

**Title:**

Neural correlates of empathic accuracy in adolescence

**Running title:**

fMRI of empathic accuracy in adolescence

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## **Abstract**

Empathy, the ability to understand others' emotions, can occur through perspective taking and experience sharing. Neural systems active when adults empathize include regions underlying perspective taking (e.g. medial prefrontal cortex; MPFC), and experience sharing (e.g. inferior parietal lobule; IPL). It is unknown whether adolescents utilize networks implicated in both experience sharing and perspective taking when accurately empathizing. This question is critical given the importance of accurately understanding others' emotions for developing and maintaining adaptive peer relationships during adolescence. We extend the literature on empathy in adolescence by determining the neural basis of empathic accuracy, a behavioral assay of empathy that does not bias participants toward the exclusive use of perspective taking or experience sharing. Participants (N=155, aged 11.1-15.5 years) watched videos of "targets" describing emotional events and continuously rated the targets' emotions during functional magnetic resonance imaging scanning. Empathic accuracy related to activation in regions underlying perspective taking (MPFC, temporoparietal junction, and superior temporal sulcus), while activation in regions underlying experience sharing (IPL, anterior cingulate cortex, and anterior insula) related to lower empathic accuracy. These results provide novel insight into the neural basis of empathic accuracy in adolescence, and suggest that perspective taking processes may be effective for increasing empathy.

**Keywords:** empathy, adolescence, perspective taking, empathic accuracy, experience sharing

## Introduction

Empathy, or the ability to understand others' emotions, is a critical skill for effective social interaction and may be a first step towards altruistic behavior (Eisenberg et al., 1991; Knafo et al., 2008). Adolescents place greater value on relationships with peers relative to those with family, which is reflected in part by an increasing proportion of time spent with peers (Brown, 2004). This change likely necessitates greater use of complex social communication skills such as empathy, as family relationships entail interactions with familiar people, whereas adolescents form new types of relationships with their peers. Research also indicates that adolescents with greater empathy have less internalizing problems, and are less often the victims of bullying (Gleason et al., 2009). Thus, it is critical to understand the processes leading to successful empathy in order to improve adolescents' well-being.

Zaki and Ochsner describe two processes supporting empathy: perspective taking and experience sharing (2012). Experience sharing (or affective empathy; Zahn-Waxler et al., 1992) involves an affective response whereby a perceiver vicariously feels an emotion similar to another person. Research targeting neural processes associated with experience sharing – for example, using stimuli depicting bodily injury – indicates that this process involves activation in some of the same regions that are active during first-hand experience in adults (Hein and Singer, 2008; Singer et al., 2004; Van Overwalle and Baetens, 2009) and in children aged 7 – 12 years (Decety et al., 2008). Regions associated with experience sharing include inferior parietal lobule (IPL), anterior cingulate cortex (ACC) and premotor cortex (PMC; Zaki and Ochsner, 2012), as well as anterior insula (AI; Singer et al., 2004). AI has been implicated in experience

sharing specifically for pain, and with ACC it is involved in first-hand experience of pain (Hein and Singer, 2008). Activation in PMC and IPL is associated with experience sharing in tasks involving motor action (Chong et al., 2008), particularly when intention can be inferred (Iacoboni et al., 2005). PMC is also involved in motor planning and control (Culham, 2015; Lamm et al., 2011).

Perspective taking (or cognitive empathy) does not require an affective response, but rather inferring another person's thoughts (Ruby and Decety, 2004). Activation in regions including medial prefrontal cortex (MPFC), precuneus, superior temporal sulcus (STS), and right temporal-parietal junction (RTPJ) relates to perspective taking when adults infer a target's thoughts based on actual or implied motion (Allison et al., 2000), written narratives, and cartoon vignettes (Gallagher et al., 2000). Research in adolescents with cartoon vignettes (Sebastian et al., 2012), pictures of positive and negative social interactions (Overgaauw et al., 2014), and simulated interactions with avatars (i.e. Cyberball; Gunther Moor et al., 2012; Masten et al., 2013) has also revealed activation in MPFC, RTPJ, and STS. Additionally, this network relates to cognitive processes such as autobiographical memory, prospection, and task-unrelated processing (i.e. 'default mode' activation; Spreng et al., 2008). Thus, the neural regions associated with perspective taking likely serve a more general function of inferring goals (Buckner and Carroll, 2007; Van Overwalle and Baetens, 2009).

These two sub-components of empathy, perspective taking and experience sharing, are thus associated with activation in distinct neural networks. Notably, regions associated with perspective taking (and, to a lesser extent, experience sharing) undergo substantial changes during adolescence. The neural regions underlying perspective

taking mature much later than those underlying experience sharing, and the MPFC in particular does not fully mature up to 25 years of age (Singer, 2006). There are also developmental differences between adolescents and adults in resting state (Blakemore, 2012) and task-based (Burnett and Blakemore, 2009) connectivity of regions within the network underlying perspective taking, and with intrinsic connectivity of the ACC (Kelly et al., 2009). Moreover, behavioral data indicates adolescents perform worse than adults on a perspective taking task (Dumontheil et al., 2010).

Given these neurodevelopmental differences and the importance of peer relationships during this period, it is important to characterize the neural correlates of empathy in adolescents. While the studies described above have investigated the neural basis of perspective taking (Gunther Moor et al., 2012; Masten et al., 2009; Sebastian et al., 2012) and witnessing others' pain (Decety et al., 2008) in adolescents, none have utilized complex, realistic social stimuli. One exception is the study by Overgaauw et al., which included posed photographs of social scenes that provided more complex information, however this study focused on punishment behavior (in the dictator game) and differences between positive and negative scenes, rather than the accuracy by which participants understood others' emotions. The majority of research to date in adolescents has focused on isolating brain activation related to either experience sharing or perspective taking with paradigms targeting one of these two processes. For example, while Cyberball and cartoon vignettes provide valuable insight into mechanisms underlying perspective taking, these stimuli do not permit direct access to another person's emotional expressions and the opportunity for simulation that is a precursor of experience sharing (Sato et al., 2013). Conversely, tasks using

images of bodily injury (Decety et al., 2008) or the pictures of eyes used in the mind in the eyes paradigm (Baron-Cohen et al., 1997) might allow for mimicry but lack a narrative component that is present in perspective taking tasks. In order to fully understand empathy we need to move beyond reductive paradigms to study how these two processes support empathic behavior with realistic social stimuli.

Empathic accuracy paradigms provide ecological validity through the use of videos of a real person (the “target”) expressing actual emotions while sharing emotional memories. In the empathic accuracy task participants have access to contextual, narrative information by way of the story told in the video, have the opportunity for simulation from the emotional facial expressions in the video, and are not instructed to use a cognitive (i.e., perspective taking) or affective (i.e., experience sharing) strategy. Thus, participants are able to utilize either perspective taking or experience sharing. In this way, empathic accuracy paradigms are theory-neutral with respect to the type of process engaged during empathy. Indeed, neuroimaging research in adults demonstrates that the complex video stimuli in the empathic accuracy task elicit activation in regions involved in perspective taking (e.g. STS, TPJ, and MPFC) and experience sharing (e.g. IPL and bilateral dorsal PMC; Zaki et al., 2009).

In addition to allowing use of either a perspective taking or experience sharing strategy, empathic accuracy tasks are grounded in a behavioral measure critically important for peer relations and adjustment in young adolescents. Empathic accuracy is measured from the correlation between perceiver’s ratings of a target’s emotions relative to the target’s ratings of their own emotions in the video. Adolescents (average age 12.2 years) with lower scores on this behavioral measure of empathy (empathic

accuracy) were more likely to suffer from bullying and internalizing problems such as depression, while higher empathic accuracy mitigated the negative impact of poor peer relations on personal adjustment (Gleason et al., 2009). Furthermore, this study showed that self-reported empathy did not relate to outcomes such as depression and bullying (consistent with the finding that self-reported empathy is not correlated with empathic accuracy in adults; Simpson, Minda, & Ickes, 2003). Thus empathic accuracy affords a unique behavioral measure with important consequences for young adolescents.

