imaging, empathy, mirror neurons, social cognition, superior longitudinal fasciculus

### Introduction

Understanding cues to the internal states of others is central to normal human functioning. Past research suggests that there are 2 ways to process these cues: Through visceral, affective reactions (i.e., emotional empathy or “feeling” for others) and through more reasoned, cognitive responses (i.e., cognitive empathy or understanding how others might think or feel; Davis 1983a; De Waal 2007). Individuals vary substantially in how much they experience empathy in everyday life, and more specifically, in the relative frequency with which they use emotional or cognitive strategies to understand cues to the internal experiences of others (Davis 1983a). Although both emotional and cognitive aspects of empathy are thought to rely on networks of widely distributed cortical areas that interact via long-range white matter (WM) connections (Carr et al. 2003; Zaki and Ochsner 2012), the role of anatomical connectivity in empathy remains largely unexplored. The current study sought to test whether individuals with the capacity and predisposition to empathize with others exhibit structural differences in anatomical connectivity and further, to identify the characteristics of WM microstructure that underlie individual differences in the tendency to employ cognitive and emotional empathy to understand others.

Behavioral evidence strongly suggests that cognitive and emotional empathy are subserved by distinct systems (De Waal 2007). Cognitive empathy undergoes a protracted

development in humans (Decety and Jackson 2004; Saxe et al. 2004) and appears to comprise an evolutionarily recent capacity, as it is observable in great apes (De Waal 2007) but not in other primates (Cheney and Seyfarth 1990). Cognitive empathy requires considerable mental sophistication and resources, as it requires that we simultaneously keep in mind and distinguish between multiple possible perspectives on a given situation (Decety and Jackson 2004; Decety and Lamm 2007). By contrast, emotional empathy often does not require a self-other distinction (De Waal 2007). Emotional forms of empathy appear to rely on phylogenetically ancient mechanisms, as they are present even in rodents (Langford et al. 2006), and may comprise an innate tendency in humans, as emotion contagion is observable even during the first day of life (Singer 2006). Additionally, while emotional empathy is characterized by fast, automatic reactions (Dimberg et al. 2000), cognitive perspective taking comprises a more effortful, reasoned process similar to nonsocial forms of perspective taking (e.g., visuospatial perspective taking; Aichhorn et al. 2006; Hamilton et al. 2009) and is likely reliant on more domain-general computations (Decety and Lamm 2007). Cognitive and emotional forms of empathy can also be clinically dissociated. For instance, in psychopathy, emotional empathy is compromised, but cognitive perspective taking abilities are preserved (Soderstrom 2003).

Consistent with behavioral dissociations, distinct neural systems appear to support cognitive and emotional aspects of empathy. Emotional empathic responses seem to rely on activity in the putative human mirror neuron system (hMNS; Iacoboni and Dapretto 2006) or action observation network (AON; Grafton et al. 1996)—the inferior frontal gyrus (IFG; Carr et al. 2003; Pfeifer et al. 2008), inferior parietal lobule (Gazzola et al. 2006), and posterior superior temporal sulcus (pSTS; Carr et al. 2003)—as well as the insula and amygdala (Carr et al. 2003). Contrastingly, tasks eliciting cognitive empathic responses (e.g., mentalizing, perspective taking) preferentially recruit the medial prefrontal cortex (MPFC; Mitchell et al. 2005; Amodio and Frith 2006), temporoparietal junction (TPJ; Saxe and Kanwisher 2003), pSTS, and temporal poles (Frith 2001; for a review see Zaki and Ochsner 2012) rather than core AON/hMNS or limbic areas. While cognitive forms of empathy are sometimes associated with AON/hMNS activity (e.g., Montgomery et al. 2009), emotional empathic responses appear to recruit the AON/hMNS more strongly than cognitive empathic responses (Nummenmaa et al. 2008), consistent with a central role for linking action perception and production in emotional empathy. Neuropsychological evidence also suggests that distinct cortical regions contribute to emotional and cognitive forms of empathy. Patients with lesions to the MPFC have low self-reported cognitive

empathy, but have emotional empathy scores within the normal range, whereas patients with IFG lesions report low emotional empathy, but have cognitive empathy scores within the normal range (Shamay-Tsoory et al. 2009). Thus, converging evidence from comparative and developmental cognition, clinical populations, and neuroimaging studies suggests that emotional and cognitive empathic responses are subserved by distinct neural systems.

While a growing body of evidence suggests that empathy is not a unitary construct, only one personality scale is rooted in a multidimensional conceptualization of empathy (Konrath et al. 2011): The Interpersonal Reactivity Index (IRI; Davis 1980). The IRI was designed to assess 2 affective (empathic concern, EC; personal distress, PD) and 2 cognitive (fantasy scale, FS; perspective taking, PT) constructs related to interpersonal reactivity. EC and PT are of primary interest to the present study as they correspond most clearly to common conceptualizations of emotional and cognitive empathy, respectively (Baron-Cohen and Wheelwright 2004; Lawrence et al. 2004). Consistent with this assertion, PT is the IRI subscale most correlated with the Hogan Empathy Scale (Hogan 1969), a widely used measure of cognitive empathy ( $r=0.42$  for males;  $r=0.37$  for females; Davis 1983a), whereas EC is the subscale most related to the Questionnaire Measure of Emotional Empathy (QMEE; Mehrabian and Epstein 1972), a popular measure of emotional empathy ( $r=0.63$  for males;  $r=0.56$  for females; Davis 1983a). In particular, EC is considered to be the most prototypical dimension of empathy and remains the subscale most often used to study empathy (Konrath et al. 2011). EC has repeatedly been associated with prosocial behavior in both naturalistic and laboratory settings (Davis 1983b; Unger and Thumhuri 1997; Eisenberg et al. 2002; Wilhelm and Bekkers 2010). Consistent, robust associations with spontaneous helping behavior appear to be specific to EC (Davis 1983b; Konrath et al. 2011). When people are reminded to adopt the perspectives of those in need, the PT subscale also predicts prosocial behavior (Davis 1983b). Additionally, low PT scores predict antisocial behavior. Criminal offenders score lower than nonoffenders on PT, but not on any other subscale of the IRI (Jolliffe and Farrington 2004).

Neither FS nor PD appears to have consistent antisocial or prosocial behavioral correlates (Konrath et al. 2011), perhaps because they measure constructs that are related, rather than identical, to empathy—imagination and emotion regulation, respectively (Baron-Cohen and Wheelwright 2004; Lawrence et al. 2004; Stueber 2008). In contrast to EC and PT, which measure other-oriented reactions to social information, PD and FS subscale items concern self-oriented reactions that can occur in response to nonsocial information: 5 of the 7 PD subscale items do not mention other people (e.g., “In emergency situations, I feel apprehensive and ill-at-ease”), and all FS items relate to engaging with fictional characters in books and movies. Additionally, while FS and PT scores are sometimes summed to obtain a measure of cognitive empathy, Davis (1983b) later determined that FS “is more a measure of emotional than cognitive empathy” based on its correlations with other IRI subscales and with measures of emotionality, and has recommended against summing IRI subscales to obtain composite empathy scores (D’Orazio 2004). In sum, PT and EC closely correspond to classical definitions of cognitive and emotional empathy, while FS and PD assess self-oriented reactions not specific to social information and may

not comprise valid approximations of empathy in itself (Baron-Cohen and Wheelwright 2004; Lawrence et al. 2004; Stueber 2008). PT and EC subscales are most related to cognitive and emotional empathic responses to other people as measured by existing self-report measures, by the content of their constituent items and by their real-world behavioral correlates. Thus, in order to characterize the patterns of anatomical connectivity specifically related to cognitive and emotional empathy, our primary analyses involved probing the WM microstructural correlates of PT and EC scores.

While the neural systems thought to support empathy rely on the coupling of activity between distant brain regions, the anatomical characteristics that support this coupling have not yet been well characterized. Rapid coupling of far-off brain regions (e.g., between frontal areas implicated in motor planning and parietal areas implicated in action representation) may be particularly central to emotional empathy. Individuals high in emotional empathy as assessed by the QMEE (Mehrabian and Epstein 1972), which corresponds to the EC subscale of the IRI (Davis 1983a), tend to rapidly and automatically mimic observed facial expressions of emotion more than individuals low in emotional empathy (Sonnby-Borgström 2002; Dimberg et al. 2011). Moreover, emotional resonance is characterized not only by after the fact mimicry, but also by the synchronization of postures, movements, facial expressions, and vocalizations, necessitating rapid coupling between perception and action (Hatfield et al. 1993). However, the anatomical pathways that support this coupling remain unexplored. More specifically, it is unknown whether people with the capacity and predisposition to empathize with others exhibit structural differences in WM architecture compared with individuals lower in empathy, and whether specific kinds of empathic tendencies—i.e., tending to empathize emotionally or to engage in cognitive perspective taking to understand others—are rooted in specific patterns of anatomical connectivity.