In the current study we expanded on prior research on empathy in adolescence to determine the neural systems supporting empathic accuracy during functional magnetic resonance imaging (fMRI) scanning. We investigated whether adolescents would have greater empathic accuracy when activating networks underlying experience sharing and perspective taking by using an empathic accuracy paradigm that allowed us to uniquely examine the relationship between brain activation and behavior. We hypothesized that adolescents would recruit regions related to experience sharing (e.g. IPL, ACC, AI and PMC) when making empathically accurate responses since regions underlying perspective taking (e.g., MPFC, RTPJ and STS) are not fully developed at this age, and behavioral research indicates that perspective taking skills are still developing during adolescence (Crone, 2013; Dumontheil et al., 2010). Since previous research indicates empathic accuracy provides a behavioral measure of empathy that is not fully captured by self-report measures of empathy (Gleason et al., 2009; Simpson et al., 2003), we hypothesized that empathic accuracy would not be strongly related to self-reported empathic concern nor perspective taking. Additionally, given the mixed evidence on gender differences in empathy (Ickes et al., 2000; Michalska et al., 2013;

Van der Graaff et al., 2014) we did not have a specific hypothesis with regard to gender differences in empathy, and rather we capitalized on the large sample size in the current study to thoroughly investigate gender differences across multiple measures of empathy in exploratory analyses.

## **Materials and methods**

### *Participants*

We recruited 192 healthy adolescents (average age 12.8 years  $\pm$  8.8 months, age range 11.1-15.5 years, 69 female) from the Madison, WI community online and in local print and broadcast media to participate in a study on the impact of games on behavior and brain function. Participants had to be enrolled in the 7<sup>th</sup> or 8<sup>th</sup> grade, fluent English speakers, safe for MRI scanning, not using psychotropic medications, and with no current or previous diagnosis of a mental illness. The results presented here are from participants' first visit (baseline data), which was collected prior to randomization to an intervention. Participants completed other tasks as a part of the larger study to measure performance in domains we expected to be affected by the intervention, such as response inhibition measured with a Stroop task. Thirty-three participants' data were unusable due to technical issues (21), inability to see or hear the stimuli (8), or not completing the task (4). Thus the sample size for analysis of empathic accuracy was 159 (average age 13.3 years  $\pm$  8.3 months, age range 11.1-15.5 years, 54 female). UW-Madison's Health Sciences Institutional Review Board approved the protocol, and all participants provided informed assent and were given monetary compensation for participating. Legal guardians provided informed consent.

### *Questionnaires*



Participants completed a battery of questionnaires as a part of the larger study of the impact of games on behavior and brain function, including the Interpersonal Reactivity Index (IRI; Davis, 1983) and the Pro-social Norms Survey (PNS; The American National Election Studies (ANES), 2015). The IRI contains four sub-scales, two of which measure constructs related to empathy and are relevant for the current analysis: empathic concern and perspective taking. We also explored the personal distress sub-scale a post-hoc manner. The PNS provided a measure of adherence to pro-social norms in which participants select one of five responses from “Strongly Disagree” to “Strongly Agree” with “Disagree”, “Neither Agree nor Disagree”, and “Agree” in between the two polar options. Example items from this scale include: “It is important to help one another so that the community in general is a better place” and “These days people need to look after themselves and not overly worry about others” (the latter example being reverse scored). Following completion of the study, participants were asked to retroactively rate their pubertal development using the Tanner Scale (Taylor et al., 2001). Since participants were re-contacted the sample size for the Tanner scale was further reduced, but this did not affect the sample size for any of the other measures. In total, 105 participants who completed the empathic accuracy task also completed the post-study questionnaire (average age 13.4 years  $\pm$  8.5 months, 34 female).

### *Empathic Accuracy Task*

The empathic accuracy task was created by Ickes (1993) to assess a participant’s ability to judge the emotions of a target person presented in a video. Participants’ (the “perceivers”) empathic accuracy scores are based on the targets’

ratings of their own emotions. The task used in the current study was based on a version adapted by Zaki et al. (2009) for use during fMRI scanning (Figure 1). The only modifications to the task for the current study were to present videos of older adolescent *targets* (aged 18-21 years) describing events from their adolescence in order to appear more relevant to the adolescent perceivers (i.e. rather than adults). Targets were videotaped while discussing emotional events such as the death of a grandparent or winning a sports competition. Targets were instructed to think of the 4 most negative and 4 most positive events from their adolescence, which they had time to recollect and write down before the videos were recorded. For each video, the targets were randomly cued to one of the events, and given a few minutes to read their recollections and put themselves in that moment before retelling on video. Targets did not read from their written responses, but simply used them as a reminder. After recording, the targets watched their own videos and made ratings of their emotions as displayed in the videos, which served as the “correct” response to which perceivers’ ratings were compared. The ratings were collected on a Likert scale from 1-9 with “Very Negative” at 1 on the left and “Very Positive” at 9 on the right (Figure 1A). The targets were asked to adjust their rating every time their emotion changed in the video, and ratings were collected continuously throughout the entire video.

Eight videos were recorded of 19 different target individuals, and for each target individual there were 8 videos evenly split between descriptions of negative and positive events from their adolescence. This resulted in a total of 154 videos from which we selected 2 sets of 18 videos for the empathic accuracy task. Thus, 36 different videos were used in total. Participants were shown one set of videos, and the set used was

counterbalanced across participants. The particular videos for each set were selected based on a number of criteria. We needed to select an equal number of male and female targets from as diverse a set of ethnic backgrounds as possible. Targets needed to have at least 2 positive and 2 negative videos, so that the same targets appeared across video sets and valences. Videos could not include content deemed inappropriate for minors (e.g. swearing). Finally, we had to organize the videos into sub-sets for each of the 3 scan runs (for each of the 2 video sets), such that each sub-set of 6 videos (per scan run) included an equal number of videos by valence and gender, and the total length for each run was equivalent.

Participants in the current study (identified as “perceivers” in Figure 1) completed the empathic accuracy task in 3 fMRI scan runs, each lasting approximately 5 minutes. In the empathic accuracy fMRI task a cue word was displayed for 3 seconds, followed by a fixation cross for 2 seconds and then a video, which ranged from 28 to 144 seconds (mean=90 seconds, Figure 1B). The cue instructed participants how to rate the videos, corresponding to 3 different conditions, and ratings were made continuously throughout the videos. If the cue “OTHER” appeared participants were instructed to rate the emotion of the target in the video from negative to positive, exactly as the targets had rated themselves. If the cue “SELF” appeared participants were instructed to rate their own emotions from negative to positive using the same scale. If the cue “GAZE” appeared participants were instructed to rate the direction of the target’s eye-gaze from left to right using a 1-9 Likert scale with 1 labeled “Left” and 9 labeled “Right”. The order of conditions was pseudo-randomized such that participants saw a different order of 6 trial blocks in each of the task runs, and targets were half male and half female. There

were 18 trial blocks, 6 per condition, and each had a unique video stimulus. This report focuses on the “OTHER” condition, which corresponded to empathic accuracy trials. Prior to the scan participants completed three practice trials with videos not used in the fMRI task. Empathic accuracy was determined from the OTHER trials by calculating the correlation between the time-course of target and perceiver ratings for each video (Figure 1C), and then  $r$ - to  $Z$ -transforming them with Fisher’s method. One trial was excluded due to large disagreement between the target’s rating and the majority of participant ratings, which resulted in extremely low average empathic accuracy scores across participants (mean  $r < 0.10$ ).

### *Statistical Analysis*

See Supplementary Methods for information on MRI data acquisition and processing. We studied the relationship between blood-oxygen-level dependent (BOLD) activation and empathic accuracy across trials, within subject for “OTHER” trial blocks. For the first level, time series analysis for each of 18 blocks was modeled with a separate regressor. Only the 6 estimates for the "OTHER" trial blocks provided a measure of empathic accuracy and were considered in higher-level analyses. In a within subject, fixed effects analysis, the linear relationship between the block-based BOLD activation and within-block empathic accuracy was estimated. The group analysis then estimated the average of this linear slope across subjects in a mixed effects Flandermans 1 analysis. The number of ratings made per minute for each trial was an additional regressor of no interest to control for differences in the amount of ratings.  $Z$  (Gaussianised T/F) statistic images were thresholded using clusters determined by  $Z > 3.1$  and a (corrected) cluster significance threshold of  $p = 0.05$  (Worsley, n.d.).

We conducted region of interest (ROI) analyses using 12 *a priori* ROIs previously related to perspective taking, experience sharing or empathic accuracy (right ventral and left dorsal MPFC – VMPFC and DMPFC, right STS and ACC, 2 right IPL ROIs, and right and left TPJ, PMC, and AI). ROIs were defined as 6mm spheres from coordinates provided in the supplementary material by Zaki et al. (2009), which to our knowledge is the only study to determine the neural correlates of empathic accuracy in healthy adults. The ROI analysis allowed us to directly replicate the analysis used by Zaki et al., and to test whether ROIs related to perspective taking versus experience sharing differentially contributed as a *set* to empathic accuracy in adolescents. We extracted the mean percent signal change for each participant from the empathic accuracy-modulated contrast, and tested the mean for each ROI against zero using a two-tailed *t*-test. We controlled for multiple comparisons using family-wise error control over the 12 ROIs according to maximum-*t* based null estimated non-parametrically with a total of 5000 permutations (indicated by *p*\*; Nichols and Holmes, 2002). All other reported statistics correspond to uncorrected results. In order to test whether activation in a set of regions underlying perspective taking (PT; VMPFC, DMPFC, STS, right and left TPJ) had a stronger relationship with empathic accuracy than regions underlying experience sharing (ES; two IPL ROIs, right and left AI and PMC, and ACC), we computed the average of the empathic accuracy-related activations across each set. We then ran a repeated measures linear mixed effects model including the network type (ES or PT) as a fixed effect and subject number as a random effect using the *lmer* function from the *lme4* library (Bates et al., 2014) in the statistical analysis software R (version 3.2.2; R Core Team, 2015). *P*-value computation used the *modelSummary* function of the

lmSupport package, which is based on the Kenward-Rogers approximation for degrees of freedom (Kenward and Roger, 1997).

Results are reported after removing outliers based on Cook's D using a cutoff threshold of  $4/(N-P)$  for data points disconnected from the distribution, and outliers were removed from the corresponding figures. All results remained the same without outliers removed, except in 3 cases as indicated in the results. We tested for gender differences at each stage of the analysis, and controlled for gender in analyses where we found gender differences in one or more variables. The results specify when gender was included as a covariate, and all the significant results remain without this covariate.

Two participants were removed from all group analyses due to extreme motion across multiple scan runs (defined as runs with a framewise displacement greater than 0.9mm in over 25% of the TRs), and 2 participants were removed due to extreme signal intensity based on the Cook's D threshold across *t*-tests assessing whether the mean brain activation for each of the ROIs (across participants) was different from zero. Thus the sample size for analysis with fMRI data was 155 (average age = 12.8 years  $\pm$  8.6 months, N = 53 female). Of the participants with fMRI data, 127 were right-handed, 11 were left-handed, 5 were ambidextrous, and the remaining 12 did not provide handedness information. All results remain the same when limited to right-handed participants, except in one case where the effect became marginal, which is indicated in the results.

## **Results**

### *Empathic Accuracy and Self-Report Measures*

The average  $r$  value for empathic accuracy across all participants (prior to Fisher transformation) was 0.68 (SD = 0.25, range = -0.56 - 0.99). All analyses used Fisher Z-transformed empathic accuracy to normalize the distribution of correlation values. Females ( $M=1.03$ ,  $SD=0.18$ ) had significantly higher empathic accuracy than males ( $M=0.96$ ,  $SD=0.14$ ;  $t(152)=-2.21$ ,  $p=0.029$ ,  $b=-0.08$ ,  $CI=[-0.14,-0.01]$ , 5 outliers removed; Figure 2). The gender difference in empathic accuracy remained significant while controlling for pubertal level ( $t(101)=-2.67$ ,  $p=0.009$ ,  $b=-0.12$ ,  $CI=[-0.21,-0.03]$ , 1 outlier removed), however it dropped to a trend level when controlling for age ( $t(151)=-1.67$ ,  $p=0.097$ ,  $b=-0.06$ ,  $CI=[-0.13, 0.01]$ , 5 outliers removed). This effect also became marginal without outliers removed ( $p=0.051$ ). There was no gender difference in age ( $t(153)=-0.24$ ,  $p=0.81$ ,  $b=-0.31$ ,  $CI=[-2.81,2.20]$ , 4 outliers removed).

We found gender differences in the questionnaire measures, all of which had 1 outlier removed. Self-reported empathic concern (IRI;  $M=17.27$ ,  $SD=4.16$ ) was higher in females ( $M=19.30$ ,  $SD=3.47$ ) than males ( $M=16.37$ ,  $SD=4.04$ ),  $t(156)=-3.93$ ,  $p<0.001$ ,  $b=-2.63$ ,  $CI=[-3.93,-1.31]$  (Supplementary Figure 1A). Self-reported perspective taking (IRI;  $M=14.75$ ,  $SD=4.56$ ) was higher in females ( $M=15.77$ ,  $SD=3.89$ ) than males ( $M=14.13$ ,  $SD=4.67$ ),  $t(156)=-2.47$ ,  $p=0.015$ ,  $b=-1.87$ ,  $CI=[-3.36,-0.37]$  (Supplementary Figure 1B). Self-reported adherence to pro-social norms (PNS;  $M=31.66$ ,  $SD=3.79$ ) was higher in females ( $M=32.79$ ,  $SD=3.87$ ) than males ( $M=31.19$ ,  $SD=3.51$ ),  $t(156)=-2.19$ ,  $p=0.030$ ,  $b=-1.38$ ,  $CI=[-2.63,-0.13]$  (Supplementary Figure 1C). All of these gender differences remained significant when controlling for either pubertal development or age.

In separate analyses, we regressed empathic accuracy on self-reported empathic concern, perspective taking, or pro-social norms while controlling for gender. Greater empathic accuracy was not associated with more empathic concern ( $t(149)=1.61$ ,  $p=0.109$ ,  $b=0.01$ ,  $CI=[-0.001,0.015]$ , 7 outliers removed; Supplementary Figure 2A), however this effect was significant with outliers included ( $p=0.029$ ) or if gender was not included as a covariate ( $p=0.017$ ). Empathic accuracy was not related to self-reported perspective taking ( $t(150)=1.41$ ,  $p=0.161$ ,  $b=0.005$ ,  $CI=[-0.002,0.01]$ , 6 outliers removed; Supplementary Figure 2B), or with self-reported adherence to pro-social norms ( $t(152)=0.75$ ,  $p=0.453$ ,  $b=0.004$ ,  $CI=[-0.01, 0.01]$ , 4 outliers removed; Supplementary Figure 2C) unless the outliers were included ( $p=0.031$ ).

We conducted a post-hoc analysis regressing empathic accuracy on personal distress while controlling for gender ( $M=10.79$ ,  $SD=3.62$ ) and did not find a significant relationship ( $t(153)=0.44$ ,  $p=0.661$ ,  $b=0.002$ ,  $CI=[-0.01,0.01]$ , 3 outliers removed).

#### *Voxelwise Analysis of Empathic Accuracy*

A voxel-wise analysis of the relationship between BOLD activation and empathic accuracy revealed that empathic accuracy related to greater activation in regions underlying perspective taking, including VMPFC, DMPFC, RTPJ, precuneus, and STS (depicted in orange/yellow, Figure 3A). Conversely, in regions underlying experience sharing, including ACC, and right IPL, activation was related to *lower* empathic accuracy (or greater empathic accuracy related to less activation in these regions; depicted in blue in Figure 3A). A summary of clusters with activation related to empathic accuracy is provided in Table 1. We ran a voxelwise independent samples *t*-test between males and



females, and did not identify any significant gender differences in the relationship between empathic accuracy and BOLD activation.