While linking anatomical connectivity with behavioral outcomes has received increased attention recently, most research has focused on characterizing the consequences of disruptions to WM connectivity associated with lesions, clinical conditions, or developmental disorders (Catani and Mesulam 2008; Loui et al. 2009; Whitfield-Gabrieli et al. 2009; Cheon et al. 2011; Jou et al. 2011). Far less is known about how graded individual differences in behavior relate to anatomical connectivity among healthy individuals (Loui, Li, Hohmann, et al. 2011). While local hypoconnectivity tends to be associated with functional deficits in domains of cognition supported by a given set of anatomical connections, hyperconnectivity often supports above average functioning in those domains (Loui, Li, Hohmann, et al. 2011). For instance, individuals with tone deafness, characterized by mismatches between the perception and production of auditory pitch, exhibit abnormally reduced WM connectivity of the right arcuate fasciculus (Loui et al. 2009), an association fiber tract comprising part of the superior longitudinal fasciculus (SLF) that connects superior temporal regions implicated in pitch perception and inferior frontal regions implicated in pitch production. Contrastingly, individuals with absolute pitch (i.e., who can name and reproduce any given auditory pitch without a reference; Miyazaki 1989) exhibit hyperconnectivity in portions of the SLF (Loui, Li, Hohmann, et al. 2011).

Because emotional empathy relies on an analogous coupling of regions implicated in action production and

perception, it was predicted that individual differences in EC would be associated with local differences in anatomical connectivity between AON/hMNS regions. More specifically, because vocal expressions of emotion (i.e., prosody) rely on similarly intricate and relational patterns of auditory pitch as those present in melodies, and because melodic processing ability appears to scale continuously with level of connectivity within the right SLF (Loui et al. 2009, Loui, Li, Hohmann, et al. 2011, Loui, Li, Schlaug 2011; Halwani et al. 2011), it was predicted that more robust WM microstructure in the right SLF would be associated with greater levels of EC. Further, because empathy is thought to result in part from the modulation of AON/hMNS activity from the amygdala via the insula (Carr et al. 2003), it was predicted that WM integrity in these regions (Augustine 1996) would be more robust among individuals with higher levels of emotional empathy. Correspondingly, it was predicted that WM integrity in tracts connecting areas involved in mentalizing (e.g., TPJ, temporal poles, MPFC, precuneus; Zaki and Ochsner 2012) would be more robust among individuals higher in cognitive empathy. Additionally, previous research in lesion patients suggests that long-range fiber tracts in the sagittal stratum, such as those linking the occipital cortex with areas implicated in affective processing in the anterior temporal lobe, amygdala, and orbitofrontal cortex (OFC; i.e., inferior longitudinal fasciculus, ILF; inferior fronto-occipital fasciculus, IFOF; Catani et al. 2002, 2003), support the rapid interactions between sensory and emotional processing that underlie emotion recognition (Rudrauf et al. 2008; Philippi et al. 2009), which is closely tied to emotional empathy (Shamay-Tsoory et al. 2009). Autism spectrum disorder (ASD), characterized by deficits in mentalizing (Baron-Cohen et al. 1985), mimicry (Smith and Bryson 1994) and appropriately engaging the AON/hMNS (Rizzolatti and Fabbri-Destro 2008), is also associated with widespread reductions in WM connectivity in tracts including the forceps minor (FM), forceps major, corticospinal tract (CST), cingulum, SLF, ILF, IFOF, anterior thalamic radiations (ATR), uncinate fasciculus (UF), and corpus callosum (CC; Cheon et al. 2011; Jou et al. 2011). Thus, previous clinical and neuroimaging evidence suggests that several cerebral circuits may be implicated in both cognitive and emotional dimensions of empathy. Therefore, tract-based spatial statistics (TBSS; Smith et al. 2006) were used to correlate diffusion tensor imaging (DTI)-derived indices of WM microstructural integrity throughout a skeleton of WM tracts common to all participants in the current study with self-reported empathy. While multiple cortical circuits likely underlie inter-individual variability in cognitive and emotional empathic tendencies, it was predicted that the most robust relationships would be found between emotional empathy and WM microstructure in networks connecting frontal, parietal, and limbic brain regions.

## Materials and Methods

### Participants

Sixty-four English speakers (37 females) between 18 and 28 years of age ( $M = 19.45$  years; standard deviation,  $SD = 1.65$  years) participated in this study. All participants provided written informed consent prior to scanning, and the experimental procedure was approved by the Dartmouth College Committee for the Protection of Human Subjects. All participants were right-handed and had no known history of neurological disorders.

## Behavioral Measures

### Measuring Empathy

Participants were given the IRI (Davis 1980) as part of a large battery of self-report measures administered during an undergraduate introductory psychology class prior to participation. The IRI is a 28-item self-report questionnaire with four 7-item subscales (EC, FS, PD, and PT). Respondents rate how well each statement describes them from 0 (“does not describe me well”) to 4 (“describes me very well”). The IRI subscales have been shown to have good internal consistency, with alpha coefficients ranging from 0.71 to 0.77, as well as good test-retest reliability, with test-retest reliability coefficients ranging from 0.61 to 0.81 (Davis 1980; Christopher et al. 1993). While it is a self-report measure, there is a high degree of self-other agreement on IRI scores (Cliffordson 2001). Its 4-factor structure has been confirmed in large adult samples (e.g., Davis 1980; Carey et al. 1988). This measure has high discriminant and convergent validity (Davis et al. 1994), indicating that its 4 subscales measure distinct components of empathy. Because not all IRI subscales are positively correlated (Davis 1980, 1983a; Eisenberg and Fabes 1990), previous authors, including the scale’s creator, have advised against summing IRI subscales to obtain composite empathy scores (D’Orazio 2004).

The EC subscale includes statements describing the tendency to experience concern, warmth, and sympathy for others (e.g., “Other people’s misfortunes do not usually disturb me a great deal”). Statements on the PD subscale pertain to respondents’ tendency to experience self-oriented anxiety and stress in tense situations (e.g., “I tend to lose control during emergencies”). PT subscale items describe the tendency to spontaneously adopt others’ points of view in everyday life (e.g., “I sometimes try to understand my friends better by imagining how things look from their perspective”). Finally, FS subscale items assess how much participants engage with fictional characters (e.g., “When I am reading an interesting story or novel, I imagine how I would feel if the events in the story were happening to me”). Females tend to score more highly than males on all subscales; the greatest gender difference is associated with the FS subscale (Davis 1980). Only EC, and, to a lesser extent, PT, are associated with prosocial outcomes (Konrath et al. 2011). Similarly, PT and EC measure prototypical cognitive and emotional empathy, respectively, while PD and FS have been argued to assess broader psychological constructs (Baron-Cohen and Wheelwright 2004; Lawrence et al. 2004; Stueber 2008).

### Assessing Musical Training History

After scanning, participants were contacted with questions regarding their musical training experience to ensure that any observed relationships between WM microstructure and empathy were not mediated by musical training history (musical training has previously been correlated with structural differences in WM tracts connecting areas involved in action perception and production; Halwani et al. 2011). Fifty participants provided this information. These participants answered the following questions: 1) “Have you ever taken music lessons (e.g., piano, violin or singing lessons) or otherwise practiced music on a regular basis?” and 2) “If yes, (a) at what age did you begin receiving musical training, and (b) how many years cumulatively have you played music on a regular basis?”

### Image Acquisition

Structural images were acquired on a Philips Intera Achieva 3-T scanner (Philips Medical Systems) with a SENSE (SENSEitivity Encoding) 8-channel head coil. Participants’ heads were stabilized using foam padding and masking tape was placed across participants’ foreheads to prevent motion and to ensure that subjects were aware of small movements. Diffusion-weighted images were acquired using echo-planar imaging (32 diffusion gradient directions;  $b$ -value = 1000  $s/mm^2$ ;  $1.75 \times 1.75 \times 2.00$   $mm^3$  voxels; 60 axial slices; field of view =  $224 \times 224$   $mm$ ; repetition time = 4115 ms; time echo = 82 ms). This DTI protocol was repeated twice consecutively with dynamic stabilization, yielding a total image acquisition time of 10 min, 26 s. Data were concatenated into a single 4-dimensional data set. Gradient

direction vectors were extracted using the DTL\_gradient\_table\_creator JAVA applet provided by Jonathan A.D. Farrell (John Hopkins University, Baltimore, MA, United States of America), supported by NIH/NICRR grant RR15241 to the Kennedy Krieger Institute, RO1AG20012 and U24 RR021382-02 (Morphometry group of the Biomedical Informatics Research Network, BIRN; Farrell et al. 2007).

### Diffusion Tensor Imaging Analysis

TBSS (Smith et al. 2006) in FMRIB's software library (FSL) (Smith et al. 2004) was used to carry out voxelwise statistics. First, all participants' diffusion-weighted images were corrected for eddy currents and head motion. Next, fractional anisotropy (FA) images were created by fitting a tensor model to raw diffusion data with FMRIB's diffusion toolbox in FSL, and brain extraction was performed using FSL's brain extraction tool (Smith 2002). FA comprises a general marker of axonal integrity. Larger FA values can reflect increased myelination, increased axonal coherence, and/or increased axonal caliber (Beaulieu 2002). All subjects' FA images were aligned to the MNI152 FA template using the nonlinear registration tool FNIRT (Andersson et al. 2007a, 2007b). Next, a mean FA image was created and thinned to produce a group mean FA skeleton representing the centers of tracts common to all participants in the study. Finally, each subject's spatially normalized FA data were projected onto this common skeleton, and these data were fed into voxelwise cross-subject statistics (Smith et al. 2006).