### *Region of Interest Analysis of Empathic Accuracy*

The results of the ROI analyses paralleled the voxelwise results, such that higher empathic accuracy was related to greater activation in regions underlying perspective taking: STS ( $t(152)=3.49$ ,  $p^*=0.006$ ,  $p=0.001$ ,  $b=0.11$ , 2 outliers removed), and VMPFC at a trend level ( $t(152)=2.71$ ,  $p^*=0.073$ ,  $p=0.008$ ,  $b=0.07$ , 2 outliers removed). In contrast, greater activation in regions underlying experience sharing related to *lower* empathic accuracy: ACC ( $t(150)=-2.48$ ,  $p^*=0.042$ ,  $p=0.014$ ,  $b=-0.12$ , 4 outliers removed), right IPL ( $t(153)=-2.90$ ,  $p^*=0.038$ ,  $p=0.004$ ,  $b=-0.11$ , 1 outlier removed), right AI ( $t(149)=-4.83$ ,  $p^*<0.001$ ,  $p<0.001$ ,  $b=-0.10$ , 5 outliers removed), and left AI ( $t(152)=-3.34$ ,  $p^*=0.008$ ,  $p=0.001$ ,  $b=-0.10$ , 2 outliers removed). There were no significant gender differences in empathic accuracy-related activation in any of the ROIs.

We compared activation across ROIs in the network associated with perspective taking to those associated with experience sharing. Mean activation extracted from the set of perspective taking regions was associated with greater empathic accuracy than activation from experience sharing regions,  $F(1,150)=26.8$ ,  $p<0.001$ ,  $b=0.12$ ,  $CI=[0.07,0.16]$  (Figure 3B). BOLD activation within the perspective taking regions was significantly positively related to empathic accuracy ( $t(150)=2.70$ ,  $p=0.008$ ,  $b=0.06$ ,  $CI=[0.02, 0.11]$ ). Conversely, activation within the experience sharing network was significantly negatively associated with empathic accuracy ( $t(150)=-2.55$ ,  $p=0.012$ ,  $b=-0.06$ ,  $CI=[-0.10,-0.01]$ ). All three results are reported with 4 outliers removed but remain the same if including these outliers.

We tested whether individual differences in empathic accuracy-related activation in each of the 12 ROIs related to self-reported empathic concern, perspective taking, or adherence to pro-social norms (while controlling for gender). Greater empathic accuracy-related activation in RTPJ was associated with greater empathic concern ( $t(149)=3.02$ ,  $p^*=0.045$ ,  $p=0.003$ ,  $b=2.33$ ,  $CI=[0.81,3.86]$ , 3 outliers removed; Figure 4A) and only marginally with perspective taking ( $t(148)=2.15$ ,  $p^*=0.066$ ,  $p=0.034$ ,  $b=2.15$ ,  $CI=[0.16,3.80]$ , 4 outliers removed; Figure 4B). Greater empathic accuracy-related activation in STS was associated with higher adherence to pro-social norms at a trend level ( $t(151)=2.79$ ,  $p^*=0.054$ ,  $p=0.006$ ,  $b=2.08$ ,  $CI=[0.61,3.56]$ , 1 outlier removed; Figure 4C). Conversely, greater empathic accuracy-related activation in right IPL was marginally associated with lower self-reported adherence to pro-social norms ( $t(151)=-2.74$ ,  $p^*=0.066$ ,  $p=0.007$ ,  $b=-1.70$ ,  $CI=[-2.92,-0.47]$ , 1 outlier removed; Figure 4d), however this effect was marginal without outliers removed ( $p=0.052$ ).

We performed a post-hoc analysis to separately test for relationships between empathic accuracy-related activation in the 12 ROIs and self-reported personal distress. There was no relationship between personal distress and empathic accuracy-related activation in RTPJ ( $p=0.364$ ), STS ( $p=0.838$ ) or right IPL ( $p=0.151$ ), or with any of the other ROIs.

## Discussion

This study provides the first evidence that empathic accuracy in adolescents is associated with greater BOLD activation in a network implicated in perspective taking. Previous work also implicates regions underlying perspective taking in adolescents' empathic processing, however these studies used tasks lacking realistic stimuli and

opportunities for experience sharing through mimicry (Blakemore, 2008; Masten et al., 2009; Sebastian et al., 2012). The current study expands upon prior work with a much larger sample and with videos depicting actual people that allow participants to utilize either perspective taking or experience sharing. This is in contrast to tasks that utilize avatars or cartoons, which do not provide opportunities for simulation and experience sharing, or tasks without a narrative component such as images of bodily injury (Decety et al., 2008).

Interestingly, regions involved in experience sharing exhibited either a non-significant or negative relationship with empathic accuracy. This contrasts with previous findings that adults engaged regions underlying perspective taking and experience sharing to the same degree when making empathically accurate ratings (Zaki et al., 2009). These results are also contrary to our hypothesis that adolescents would recruit regions underlying experience sharing (e.g. IPL, PMC, ACC, and AI) rather than regions underlying perspective taking (e.g. VMPFC, DMPFC), which are still maturing at this age. However, this finding is consistent with literature showing adolescents can flexibly engage cognitive control systems in motivationally salient contexts, and at times can outperform adults (Crone and Dahl, 2012; Kleibeuker et al., 2013). Therefore adolescents are not completely lacking in many executive functions subserved by the PFC, such as perspective taking. However, one process in which the PFC plays a central role, and that is still developing in adolescents is self-regulation (Steinberg, 2005), specifically emotion regulation. While perspective taking alone does not require self-regulation, as it does not necessarily entail an affective response, experience sharing in a highly emotional context would very likely necessitate emotion regulation.

One interpretation of the negative relationship between empathic accuracy and activation in experience sharing regions is that adolescents became immersed in their own emotions when sharing the emotional experience of the target. While personal distress can occur with experience sharing (Decety and Ickes, 2011), and potentially reduce empathic accuracy, we were unable to directly test this interpretation in the current study. Without the ability to effectively regulate their emotions, adolescents who experience personal distress from experience sharing may not be able to disengage with their own emotions in order to attend to and accurately identify the target's emotions. Another possibility is that experience sharing could interact with an inaccurate perspective of the target's emotions and further degrade the perceiver's empathic accuracy. Previous findings that adolescents have increased activation in two regions of the experience sharing network (ACC and insula) with greater rejection-related personal distress provide additional support for this idea (Gunther Moor et al., 2012; Masten et al., 2009). Moreover, in another study adolescents had less activation in dorsolateral PFC compared to adults, which may otherwise serve to down-regulate distress (Sebastian et al., 2010). However, post-hoc analyses in the current study did not reveal any significant relationships between self-reported personal distress (from the IRI) and empathic accuracy, or with empathic accuracy-related BOLD activation in any of the ROIs. The questionnaire measuring personal distress was administered outside the scan session, and individual differences in this measure may not have accurately reflected levels of personal distress during the empathic accuracy task. One limitation was a lack of measures of emotion regulation or personal distress following each video,

which would allow us to better test the interpretation that experience sharing caused personal distress, and led to lower empathic accuracy.

Consistent with prior work (Gleason et al., 2009) we did not find significant relationships between empathic accuracy and self-report measures of empathy (e.g., empathic concern or perspective taking). Thus empathic accuracy provides a behavioral measure of empathic ability that is not captured by questionnaires. We also replicated research showing gender differences in self-reported empathy and empathic accuracy (Van der Graaff et al., 2014). Females scored higher on empathy measures in addition to self-reported adherence to pro-social norms. However, similar to Michalska et al. (2013) there were no gender differences in empathic accuracy-related brain activation. Given that gender differences in self-reported empathy in adults may be due to motivational factors (Ickes et al., 2000), similar motivational factors based on gender roles may have contributed to gender differences in the current study. However, we are unable to adequately test this interpretation and future work will be needed to disentangle factors contributing to gender differences in adolescents' empathic ability.

The current study utilized videos of late adolescents in the empathic accuracy task. Although younger adolescent targets would be preferable, it was not possible to obtain videos of minors due to confidentiality considerations and timeline constraints related to IRB approval. The younger appearance of the targets made them more relatable to adolescents, in contrast to the videos of adults used by Zaki et al. (2009). The content of the targets' stories and their emotional reactions were also more vivid, as these events from their adolescence occurred within the past few years. Future work should aspire to include videos from same-aged peers to compare with the present

results, as results of the current study may not generalize to adolescents' empathic abilities with regard to same-aged peers. Moreover, the current study captured empathic accuracy processing during early- to mid-adolescence, and the underlying brain regions may be differentially recruited at different points during this developmental period. Thus, future work with a longitudinal design, combined with videos of targets matched for the age of the perceiver at each point, would provide the strongest test of development of empathic accuracy and the underlying neural networks during adolescence.

The current study also lacked measures to determine the strategy participants used during the empathic accuracy task (i.e. perspective taking, experience sharing or another strategy). The empathic accuracy task provides stimuli that allow utilization of experience sharing or perspective taking strategies, however participants may have been more likely to engage in one strategy over another. While activation in regions underlying these two processes was differentially related to empathic accuracy we cannot determine whether activation was caused by engagement with perspective taking or experience sharing. These regions are involved in other processes that may be related to but distinct from perspective taking or experience sharing. However, the fact that activation across the set of regions associated with perspective taking, both as a group and individually, consistently related to empathic accuracy, and activation in the set of regions associated with experience sharing consistently related to *lower* empathic accuracy lends support to this inference. Furthermore, participants who had greater self-reported empathy and adherence to pro-social norms also made more empathically accurate responses when they had greater activation in perspective taking regions

(RTPJ and STS, respectively), and less activation in right IPL, a region underlying experience sharing. Taken together, the results of the current study suggest that adolescents may be more empathically accurate when engaged in perspective taking than experience sharing.

The pattern of findings uncovered in this study has important implications for how to effectively train empathy in adolescents (possibly through perspective taking). In conclusion, perspective taking networks appear to play a key role in empathic accuracy in adolescents and could be potentially harnessed in programs seeking to cultivate empathy (e.g. social emotional learning, compassion-based training methods; Durlak et al., 2011; Mascaro et al., 2012; Reddy et al., 2012). Additional research is needed to directly assess the strategy adolescents engage when they are empathically accurate to fully characterize effective empathic responding during this important developmental period.

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### **Conflicts of Interest**

Dr. Richard J. Davidson is the founder, president, and serves on the board of directors for the non-profit organization, Healthy Minds Innovations, Inc. In addition, Dr. Davidson serves on the board of directors for the Mind and Life Institute.

### **Figure Captions**

**Figure 1.** Empathic Accuracy Task. Targets were filmed describing emotional events from their adolescence. The target then watched his or her videos while continuously rating his or her emotions as expressed in the video on a scale from “Very Negative” to “Very Positive” (A). These videos were shown to participants in the current study, the perceivers, during an fMRI scan. Perceivers made continuous ratings of the target’s emotions in the video on the same rating scale used by the targets (B). Finally, empathic accuracy scores were determined by calculating the correlation between the perceiver’s ratings with the target’s ratings of his or her emotions (C).

**Figure 2.** Empathic Accuracy by Gender. Females had greater empathic accuracy than males ( $t(152)=-2.21, p=0.029$ ). Error bars represent 95% CIs above and below the point estimates of the means (displayed as triangles). Raw data points are overlaid in gray.



**Figure 3.** BOLD Activation Related to Empathic Accuracy. Voxelwise, wholebrain analysis (A) with regions where increased activation related to higher empathic accuracy are in orange/yellow, and regions where activation related to lower empathic accuracy are in light blue, thresholded using clusters determined by  $Z > 2.3$  and a corrected threshold of  $P < 0.05$ . *A priori* ROIs are labeled and overlaid in red for regions related to perspective taking and in dark blue for regions related to experience sharing, as provided in Zaki et al. (2009), although not all 12 ROIs are depicted here. The ROIs are the same in the top of the panel. The underlay and coordinates are in MNI space. TPJ: temporal parietal junction; IPL: inferior parietal lobule; STS: superior temporal sulcus; VMPFC: ventral medial prefrontal cortex; DMPFC: dorsal medial prefrontal cortex; ACC: anterior cingulate cortex. ROI analysis (B) depicting that empathic accuracy-related activation across the perspective taking (PT) network was greater than the experience sharing (ES) network ( $F(1, 151) = 28.8, p < 0.001$ ). Error bars represent 95% CIs above and below the point estimates of the means (displayed as triangles). Raw data are overlaid in grey.

**Figure 4.** Empathic Accuracy-Related Activation and Questionnaire Measures.

Greater empathic accuracy-related activation extracted from right temporal parietal junction (TPJ) was associated with higher self-reported empathic concern (A;  $t(151) = 2.70, p = 0.008$ ) and perspective taking (B;  $t(151) = 2.59, p = 0.010$ ). Greater self-reported adherence to pro-social norms was associated with more empathic accuracy-related activation extracted from right superior temporal sulcus (STS) (C;  $t(151) = 2.79, p = 0.006$ ), and the opposite relationship was found for right inferior parietal lobule (IPL)

(D;  $t(151)=-2.74$ ,  $p=0.007$ ). Regression lines and data points are adjusted for gender. Precision envelopes represent 95% CIs above and below the point estimates.

### **Table 1.**

Coordinates are provided in MNI space (mm) and Z-values were extracted from the group level analysis of the interaction of EA with BOLD, thresholded using clusters determined by  $Z>2.3$  and a corrected threshold of  $P<0.05$ .

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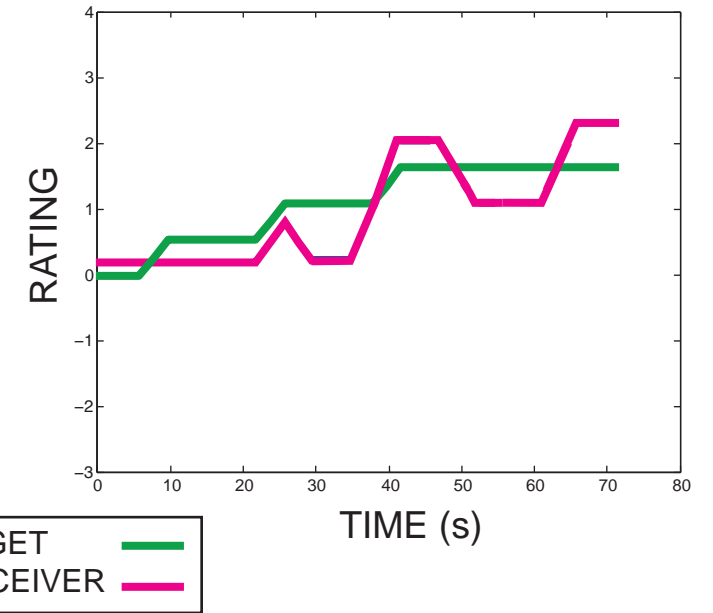
doi:10.1073/pnas.0902666106



STEP 1: Record videos of target describing emotional events from adolescence.



STEP 2: Target watches and rates emotion intensity in their own videos from "Very Negative" to "Very Positive".