In hopes of better characterizing which diffusion component was contributing to any observed FA differences, axial diffusivity (AD—diffusivity along the axons) and radial diffusivity (RD—diffusivity perpendicular to the axons) maps were also created for each subject. Previous research suggests that lower RD values may be associated with increased myelination, whereas AD may indicate degree of axonal coherence (Song et al. 2002, but see Wheeler-Kingshott and Cercignani 2009). AD was defined as the largest eigenvalue ( $\lambda_1$ ), and RD was defined as the mean of the second and third eigenvalues ( $(\lambda_2 + \lambda_3)/2$ ; Alexander et al. 2007). AD and RD maps were calculated using eigenvalue maps created by dtifit in FSL. The nonlinear transformations derived from aligning FA images to the MNI152 FA template were applied to each subject's AD and RD images. Projection vectors used to project each subject's FA data onto the group mean tract skeleton were also used to project each subject's AD and RD data onto the tract skeleton.

### Statistical Analysis

#### Primary Analyses

Cross-subject analyses relating voxelwise FA values to empathy were completed using the general linear model (GLM) tool in conjunction with permutation tests using Randomise in FSL. The primary analyses entailed probing positive and negative correlations between FA values within WM tracts in the group mean skeleton and empathy scores across subjects. Previous work has consistently found both positive and negative correlations among IRI subscales (Davis 1980, 1983a; Eisenberg and Fabes 1990; D'Orazio 2004). Additionally, systematic relationships between empathy scores, age (Schieman and Van Gundy 2000), and gender (Davis 1980, 1983b), as well as between FA and both gender and age (Schmithorst et al. 2008), have been documented. Therefore, to assess the unique relationship between WM microstructure and cognitive empathy, centered PT subscale scores were entered into the GLM with the remaining IRI subscales, age, and gender included in the model as centered nuisance variables. To assess specific associations between emotional empathy and WM microstructure, an analogous analysis was performed with EC as the variable of interest.

Significance of correlation inferences was assessed using 5000 Monte Carlo simulations to test for associations between FA values and cognitive and emotional empathy. Threshold-free cluster enhancement (TFCE; Smith and Nichols 2009) was used in lieu of setting arbitrary cluster-forming thresholds, with height set at 2 and cluster extent set at 0.5. All presented results are significant at  $P < 0.05$  after controlling for family-wise error rate (FWE) using TFCE, and employing an additional Bonferroni adjustment for having performed 4 statistical contrasts (i.e., positive and negative correlations between

FA and EC; positive and negative correlations between FA and PT). More specifically, to correct both for multiple comparisons across space and for multiple statistical contrasts, FWE-corrected  $P$ -value maps were thresholded at a Bonferroni-adjusted significance level of  $P < 0.0125$ . Clusters where local microstructure differed as a function of empathy scores were labeled with reference to atlas-based images (Mori et al. 2005, 2008).

#### Secondary Analyses

In addition to our primary analyses, 2 sets of secondary exploratory analyses were performed. First, in order to explore the WM microstructural correlates of other aspects of interpersonal sensitivity assessed by the IRI, exploratory analyses analogous to those described above were performed with FS and PD as variables of interest.

Finally, to clarify which diffusion component was driving any correlations between FA and empathy observed in the primary analyses, for each statistical contrast, the same GLM procedures described above were performed on subjects' AD and RD maps within voxels whose FA values were significantly related to individual differences in empathy scores.

## Results

### Behavioral Data

#### Empathy Scores

Scores on the EC subscale ranged from 7 to 28 ( $M = 20.12$ ;  $SD = 5.63$ ), FS subscale scores ranged from 4 to 28 ( $M = 19.03$ ;  $SD = 5.74$ ), PD subscale scores ranged from 0 to 22 ( $M = 12.08$ ;  $SD = 4.99$ ), and scores on the PT subscale ranged from 3 to 28 ( $M = 17.81$ ;  $SD = 4.99$ ). Means and SDs by gender for each subscale are displayed in Table 1, along with those from previously reported normative data (Davis 1980). Compared with males ( $M = 10.59$ ;  $SD = 4.86$ ), females ( $M = 13.16$ ;  $SD = 4.86$ ) had significantly higher PD scores  $t(56.23) = 2.09$ ,  $P < 0.05$ . There was also a trend such that females ( $M = 20.24$ ;  $SD = 6.04$ ) tended to score higher than males ( $M = 17.37$ ;  $SD = 5.27$ ) on the FS subscale  $t(51.43) = 1.98$ ,  $P = 0.05$ . While this pattern of gender differences differs from the first studies using the IRI, it is consistent with a recent meta-analysis of investigations using the IRI over the past 30 years, which found that samples with more males tend to have lower PD scores, but found no significant relationship between gender and any other IRI subscale (Konrath et al. 2011).

Pairwise correlations between all behavioral measures are reported in Table 2. Consistent with previous reports (Davis 1983a; Davis et al. 1994), the strongest correlation was between the PT and EC subscales ( $r = 0.60$ ,  $P < 0.001$ ), followed by the EC and FS subscales ( $r = 0.34$ ,  $P < 0.01$ ). The PD and FS subscales were also significantly positively correlated

**Table 1**

IRI subscale scores by gender for the current sample and normative data

Variable	Current sample		Normative data	
	Males	Females	Males	Females
Empathic concern	19.04 (5.40)	20.92 (5.74)	19.04 (4.21)	21.67 (3.83)
Perspective taking	17.59 (5.18)	17.97 (4.92)	16.78 (4.72)	17.96 (4.85)
Fantasy	17.37 (6.04)	20.24 (5.27)	15.73 (5.60)	18.75 (5.17)
Personal distress	10.59 (4.86)	13.16 (4.87)	9.46 (4.55)	12.28 (5.01)
<i>n</i>	27	37	573	582

Note: Means are presented with SDs in parentheses for the current sample and normative data (Davis 1980). Italics indicate a significant gender difference ( $P < 0.05$ ). IRI, Interpersonal Reactivity Index (Davis 1980).

**Table 2**  
Correlations between behavioral variables

	EC	PT	FS	PD	Age	Number of years of MT <sup>a</sup>	Age of onset of MT <sup>b</sup>
EC	1						
PT	0.60**	1					
FS	0.34*	0.22	1				
PD	0.14	-0.12	0.31*	1			
Age	-0.04	-0.09	0.01	0.11	1		
Number of years of MT <sup>a</sup>	-0.07	-0.15	0.10	0.27	0.05	1	
Age of onset of MT <sup>b</sup>	0.16	0.26	-0.03	-0.11	-0.10	-0.54**	1

*N* = 64 unless otherwise indicated.

EC, empathic concern; PT, perspective taking; FS, fantasy scale; PD, personal distress; MT, musical training.

<sup>a</sup>*N* = 50.

<sup>b</sup>*N* = 48

\**P* < 0.01, \*\**P* < 0.001.

( $r=0.31$ ,  $P<0.01$ ). Positive associations of FS with both PD and EC are consistent with suggestions that this subscale may be more associated with emotional than with cognitive responding (Davis 1983b), despite its having been originally considered a cognitive dimension of interpersonal reactivity (Davis 1980).

### Musical Training

Fifty participants provided musical training information. These participants had received between 0 and 14 years of musical training ( $M=8.17$  years;  $SD=4.21$ ). Of the 48 participants who had received musical training, age of onset of this training ranged from 4 to 19 years ( $M=7.77$  years;  $SD=2.92$ ). As shown in Table 2, age of onset and duration of musical training were significantly (negatively) correlated, but neither onset nor duration of musical training was significantly related to any IRI subscale. This suggests that correlations between emotional or cognitive empathy and FA could not be mediated by more musical training among those with high IRI subscale scores.

Pairwise correlations between IRI subscales correspond to data from all 64 participants. Reported correlations between IRI scores and number of years of musical training correspond to the subset of participants ( $n=50$ ) who provided musical training background information. Correlations between age of onset of musical training and other behavioral measures correspond only to the 48 participants who provided musical training background data and indicated that they had received some form of regular musical training.

### Primary DTI Analyses

#### Associations Between FA and Emotional Empathy

FA values were positively correlated with EC scores within several clusters of the tract skeleton (Fig. 1). These included clusters in long-range cortical association tracts, such as the SLF and IFOF bilaterally, as well as the right ILF. The SLF is a long-range association fiber tract connecting temporoparietal association areas involved in action perception with inferior frontal areas implicated in action production (Schmahmann and Pandya 2006). The IFOF links sensory and limbic regions of cortex by providing connections between ventral occipital cortex and OFC by way of the temporal lobe (Catani et al.

2002, 2003). The ILF plays a similar role, linking the occipital lobe with the amygdala and anterior temporal cortex (Catani et al. 2002, 2003). FA was also positively associated with EC within a major association tract of the limbic system, the UF (Hasan et al. 2009), which interconnects the amygdala, hippocampal formation, temporal poles, and OFC (Ebeling and von Cramon 1992; Catani et al. 2002).

Additionally, FA and EC were positively correlated in the ATR and CST bilaterally. The ATR connect the frontal cortex with dorsomedial thalamic nuclei and provide bidirectional connections between limbic structures, anterior thalamic nuclei, and the frontal lobe (Campbell 2005). The CST contains descending neurons originating in premotor and motor cortex (Dum and Strick 1991).