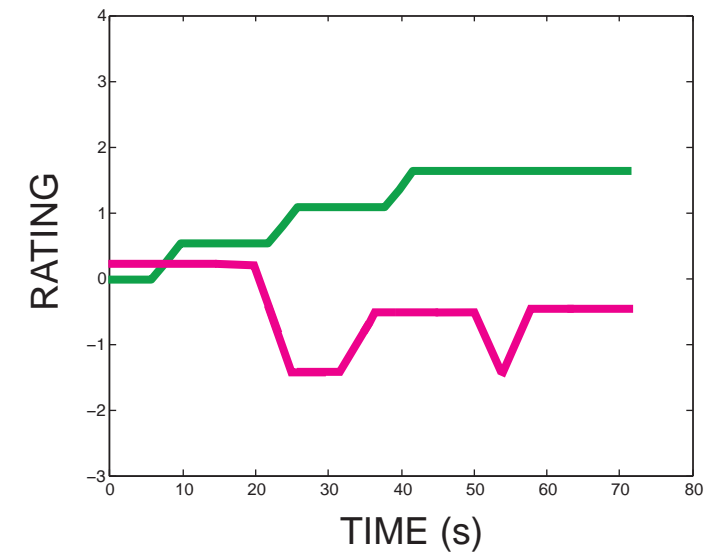


## B. PERCEIVER PROCEDURE

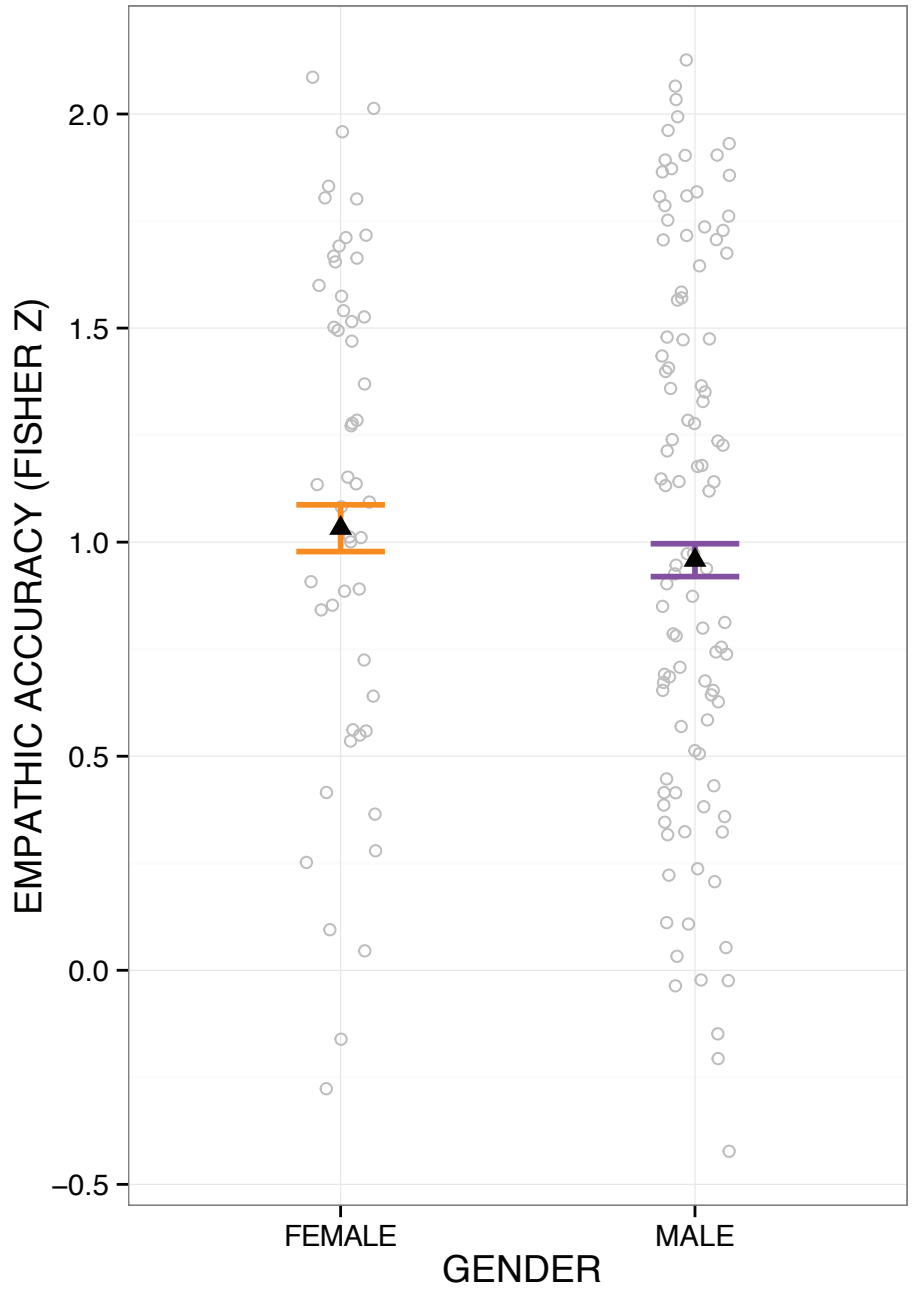


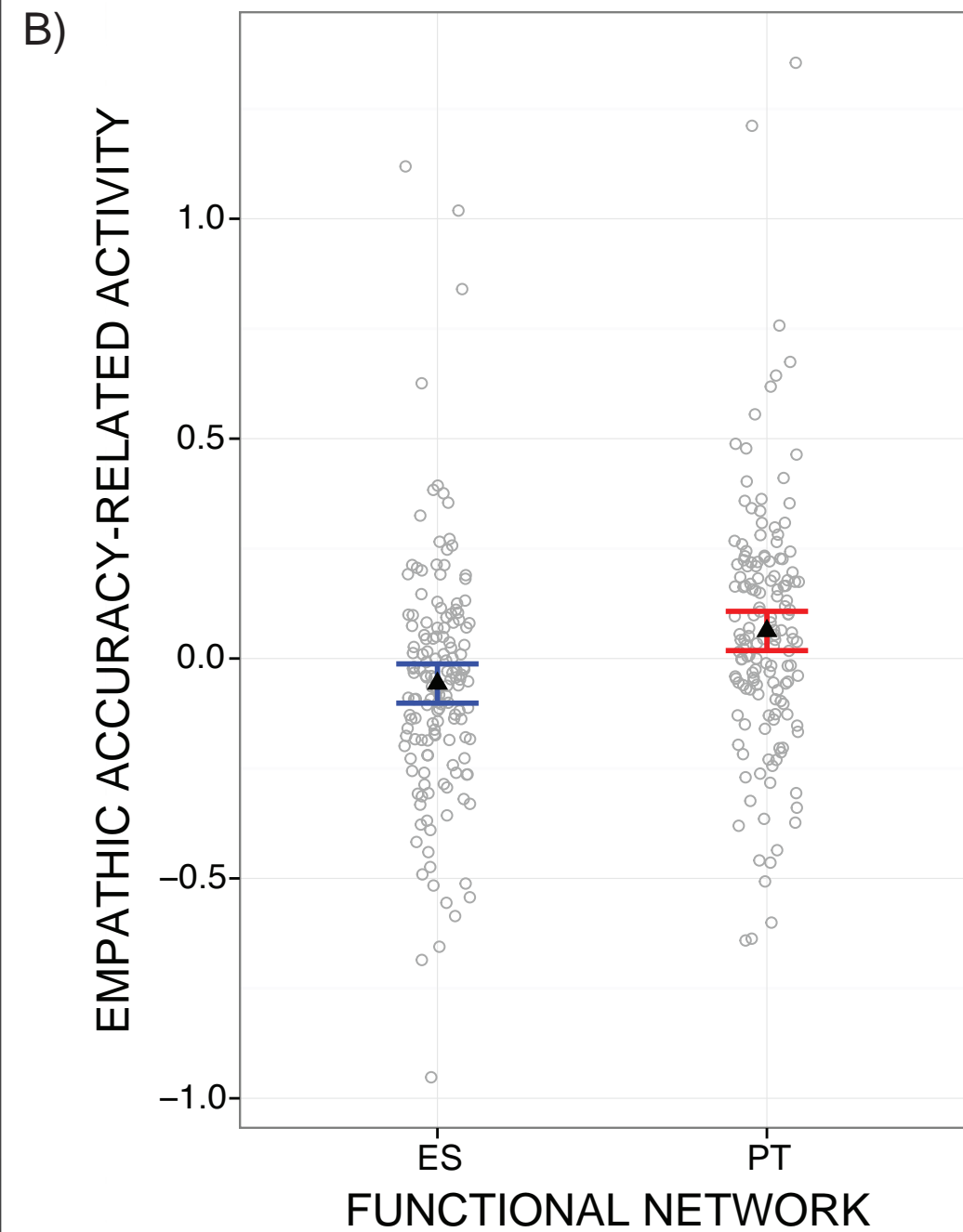