EC scores were also positively correlated with FA in the FM and an adjacent area of the CC. The FM is comprised of projections from the genu of the CC and provides interhemispheric connections between the left and right frontal lobes (Catani et al. 2002). No areas of the tract skeleton showed significant negative correlations between FA and EC.

#### Associations Between FA and Cognitive Empathy

No significant associations between cognitive empathy and WM microstructure were observed: FA values were not significantly correlated with PT scores anywhere in the group mean skeleton. All reported null findings were not significant even at a reduced threshold of  $P<0.05$ , uncorrected.

### Secondary DTI Analyses

#### Associations Between AD, RD, and Emotional Empathy

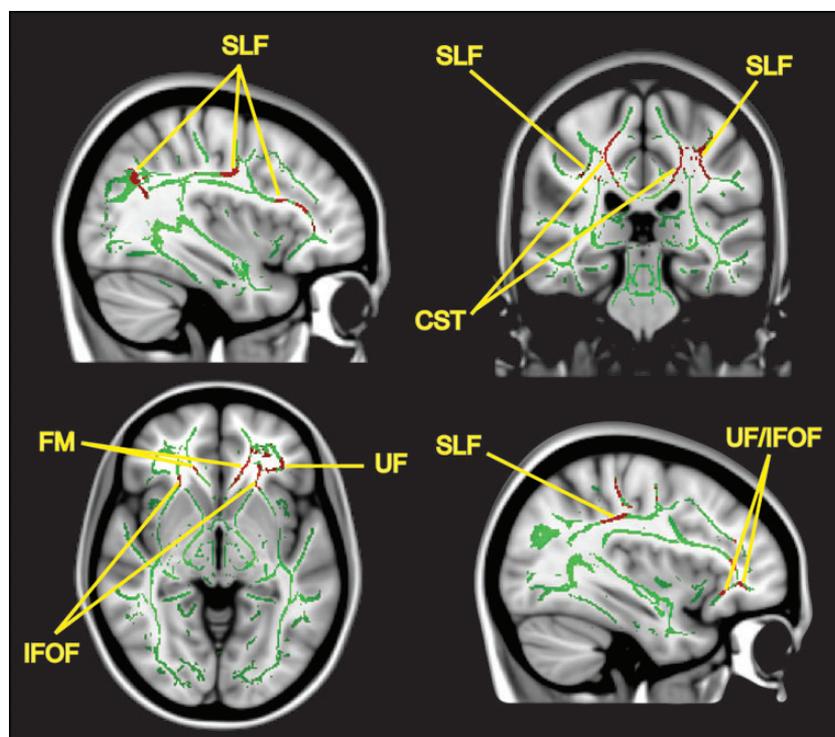
Clusters within the group tract skeleton in which FA and EC were significantly associated were interrogated further to clarify which diffusion components were contributing to the observed effects. No significant correlations between AD and EC were observed in these clusters, nor were there any significant correlations between RD and EC.

#### Associations Between FA and PD/FS

Neither PD nor FS subscale scores were significantly positively correlated with FA values in any region of the tract skeleton. Similarly, no areas of the tract skeleton exhibited a negative relationship between FA and these IRI subscales.

### Discussion

Interactions between distant brain regions (e.g., in frontal, parietal, and limbic cortex) are thought to be central to the experience of empathy (Carr et al. 2003; Zaki and Ochsner 2012). While communication between far-off regions likely depends on WM connections, the anatomical pathways that support empathic processing previously remained unexamined. The current results suggest that greater levels of EC are associated with greater WM integrity in association fiber tracts linking areas involved in action production and action perception (SLF), areas involved in visual and affective processing (ILF and IFOF), and areas within the limbic system (UF and ATR). Similar associations were observed between EC and WM integrity in the CST and in commissural fibers supporting interhemispheric communication in the frontal cortex (CC and FM). Associations with WM microstructure were specific to EC: Scores on the remaining IRI subscales were



**Figure 1.** Associations between FA and emotional empathy. Clusters where FA was significantly correlated with emotional empathy are indicated in red. Clockwise from top-left—right sagittal slice:  $x = 37$ ; coronal slice:  $y = -30$ ; left sagittal slice:  $x = -35$ ; axial slice:  $z = -4$ . Results are presented on the MNI template brain, and images are presented in radiological convention. The group mean skeleton, containing WM tracts common to all participants, is indicated in green. All displayed results are significant at  $P < 0.05$  after correcting for FWE and after Bonferroni adjustments for multiple statistical contrasts. CST, corticospinal tract; FA, fractional anisotropy; FM, forceps minor; IFOF, inferior fronto-occipital fasciculus; SLF, superior longitudinal fasciculus; UF, uncinate fasciculus.

included as nuisance variables in our primary analyses, and no other IRI subscale was significantly related to FA. These results suggest that anatomical connections, such as those between regions involved in action perception and production, and between sensory and limbic cortical regions, are of particular relevance to emotional empathy. The following section elaborates on results pertaining to each region of the tract skeleton.

### ***ILF/IFOF Microstructure and Emotional Empathy***

EC was related to more robust WM microstructure in the IFOF bilaterally, as well as the right ILF (Table 3). The IFOF and ILF run together through much of temporal and occipital cortex, linking areas involved in early visual and facial processing to more anterior areas involved in affective processing (Mori et al. 2008). The IFOF travels from the occipital lobe through medial temporal cortex before ending in OFC; the ILF begins in extrastriate visual cortex and in the fusiform gyrus and terminates in lateral temporal cortex and in medial temporal cortex in the vicinity of the amygdala and parahippocampal gyrus (Catani et al. 2002, 2003; Schmahmann and Pandya 2006). The ILF and IFOF appear to underlie the modulation of early visual processing by the amygdala (Catani et al. 2003) and have recently been linked to emotional processing in patients with focal brain lesions. Damage to these tracts impairs visual emotion recognition even in the absence of damage to the gray matter structures that they connect, suggesting that the long-range communication they provide is critical for the effective interpretation of emotional visual information (Philippi et al. 2009). Further, findings from

**Table 3**

Clusters where emotional empathy and FA were significantly correlated

Size (mm <sup>3</sup> )	FWE corrected (P-value)	Peak			COG			Hemi	Approximate tract location
		X	Y	Z	X	Y	Z		
4708	0.008	20	-35	53	22	-4	29	R	SLF, IFOF, ILF, UF, CC, FM, ATR, CST
3767	0.006	-20	36	10	-18	24	17	L	SLF, IFOF, UF, CC, FM, ATR, CST
1428	0.009	-20	-34	37	-25	-30	42	L	SLF
34	0.012	-18	16	40	-18	16	43	L	WM near premotor cortex
3	0.012	-30	50	-3	-30	50	-2	L	IFOF

FA, fractional anisotropy; FWE, family-wise error rate; COG, center of gravity; Hemi, hemisphere; SLF, superior longitudinal fasciculus; IFOF, inferior fronto-occipital fasciculus; ILF, inferior longitudinal fasciculus; UF, uncinate fasciculus; CC, corpus callosum; FM, forceps minor; ATR, anterior thalamic radiations; CST, corticospinal tract; WM, white matter.

magnetoencephalography suggest that the ILF and IFOF provide “short-cuts” for communication between early sensory cortices and more anterior areas involved in affective processing (e.g., amygdala, OFC, and temporal poles), allowing emotional visual information to modulate attention even before it has been fully visually processed (Rudrauf et al. 2008). Lesions to the ILF dampen emotional responses to visual stimuli (visual hypoemotionality; Bauer 1982). Similarly, ASD, characterized by social perception deficits and deficient interaction between the amygdala and fusiform gyrus in social contexts (Schultz 2005), is associated with a compromised ILF (Cheung et al. 2009; Pugliese et al. 2009).

Enhanced ILF and IFOF microstructure among those high in EC may enhance attention to emotional visual signals and underlie correlations between visual emotion recognition abilities and emotional empathy (Laurent and Hodges 2008; Dimberg et al. 2011).

### **WM Microstructure in the Limbic System and Emotional Empathy**

EC was also related to enhanced WM integrity in a major limbic association tract, the UF (Hasan et al. 2009), which provides reciprocal connections between the amygdala, hippocampal formation, temporal poles, and OFC (Ebeling and von Cramon 1992; Catani et al. 2002). Consistent disruption of this tract in ASD (Kumar et al. 2010; Pardini et al. 2009; Ameis et al. 2011; Lo et al. 2011) has been suggested to contribute to impaired socio-emotional functioning among individuals with ASD (Ameis et al. 2011). The current findings suggest that UF integrity does not only predict socio-emotional functioning in pathological circumstances: A more robust UF also appears to be associated with higher levels of EC among healthy individuals. Similar associations were observed between EC and FA values within the ATR, which link the thalamus and frontal lobes and interconnect limbic structures with the thalamus and frontal cortex (Campbell 2005). The ATR are included in Papez' original limbic circuit, thought to support memory and the cortical control of emotion (Papez 1937). Circuits involved in affective arousal that include the hippocampus, amygdala, and hypothalamus are thought to contribute to the affective state-sharing processes that characterize emotional facets of empathy (Decety 2011). Increased integrity of WM tracts interconnecting these regions may reflect and/or enable more rapid and prioritized processing of emotional information among individuals high in EC.

### **SLF Microstructure and Emotional Empathy**

EC was also positively correlated with FA values in the SLF bilaterally (Table 3), most extensively in the right SLF (Fig. 1), suggesting that this pathway is particularly important for EC. While the left SLF has long been implicated in language processing, providing a pathway for communication between areas involved in speech perception and speech production (Geschwind 1965; Damasio and Damasio 1980; Catani and Mesulam 2008), historically, the right SLF has received comparatively less attention (Loui et al. 2009). Recently, the right SLF has been implicated in processing melodic patterns and fine-grained auditory pitch differences, and in reproducing perceived melodies (Loui et al. 2009; Halwani et al. 2011; Loui, Li, Hohmann, et al. 2011; Loui, Li, Schlaug 2011). This tract is impoverished in tone-deaf individuals and comparatively robust in individuals with absolute pitch (Loui et al. 2009, Loui, Li, Hohmann, et al. 2011) and in those better able to learn pitch patterns (Loui, Li, Schlaug 2011), presumably because it links temporo-parietal areas involved in pitch perception with inferior frontal areas implicated in pitch production (Loui et al. 2009). The current results may reflect a similar phenomenon in which WM tracts connecting areas involved primarily in perceiving and producing emotional signals are more robust among individuals higher in EC.

This is consistent with suggestions that an automatic link between perception and action underlies emotion contagion (Chartrand and Bargh 1999), and with fMRI evidence

implicating frontal endpoints of the right SLF (right ventral premotor area—BA 6; IFG—BA 44; Schmahmann and Pandya 2006) in passive viewing of emotional expressions (Leslie et al. 2004) with higher responses to social stimuli in these regions corresponding to higher EC scores (Kaplan and Iacoboni 2006; Schulte-Rüther et al. 2007; Pfeifer et al. 2008). Enhanced anatomical connectivity between areas involved in the perception and expression of emotion could have several social consequences for high emotional empathizers. First, it could underlie high emotional empathizers' tendency to modulate their own affective signals to a greater degree in response to others' emotional expressions (Sonnby-Borgström 2002; Dimberg et al. 2011), which improves perceived rapport (Bernieri 1988; Chartrand and Bargh 1999; Miles et al. 2009; Ramseyer and Tschacher 2011) and further perpetuates emotion contagion (Laird et al. 1994). Second, more robust connections between areas involved in emotion expression and perception may underlie correlations between emotional empathy and emotion recognition ability (Shamay-Tsoory et al. 2009; Dimberg et al. 2011), potentially mediated by internal simulations of others' experiences (Gallese 2003), consistent with evidence that disrupting activity in the right premotor cortex impairs emotion discrimination, but not identity discrimination (Banissy et al. 2010) or semantic processing (van Rijn et al. 2005). Third, anticipating social cues as they unfold using cortical machinery for action prediction and simulation could improve the speed and clarity with which these cues are processed, particularly in ambiguous contexts (Stephens et al. 2010). Thus, enhanced anatomical coupling between areas involved in emotional perception and expression may enable more efficient communication between these areas when predicting social cues as they unfold in real time to minimize prediction error (Blakemore and Frith 2005; Kilner et al. 2007; Wilson and Knoblich 2005). It may also promote internal simulations of others' emotional signals to improve social understanding (Gallese 2003) or to promote mimicry and interpersonal synchrony, thus improving social cohesion (Wheatley et al. 2012). These possibilities are not mutually exclusive. For instance, anticipating others' upcoming behavior during social interactions is essential both to minimize prediction error (Wilson and Knoblich 2005) and to establish interpersonal synchrony (Keller PE et al. 2007).

### **Commissural Fiber Tracts and Emotional Empathy**

EC was positively associated with FA in the FM and adjacent areas of the CC, tracts supporting interhemispheric communication in medial and lateral prefrontal cortex (Peltier et al. 2010; Voineskos et al. 2010), which clinical evidence suggests is necessary to link psychophysiological responses to emotional stimuli with appropriate conceptual emotional information (Paul et al. 2006). The FM has previously been found to be less robust in individuals with ASD (Keller TA et al. 2007; Jou et al. 2011), and in males in comparison with females (Schmithorst et al. 2008). In the current study, correlations between FA in this area and EC cannot be explained by gender differences in dispositional emotional empathy since gender was included in the regression analysis as a nuisance variable. Future work may investigate whether gender differences in the WM microstructure of these regions are

mediated by broader dispositional variables that vary both between and within genders, such as empathic tendencies.

### ***CST Microstructure and Emotional Empathy***

EC was also significantly related to FA in the CST bilaterally. There are at least 2 possible explanations for this finding. First, observing others experience pain dramatically reduces corticospinal excitability in motor neurons corresponding to the body part being harmed, and the magnitude of this inhibition is proportional to the intensity of the observed pain (Avenati et al. 2005). This inhibition is thought to occur in response to AON/hMNS activation, preventing downward propagation of the motoric representations elicited during action observation. EC scores have previously been shown to modulate neural activity suggestive of affective “state-sharing” when observing others experience pain (Singer et al. 2004). It is possible that more robust WM microstructure in tracts connecting AON/hMNS areas (e.g., in the SLF) elicits enhanced activation in premotor and primary motor areas of cortex during action observation (Kraskov et al. 2009), which in turn requires concomitant CST inhibition to ensure that the observed or predicted action programs are not executed. A second possibility is that increases in CST microstructural integrity associated with higher EC reflect excitatory anatomical connections: Emotion can increase CST excitability (Baumgartner et al. 2007; Hajcak et al. 2007; Schutter et al. 2008), as can action observation, particularly among those high in empathy (Lepage et al. 2010). Thus, it is also possible that increased FA in the CST of those high in EC reflects excitatory connections. Some combination of these factors is also possible: In macaque ventral premotor cortex, CST neurons whose firing is facilitated or suppressed by action observation appear to be equally prevalent (Kraskov et al. 2009). While it is not possible to discern whether the WM microstructural differences observed here reflect changes in inhibitory or excitatory neural connections, future work using additional modalities of measurement may clarify the exact nature of these differences.

### ***WM Microstructure and Cognitive Empathy***

Although similar ranges of PT and EC scores were obtained, and participants' scores on these subscales closely matched previously reported normative data (Table 1), PT was not associated with any differences in WM microstructural integrity. While a null finding is difficult to interpret, there are many possible reasons why emotional empathy would be more closely associated with differences in anatomical connectivity than cognitive empathy. First, emotional empathy is characterized by rapid, obligatory perception-action coupling (Dimberg et al. 2011), whereas cognitive empathy appears to comprise a less automatic, more effortful process (Keysar et al. 2003). If emotional empathy is a more automatic process than cognitive empathy, regions belonging to the neural networks supporting emotional empathy may become “wired” together more strongly through simple Hebbian learning in everyday experience. Fittingly, our primary analyses revealed that WM integrity in the vicinity of the SLF, which links temporo-parietal areas implicated in action perception with inferior frontal regions associated with action production (Schmahmann and Pandya 2006), was specifically associated with EC, our measure of emotional empathy. In

the same vein, while PT has been suggested to be malleable to experience during development (Davis et al. 1994), EC has consistently been found to comprise the most heritable component of dispositional empathy (Matthews et al. 1981; Zahn-Waxler et al. 1992; Davis et al. 1994). Therefore, compared with individuals high in PT, individuals high in EC may have more consistently engaged regions belonging to the neural networks supporting this facet of empathy throughout their lives, and thus, may have more consistently strengthened anatomical connections between these regions. Secondly cognitive empathy may rely on domain-general mechanisms (Decety and Lamm 2007) that are shared by perspective taking functions in other domains (e.g., visuospatial perspective taking; Aichhorn et al. 2006; Hamilton et al. 2009). Recent evidence suggests that both implicit and explicit mentalizing rely in part on domain-general executive processing resources (Schneider et al. 2012). In contrast, emotional empathy involves at least in part, evolutionarily older, domain-specific neural machinery dedicated to perceiving and adjusting emotional states (Decety 2011). Thus, individual variability in the tendency to employ perspective taking in nonsocial contexts may introduce noise into correlations between social perspective taking and its structural correlates that would not affect correlations between emotional empathy and WM microstructure. Third, cognitive empathy may not depend as heavily on rapid neural coupling between distant regions compared with emotional empathy, which is associated with predicting and reacting to others' actions within milliseconds (Phillips-Silver et al. 2010; Dimberg et al. 2011).

### **Conclusions**

The current results provide the first evidence that the tendency to experience emotion in response to the perceived emotions of others is associated with specific patterns of anatomical connectivity. Importantly, individual differences in anatomical connectivity could arise from consistent behavioral patterns, or predispose them. Just as early neuroanatomical abnormalities are associated with decreased sensory-emotional and perception-action coupling in clinical disorders (Bachevalier and Loveland 2006), predispositions for hyperconnectivity may underlie heightened EC in some individuals. On the other hand, recent evidence suggests that even short-term experience can markedly alter the structure of several anatomical tracts, including those implicated in the current study (Hänggi et al. 2008; Imfeld et al. 2009; Tang et al. 2010; Halwani et al. 2011).