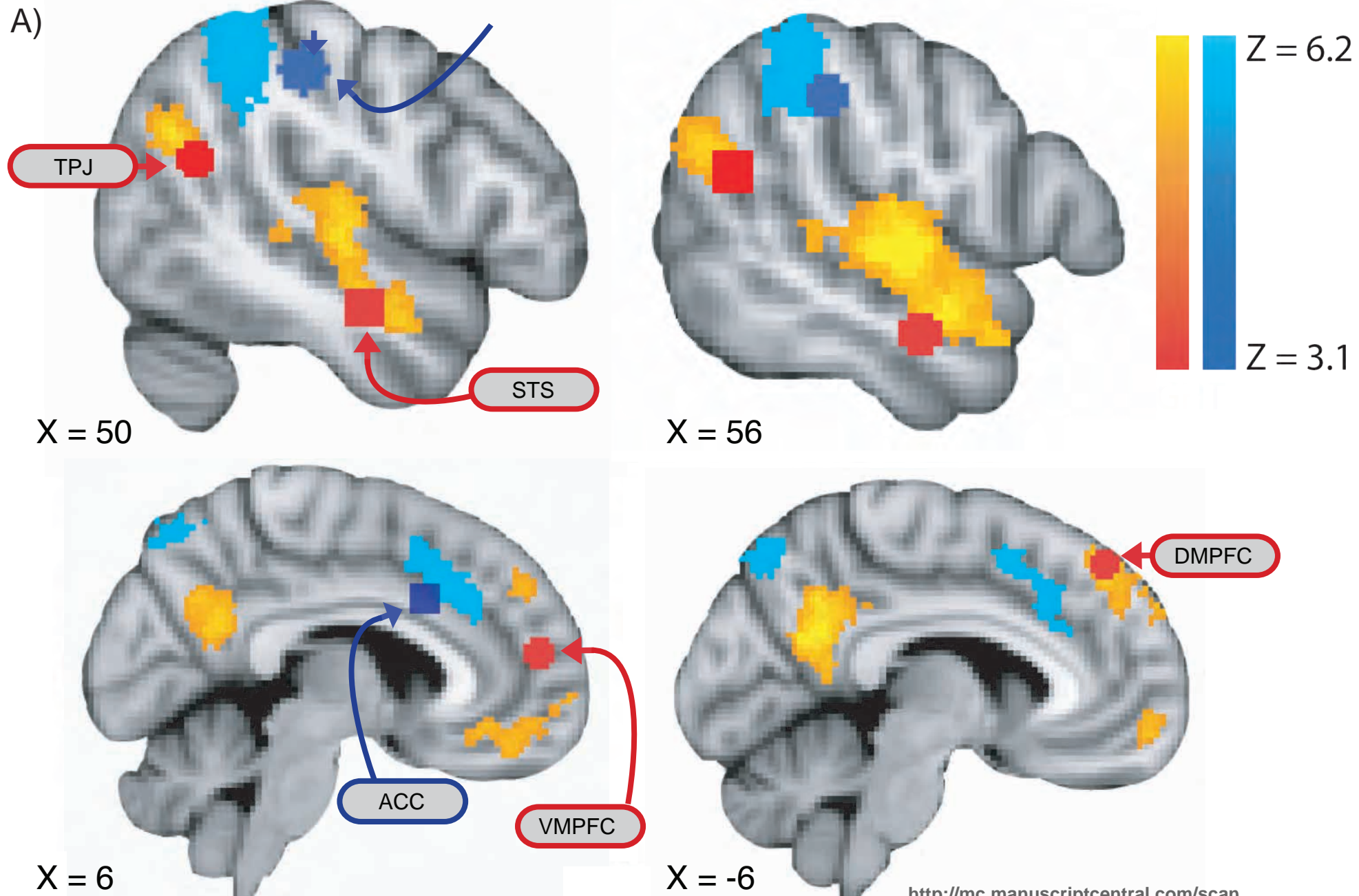
STEP 1: Perceiver rates target's emotions in videos during an fMRI scan using the identical scale as the targets used in Step 2 of Part A (above).