Deficits in long-range connectivity are thought to underlie difficulties in integrating social cues among individuals with ASD (Courchesne and Pierce 2005), particularly connections between the limbic system and areas involved in language and sensorimotor processing (Gotts et al. 2012). The collection of tracts whose microstructural integrity is compromised in ASD (e.g., Shukla et al. 2010; Jou et al. 2011) closely match those whose microstructural integrity is positively related to EC. The cortical regions connected by these tracts also correspond to those thought to support empathic accuracy among healthy individuals (Zaki et al. 2009), which is positively associated with EC (Laurent and Hodges 2008). Taken together, these facts suggest that interventions aimed at strengthening tracts associated with EC, such as those connecting areas of the AON/hMNS network (Wan et al. 2011),

could enhance social functioning both among those with clinically significant social impairments and among healthy individuals. Future work should characterize the causal direction of the relationship between EC and anatomical connectivity, and the potential for interventions to enhance social connectivity through experiences that would strengthen these anatomical connections.

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## References

- Aichhorn M, Perner J, Kronbichler M, Staffen W, Ladurner G. 2006. Do visual perspective tasks need theory of mind? *Neuroimage*. 30:1059–1068.
- Alexander AL, Lee JE, Lazar M, Boudos R, DuBray MB, Oakes TR, Miller JN, Lu J, Jeong EK, McMahon WM et al. 2007. Diffusion tensor imaging of the corpus callosum in autism. *Neuroimage*. 34:61–73.
- Ameis SH, Fan J, Rockel C, Voineskos AN, Lobaugh NJ, Soorya L, Wang AT, Hollander E, Anagnostou E. 2011. Impaired structural connectivity of socio-emotional circuits in autism spectrum disorders: a diffusion tensor imaging study. *PLoS One*. 6:e28044.
- Amodio DM, Frith CD. 2006. Meeting of minds: the medial frontal cortex and social cognition. *Nat Rev Neurosci*. 7:268–277.
- Andersson JLR, Jenkinson M, Smith S. 2007a. Non-linear optimisation. FMRIB technical report TR07JA1. Oxford, UK: Available from: [www.fmrib.ox.ac.uk/analysis/techrep](http://www.fmrib.ox.ac.uk/analysis/techrep). [cited 2012 June 5].
- Andersson JLR, Jenkinson M, Smith S. 2007b. Non-linear registration, aka spatial normalisation. FMRIB technical report TR07JA2. Oxford, UK: Available from: [www.fmrib.ox.ac.uk/analysis/techrep](http://www.fmrib.ox.ac.uk/analysis/techrep). [cited 2012 June 5].
- Augustine JR. 1996. Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Res Rev*. 22:229–244.
- Avenanti AA, Buetti DD, Galati GG, Aglioti SMS. 2005. Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. *Nat Neurosci*. 8:955–960.
- Bachevalier J, Loveland KA. 2006. The orbitofrontal-amygdala circuit and self-regulation of social-emotional behavior in autism. *Neurosci Biobehav Rev*. 30:97–117.
- Banissy MJ, Sauter DA, Ward J, Warren JE, Walsh V, Scott SK. 2010. Suppressing sensorimotor activity modulates the discrimination of auditory emotions but not speaker identity. *J Neurosci*. 30:13552–13557.
- Baron-Cohen S, Leslie AM, Frith U. 1985. Does the autistic child have a “theory of mind”? *Cognition*. 21:37–46.
- Baron-Cohen S, Wheelwright S. 2004. The empathy quotient: an investigation of adults with Asperger syndrome or high functioning autism, and normal sex differences. *J Autism Dev Disord*. 34:163–175.
- Bauer RM. 1982. Visual hypoemotionality as a symptom of visual-limbic disconnection in man. *Arch Neurol*. 39:702–708.
- Baumgartner TT, Willi MM, Jäncke LL. 2007. Modulation of corticospinal activity by strong emotions evoked by pictures and classical music: a transcranial magnetic stimulation study. *Neuroreport*. 18:261–265.
- Beaulieu C. 2002. The basis of anisotropic water diffusion in the nervous system—a technical review. *NMR Biomed*. 15:435–455.
- Bernieri FJ. 1988. Coordinated movement and rapport in teacher-student interactions. *J Nonverbal Behav*. 12:120–138.
- Blakemore SJ, Frith C. 2005. The role of motor contagion in the prediction of action. *Neuropsychologia*. 43:260–267.
- Campbell WW. 2005. DeJong’s the neurologic examination. Philadelphia (PA): JB Lippincott.
- Carey JC, Fox EA, Spraggins EF. 1988. Replication of structure findings regarding the interpersonal reactivity index. *Meas Eval Counsel Dev*. 21:102–105.
- Carr L, Iacoboni M, Dubeau MC, Mazziotta JC, Lenzi GL. 2003. Neural mechanisms of empathy in humans: a relay from neural systems for imitation to limbic areas. *Proc Natl Acad Sci USA*. 100:5497–5502.
- Catani M, Howard RJ, Pajevic S, Jones DK. 2002. Virtual in vivo interactive dissection of white matter fasciculi in the human brain. *Neuroimage*. 17:77–94.
- Catani M, Jones DK, Donato R, Ffytche DH. 2003. Occipito-temporal connections in the human brain. *Brain*. 126:2093–2107.
- Catani M, Mesulam M. 2008. What is a disconnection syndrome? *Cortex*. 44:911–913.
- Chartrand TL, Bargh JA. 1999. The chameleon effect: the perception-behavior link and social interaction. *J Pers Soc Psychol*. 76:893–910.
- Cheney DL, Seyfarth RM. 1990. How monkeys see the world: inside the mind of another species. Chicago (IL): University of Chicago Press.
- Cheon KA, Kim YS, Oh SH, Park SY, Yoon HW, Herrington J, Nair A, Koh YJ, Jang DP, Kim YB et al. 2011. Involvement of the anterior thalamic radiation in boys with high functioning autism spectrum disorders: a diffusion tensor imaging study. *Brain Res*. 1417:77–86.
- Cheung C, Chua SE, Cheung V, Khong PL, Tai KS, Wong TK, Ho TP, McAlonan GM. 2009. White matter fractional anisotropy differences and correlates of diagnostic symptoms in autism. *J Child Psychol Psychiatry*. 50:1102–1112.
- Christopher FS, Owens LA, Stecker HL. 1993. Exploring the dark side of courtship: a test of a model of male premarital sexual aggressiveness. *J Marriage Fam*. 55:469–79.
- Cliffordson C. 2001. Parents’ judgments and students’ self-judgments of empathy—The structure of empathy and agreement of judgments based on the interpersonal reactivity index (IRI). *Eur J Psychol Assess*. 17:36–47.
- Courchesne E, Pierce K. 2005. Why the frontal cortex in autism might be talking only to itself: local over-connectivity but long-distance disconnection. *Curr Opin Neurobiol*. 15:225–230.
- Damasio H, Damasio AR. 1980. The anatomical basis of conduction aphasia. *Brain*. 103:337–350.
- Davis MH. 1983a. Measuring individual differences in empathy: evidence for a multidimensional approach. *J Pers Soc Psychol*. 44:113–126.
- Davis MH. 1983b. The effects of dispositional empathy on emotional reactions and helping: a multidimensional approach. *J Pers*. 51:167–184.
- Davis MH. 1980. A multidimensional approach to individual differences in empathy. *Cat Sel Doc Psychol*. 10:85.
- Davis MH, Luce C, Kraus SJ. 1994. The heritability of characteristics associated with dispositional empathy. *J Pers*. 62:369–391.
- Decety J. 2011. Dissecting the neural mechanisms mediating empathy. *Emot Rev*. 3:92–108.
- Decety J, Jackson PL. 2004. The functional architecture of human empathy. *Behav Cogn Neurosci Rev*. 3:71–100.
- Decety J, Lamm C. 2007. The role of the right temporoparietal junction in social interaction: how low-level computational processes contribute to meta-cognition. *Neuroscientist*. 13:580–593.
- De Waal FBM. 2007. The “Russian doll” model of empathy and imitation. In: Bråten S, editor. *On being moved: from mirror neurons to empathy*. 1st ed. Amsterdam (NL): John Benjamins Publishing Company. p. 49–69.
- Dimberg U, Andréasson P, Thunberg M. 2011. Emotional empathy and facial reactions to facial expressions. *J Psychophysiol*. 25:26–31.

- Dimberg U, Thunberg M, Elmehed K. 2000. Unconscious facial reactions to emotional facial expressions. *Psychol Sci.* 11:86–89.
- D’Orazio DM. 2004. The journal’s publication of research that incorrectly employs Davis’ interpersonal reactivity index. *Sex Abuse J Res Tr.* 16:173–174.
- Dum RP, Strick PL. 1991. The origin of corticospinal projections from the premotor areas in the frontal lobe. *J Neurosci.* 11:667–689.
- Ebeling U, von Cramon D. 1992. Topography of the uncinate fascicle and adjacent temporal fiber tracts. *Acta Neurochir.* 115:143–148.
- Eisenberg N, Fabes RA. 1990. Empathy: conceptualization, assessment, and relation to prosocial behavior. *Motiv Emotion.* 14:131–149.
- Eisenberg N, Guthrie IK, Cumberland A, Murphy BC, Shepard SA, Zhou Q, Carlo G. 2002. Prosocial development in early adulthood: a longitudinal study. *J Pers Soc Psychol.* 82:993–1006.
- Farrell JA, Landman BA, Jones CK, Smith SA, Prince JL, van Zijl PC, Mori S. 2007. Effects of signal-to-noise ratio on the accuracy and reproducibility of diffusion tensor imaging-derived fractional anisotropy, mean diffusivity, and principal eigenvector measurements at 1.5 T. *J Magn Reson Imaging.* 26:756–767.
- Frith U. 2001. Mind blindness and the brain in autism. *Neuron.* 32:969–979.
- Gallese V. 2003. The roots of empathy: the shared manifold hypothesis and the neural basis of intersubjectivity. *Psychopathology.* 36:171–180.
- Gazzola V, Aziz-Zadeh L, Keysers C. 2006. Empathy and the somatotopic auditory mirror system in humans. *Curr Biol.* 16:1824–1829.
- Geschwind N. 1965. Disconnexion syndromes in animals and man. *Brain.* 88:237–294.
- Gotts SJ, Simmons WK, Milbury LA, Wallace GL, Cow RW, Martin A. 2012. Fractionation of social brain circuits in autism spectrum disorders. *Brain.* 135:2711–2725.
- Grafton ST, Arbib MA, Fadiga L, Rizzolatti G. 1996. Localization of grasp representations in humans by positron emission tomography. 2. Observation compared with imagination. *Exp Brain Res.* 112:103–111.
- Hajcak GG, Molnar CC, George MSM, Bolger KK, Koola JJ, Nahas ZZ. 2007. Emotion facilitates action: a transcranial magnetic stimulation study of motor cortex excitability during picture viewing. *Psychophysiology.* 44:91–97.
- Halwani GF, Loui P, Rüber T, Schlaug G. 2011. Effects of practice and experience on the arcuate fasciculus: comparing singers, instrumentalists, and non-musicians. *Front Psychol.* 2:156.
- Hamilton AF, Brindley R, Frith U. 2009. Visual perspective taking impairment in children with autistic spectrum disorder. *Cognition.* 113:37–44.
- Hänggi J, Beeli G, Oechslin MS, Jäncke L. 2008. The multiple synaesthesia E.S.: neuroanatomical basis of interval-taste and tone-colour synaesthesia. *Neuroimage.* 43:192–203.
- Hasan KM, Iftikhar A, Kamali A, Kramer LA, Ashtari M, Cirino PT, Papanicolaou AC, Fletcher JM, Ewing-Cobbs L. 2009. Development and aging of the healthy human brain uncinate fasciculus across the lifespan using diffusion tensor tractography. *Brain Res.* 1276:67–76.
- Hatfield E, Cacioppo JT, Rapson RL. 1993. Emotional contagion. *Curr Dir Psychol Sci.* 2:96–99.
- Hogan R. 1969. Development of an empathy scale. *J Consult Clin Psych.* 33:307–316.
- Iacoboni M, Dapretto M. 2006. The mirror neuron system and the consequences of its dysfunction. *Nat Rev Neurosci.* 7:942–951.
- Imfeld A, Oechslin MS, Meyer M, Loenneker T, Jäncke L. 2009. White matter plasticity in the corticospinal tract of musicians: a diffusion tensor imaging study. *Neuroimage.* 46:600–607.
- Jolliffe D, Farrington DP. 2004. Empathy and offending: a systematic review and meta-analysis. *Aggress Violent Behav.* 9:441–476.
- Jou RJ, Mateljevic N, Kaiser MD, Sugrue DR, Volkmar FR, Pelphrey KA. 2011. Structural neural phenotype of autism: preliminary evidence from a diffusion tensor imaging study using tract-based spatial statistics. *Am J Neuroradiol.* 32:1607–1613.
- Kaplan JT, Iacoboni M. 2006. Getting a grip on other minds: mirror neurons, intention understanding, and cognitive empathy. *Soc Neurosci.* 1:175–183.
- Keller PE, Knoblich G, Repp BH. 2007. Pianists duet better when they play with themselves: on the possible role of action stimulation in synchronization. *Conscious Cogn.* 16:102–111.
- Keller TA, Kana RK, Just MA. 2007. A developmental study of the structural integrity of white matter in autism. *Neuroreport.* 18:23–27.
- Keysar B, Lin S, Barr DJ. 2003. Limits on theory of mind use in adults. *Cognition.* 89:25–41.
- Kilner JM, Friston KJ, Frith CD. 2007. Predictive coding: an account of the mirror neuron system. *Cogn Process.* 8:159–166.
- Konrath SH, O’Brien EH, Hsing C. 2011. Changes in dispositional empathy in American college students over time: a meta-analysis. *Pers Soc Psychol Rev.* 15:180–198.
- Kraskov A, Dancause N, Quallio MM, Shepherd S, Lemon RN. 2009. Corticospinal neurons in macaque ventral premotor cortex with mirror properties: a potential mechanism for action suppression? *Neuron.* 64:922–930.
- Kumar A, Sundaram SK, Sivaswamy L, Behen ME, Makki MI, Ager J, Janisse J, Chugani HT, Chugani DC. 2010. Alterations in frontal lobe tracts and corpus callosum in young children with autism spectrum disorder. *Cereb Cortex.* 20:2103–2113.
- Laird JD, Alibozak T, Davainis D, Deignan K, Fontanella K, Hong J, Levy B, Pacheco C. 1994. Individual differences in the effects of spontaneous mimicry on emotional contagion. *Motiv Emot.* 18:231–247.
- Langford DJ, Crager SE, Shehzad Z, Smith SB, Sotocinal SG, Levenstadt JS, Chanda ML, Levitin DJ, Mogil JS. 2006. Social modulation of pain as evidence for empathy in mice. *Science.* 312:1967–1970.
- Laurent SM, Hodges SD. 2008. Gender roles and empathic accuracy: the role of communion in reading minds. *Sex Roles.* 60:387–398.
- Lawrence EJ, Shaw P, Baker D, Baron-Cohen S, David AS. 2004. Measuring empathy: reliability and validity of the empathy quotient. *Psychol Med.* 34:911–919.
- Lepage JF, Tremblay S, Théoret H. 2010. Early non-specific modulation of corticospinal excitability during action observation. *Eur J Neurosci.* 31:931–937.
- Leslie KR, Johnson-Frey SH, Grafton ST. 2004. Functional imaging of face and hand imitation: towards a motor theory of empathy. *Neuroimage.* 21:601–607.
- Lo YC, Soong WT, Gau SS, Wu YY, Lai MC, Yeh FC, Chiang WY, Kuo LW, Jaw FS, Tseng WY. 2011. The loss of asymmetry and reduced interhemispheric connectivity in adolescents with autism: a study using diffusion spectrum imaging tractography. *Psychiat Res.* 192:60–66.
- Loui P, Alsop D, Schlaug G. 2009. Tone deafness: a new disconnection syndrome? *J Neurosci.* 29:10215–10220.
- Loui P, Li HC, Hohmann A, Schlaug G. 2011. Enhanced cortical connectivity in absolute pitch musicians: a model for local hyperconnectivity. *J Cogn Neurosci.* 23:1015–1026.
- Loui P, Li HC, Schlaug G. 2011. White matter integrity in right hemisphere predicts pitch-related grammar learning. *Neuroimage.* 55:500–507.
- Matthews KA, Batson CD, Horn J, Rosenman RH. 1981. “Principles in his nature which interest him in the fortune of others ...”: the heritability of empathic concern for others. *J Pers.* 49:237–247.
- Mehrabian A, Epstein N. 1972. A measure of emotional empathy. *J Pers.* 40:525–543.
- Miles LK, Nind LK, Macrae CN. 2009. The rhythm of rapport: interpersonal synchrony and social perception. *J Exp Soc Psychol.* 45:585–589.
- Mitchell JP, Macrae CN, Banaji MR. 2005. Forming impressions of people versus inanimate objects: social-cognitive processing in the medial prefrontal cortex. *Neuroimage.* 26:251–257.
- Miyazaki KI. 1989. Absolute pitch identification: effects of timbre and pitch region. *Music Percept.* 7:1–14.
- Montgomery KJ, Seeherman KR, Haxby JV. 2009. The well-tempered social brain. *Psychol Sci.* 20:1211–1213.

- Mori S, Oishi K, Jiang H, Jiang L, Li X, Akhter K, Hua K, Faria AV, Mahmood A, Woods R et al. 2008. Stereotaxic white matter atlas based on diffusion tensor imaging in an ICBM template. *Neuroimage*. 40:570–582.
- Mori S, Wakana S, Nagae-Poetscher LM, van Zijl PCM. 2005. MRI atlas of human white matter. Amsterdam (NL): Elsevier.
- Nummenmaa L, Hirvonen J, Parkkola R, Hietanen JK. 2008. Is emotional contagion special? An fMRI study on neural systems for affective and cognitive empathy. *Neuroimage*. 43:571–580.
- Papez JW. 1937. A proposed mechanism of emotion. *Arch Neurol Psychiatry*. 38:725–743.
- Pardini M, Garaci FG, Bonzano L, Roccatagliata L, Palmieri MG, Congiglione F, Krueger F, Ludovici A, Floris R, Benassi F et al. 2009. White matter reduced streamline coherence in young men with autism and mental retardation. *Eur J Neurol*. 16:1185–1190.
- Paul LK, Lautzenhiser A, Brown WS, Hart A, Neumann D, Spezio M, Adolphs R. 2006. Emotional arousal in agenesis of the corpus callosum. *Int J Psychophysiol*. 61:47–56.
- Peltier J, Verclytte S, Delmaire C, Deramond H, Pruvo JP, Le Gars D, Godefroy O. 2010. Microsurgical anatomy of the ventral callosal radiations: new destination, correlations with diffusion tensor imaging fiber-tracking, and clinical relevance. *J Neurosurg*. 113:512–519.
- Pfeifer JH, Iacoboni M, Mazziotta JC, Dapretto M. 2008. Mirroring others' emotions relates to empathy and interpersonal competence in children. *Neuroimage*. 39:2076–2085.
- Philippi CL, Mehta S, Grabowski T, Adolphs R, Rudrauf D. 2009. Damage to association fiber tracts impairs recognition of the facial expression of emotion. *J Neurosci*. 29:15089–15099.
- Phillips-Silver J, Aktipis CA, Bryant GA. 2010. The ecology of entrainment: foundations of coordinated rhythmic movement. *Music Percept*. 28:3–14.
- Pugliese L, Catani M, Ameis S, Dell'Acqua F, de Schotten MT, Murphy C, Robertson D, Deeley Q, Daly E, Murphy DGM. 2009. The anatomy of extended limbic pathways in Asperger syndrome: a preliminary diffusion tensor imaging tractography study. *Neuroimage*. 47:427–434.
- Ramseyer F, Tschacher W. 2011. Nonverbal synchrony in psychotherapy: coordinated body movement reflects relationship quality and outcome. *J Consult Clin Psychol*. 79:284–295.
- Rizzolatti G, Fabbri-Destro M. 2008. The mirror system and its role in social cognition. *Curr Opin Neurobiol*. 18:179–184.
- Rudrauf D, David O, Lachaux JP, Kovach CK, Martinerie J, Renault B, Damasio A. 2008. Rapid interactions between the ventral visual stream and emotion-related structures rely on a two-pathway architecture. *J Neurosci*. 28:2793–2803.
- Saxe R, Carey S, Kanwisher N. 2004. Understanding other minds: linking developmental psychology and functional neuroimaging. *Annu Rev Psychol*. 55:87–124.
- Saxe R, Kanwisher N. 2003. People thinking about thinking people: the role of the temporo-parietal junction in “theory of mind”. *Neuroimage*. 19:1835–1842.
- Schieman S, Van Gundy K. 2000. The personal and social links between age and self-reported empathy. *Soc Psychol Quart*. 63:152–174.
- Schmahmann JD, Pandya DN. 2006. Fiber pathways of the brain. Oxford (UK): Oxford University Press.
- Schmithorst VJ, Holland SK, Dardzinski BJ. 2008. Developmental differences in white matter architecture between boys and girls. *Hum Brain Mapp*. 29:696–720.
- Schneider D, Lam R, Bayliss AP, Dux PE. 2012. Cognitive load disrupts implicit theory-of-mind processing. *Psych Sci*. 23:842–847.
- Schulte-Rüther M, Markowitsch HJ, Fink GR, Piefke M. 2007. Mirror neuron and theory of mind mechanisms involved in face-to-face interactions: a functional magnetic resonance imaging approach to empathy. *J Cogn Neurosci*. 19:1354–1372.
- Schultz RT. 2005. Developmental deficits in social perception in autism: the role of the amygdala and fusiform face area. *Int J Dev Neurosci*. 23:125–141.
- Schutter DJ, Hofman D, Van Honk J. 2008. Fearful faces selectively increase corticospinal motor tract excitability: a transcranial magnetic stimulation study. *Psychophysiology*. 45:345–348.
- Shamay-Tsoory SG, Aharon-Peretz J, Perry D. 2009. Two systems for empathy: a double dissociation between emotional and cognitive empathy in inferior frontal gyrus versus ventromedial prefrontal lesions. *Brain*. 132:617–627.
- Shukla DK, Keehn B, Müller RA. 2010. Tract-specific analyses of diffusion tensor imaging show widespread white matter compromise in autism spectrum disorder. *J Child Psychol Psychiatry*. 52:286–295.
- Singer T. 2006. The neuronal basis and ontogeny of empathy and mind reading: review of literature and implications for future research. *Neurosci Biobehav Rev*. 30:855–863.
- Singer T, Seymour B, O'Doherty J, Kaube H, Dolan RJ, Frith CD. 2004. Empathy for pain involves the affective but not sensory components of pain. *Science*. 303:1157–1162.
- Smith IM, Bryson SE. 1994. Imitation and action in autism: a critical review. *Psychol Bull*. 116:259–273.
- Smith SM. 2002. Fast robust automated brain extraction. *Hum Brain Mapp*. 17:143–155.
- Smith SM, Jenkinson M, Johansen-Berg H, Rueckert D, Nichols TE, Mackay CE, Watkins KE, Ciccarelli O, Cader MZ, Matthews PM et al. 2006. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *Neuroimage*. 31:1487–1505.
- Smith SM, Jenkinson M, Woolrich MW, Beckmann CF, Behrens TEJ, Johansen-Berg H, Bannister PR, De Luca M, Drobnjak I, Flitney DE. 2004. Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage*. 23:S208–S219.
- Smith SM, Nichols TE. 2009. Threshold-free cluster enhancement: addressing problems of smoothing, threshold dependence and localisation in cluster inference. *Neuroimage*. 44:83–98.
- Soderstrom H. 2003. Psychopathy as a disorder of empathy. *Eur Child Adolesc Psy*. 12:249–252.
- Song SK, Sun SW, Ramsbottom MJ, Chang C, Russell J, Cross AH. 2002. Demyelination revealed through MRI as increased radial (but unchanged axial) diffusion of water. *Neuroimage*. 17:1429–1436.
- Sonnby-Borgström M. 2002. Automatic mimicry reactions as related to differences in emotional empathy. *Scand J Psychol*. 43:433–443.
- Stephens GJ, Silbert LJ, Hasson U. 2010. Speaker-listener neural coupling underlies successful communication. *Proc Natl Acad Sci USA*. 107:14425–14430.
- Stueber K. 2008. Measuring empathy. Stanford encyclopedia of philosophy. Stanford (CA): Center for the Study of Language and Information. Available from: <http://plato.stanford.edu/archives/fall2008/entries/empathy/measuring.html>.
- Tang YY, Lu Q, Geng X, Stein EA, Yang Y, Posner MI. 2010. Short-term meditation induces white matter changes in the anterior cingulate. *Proc Natl Acad Sci USA*. 107:15649–15652.
- Unger LS, Thummuluri LK. 1997. Trait empathy and continuous helping: the case of volunteerism. *J Soc Behav Pers*. 12:785–800.
- van Rijn S, Aleman A, van Diessen E, Berckmoes C, Vingerhoets G, Kahn RS. 2005. What is said or how it is said makes a difference: role of the right fronto-parietal operculum in emotional prosody as revealed by repetitive TMS. *Eur J Neurosci*. 21:3195–3200.
- Voinoskos AN, Farzan F, Barr MS, Lobaugh NJ, Mulsant BH, Chen R, Fitzgerald PB, Daskalakis ZJ. 2010. The role of the corpus callosum in transcranial magnetic stimulation induced interhemispheric signal propagation. *Biol Psychiatry*. 68:825–831.
- Wan CY, Bazen L, Baars R, Libenson A, Zipse L, Zuk J, Norton A, Schlaug G. 2011. Auditory-motor mapping training as an intervention to facilitate speech output in non-verbal children with autism: a proof of concept study. *PLoS One*. 6:e25505.
- Wheatley T, Kang O, Parkinson C, Looser C. 2012. From mind perception to mental connection: synchrony as a mechanism for social understanding. *Soc Pers Psychol Compass*. 6:589–606.
- Wheeler-Kingshott CAM, Cercignani M. 2009. About “axial” and “radial” diffusivities. *Magn Reson Med*. 61:1255–1260.
- Whitfield-Gabrieli S, Thermenos HW, Milanovic S, Tsuang MT, Faraone SV, McCarley RW, Shenton ME, Green AI, Nieto-Castanon A, LaViolette P et al. 2009. Hyperactivity and hyperconnectivity of the default network in schizophrenia and in first-degree relatives

- of persons with schizophrenia. *Proc Natl Acad Sci USA*. 106:1279–1284.
- Wilhelm MO, Bekkers R. 2010. Helping behavior, dispositional empathic concern, and the principle of care. *Soc Psychol Quart*. 73:11–32.
- Wilson M, Knoblich G. 2005. The case for motor involvement in perceiving conspecifics. *Psychol Bull*. 131:460–473.
- Zahn-Waxler C, Robinson J, Emde RN. 1992. The development of empathy in twins. *Dev Psychol*. 28:1038–1047.
- Zaki J, Ochsner K. 2012. The neuroscience of empathy: progress, pitfalls and promise. *Nat Neurosci*. 15:675–680.
- Zaki J, Weber J, Bolger N, Ochsner K. 2009. The neural bases of empathic accuracy. *Proc Natl Acad Sci USA*. 106:11382–11387.