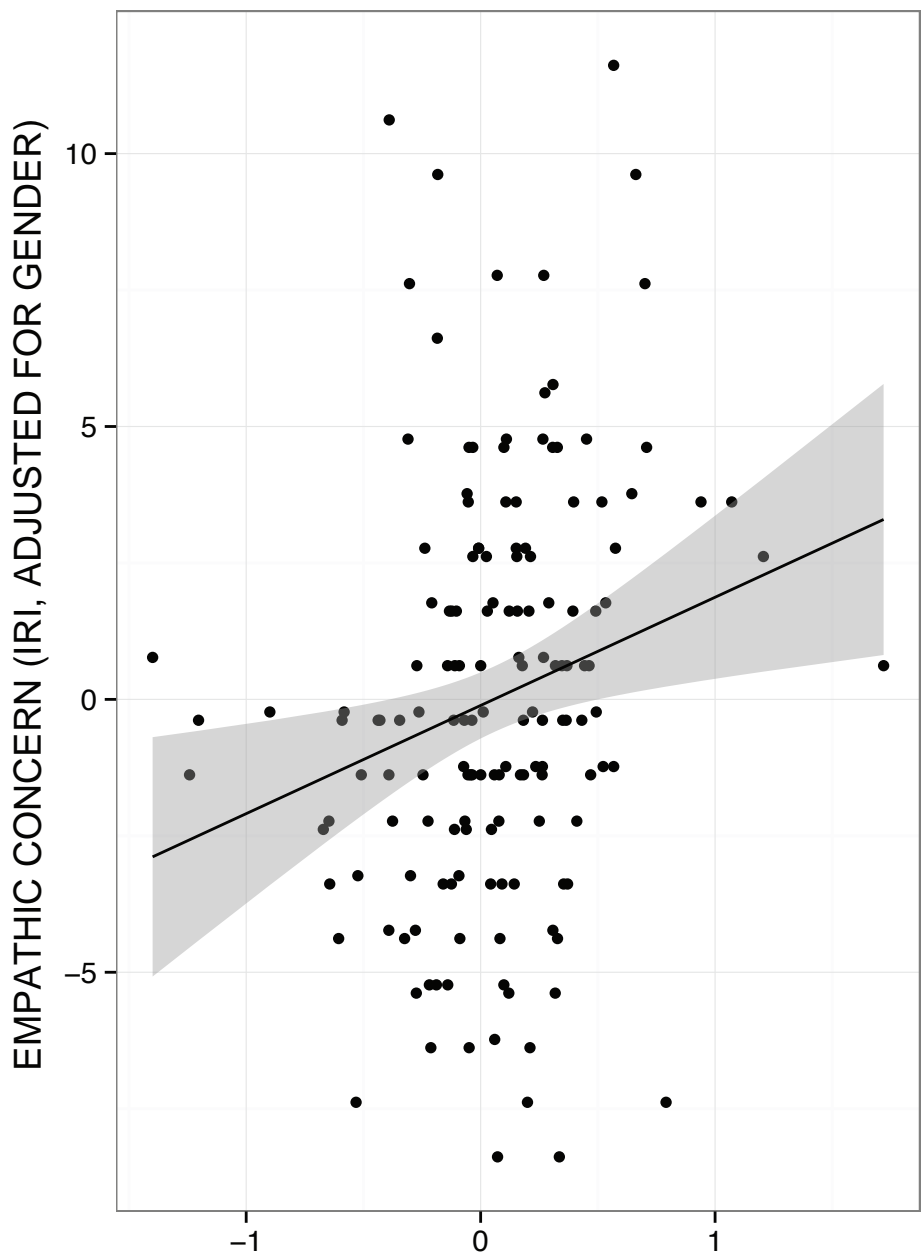
## C2. LOW EMPATHIC ACCURACY



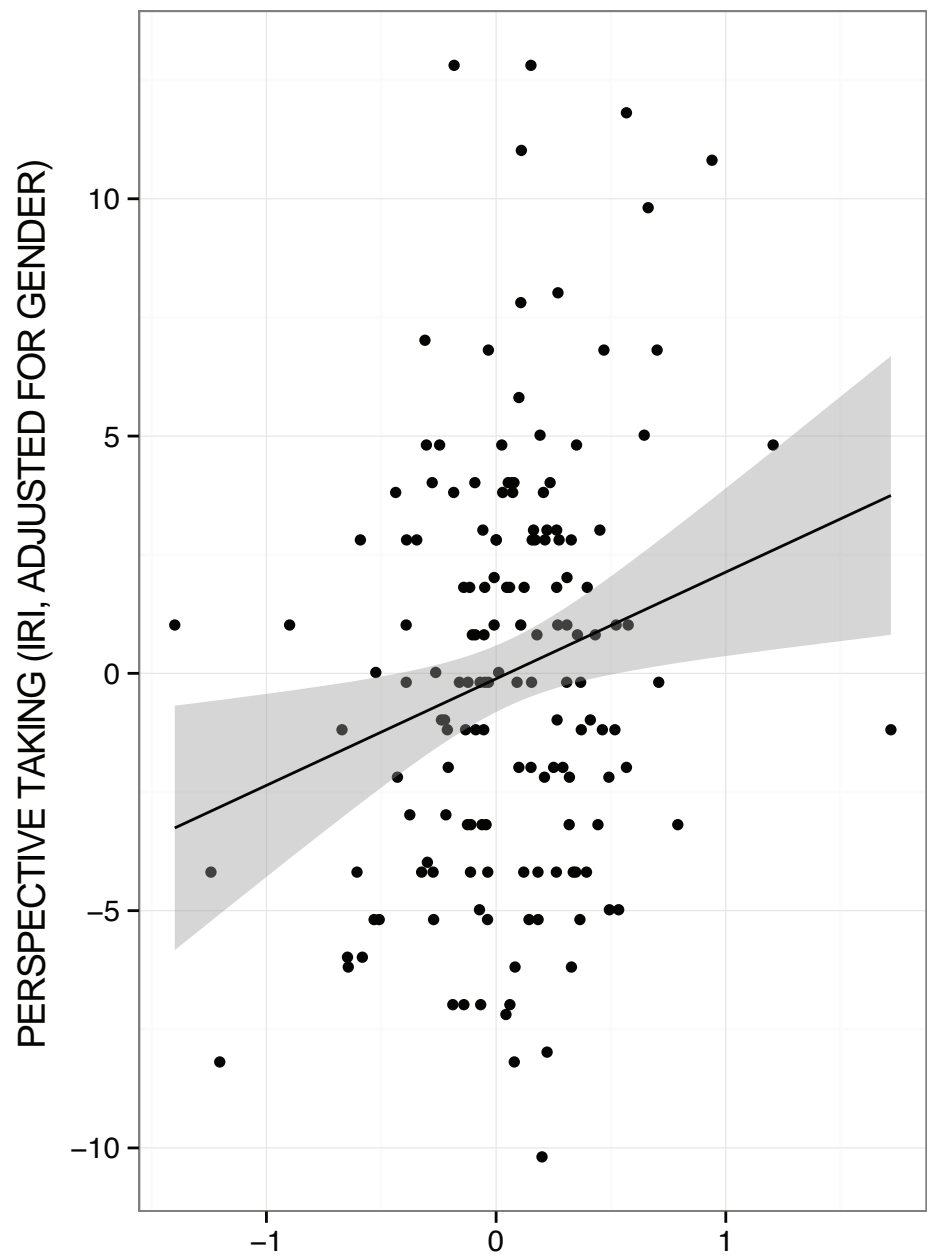
FINAL STEP: Compute empathic accuracy for the video from correlation between target (pink) and perceiver ratings (green).






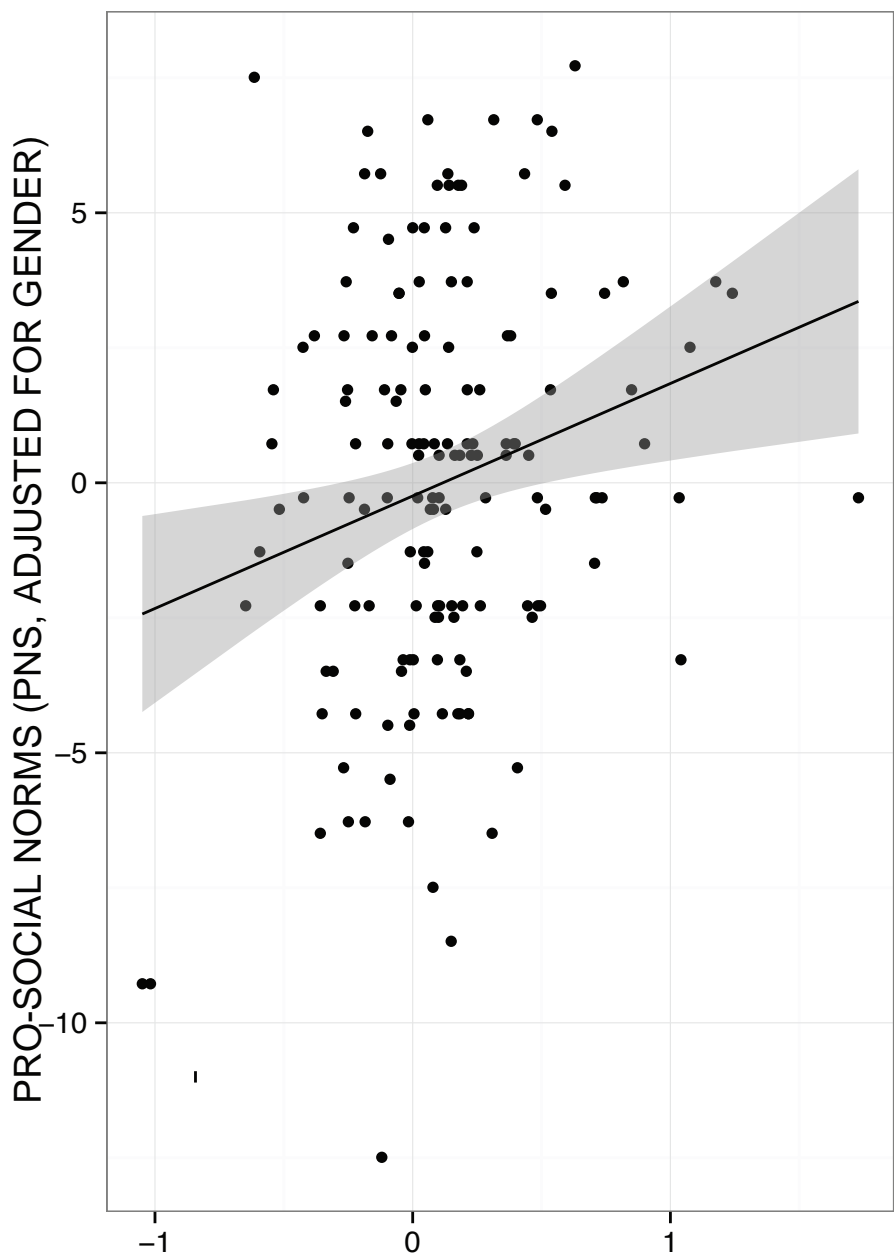


 EMPATHIC ACCURACY-RELATED **RIGHT TPJ** ACTIVATION



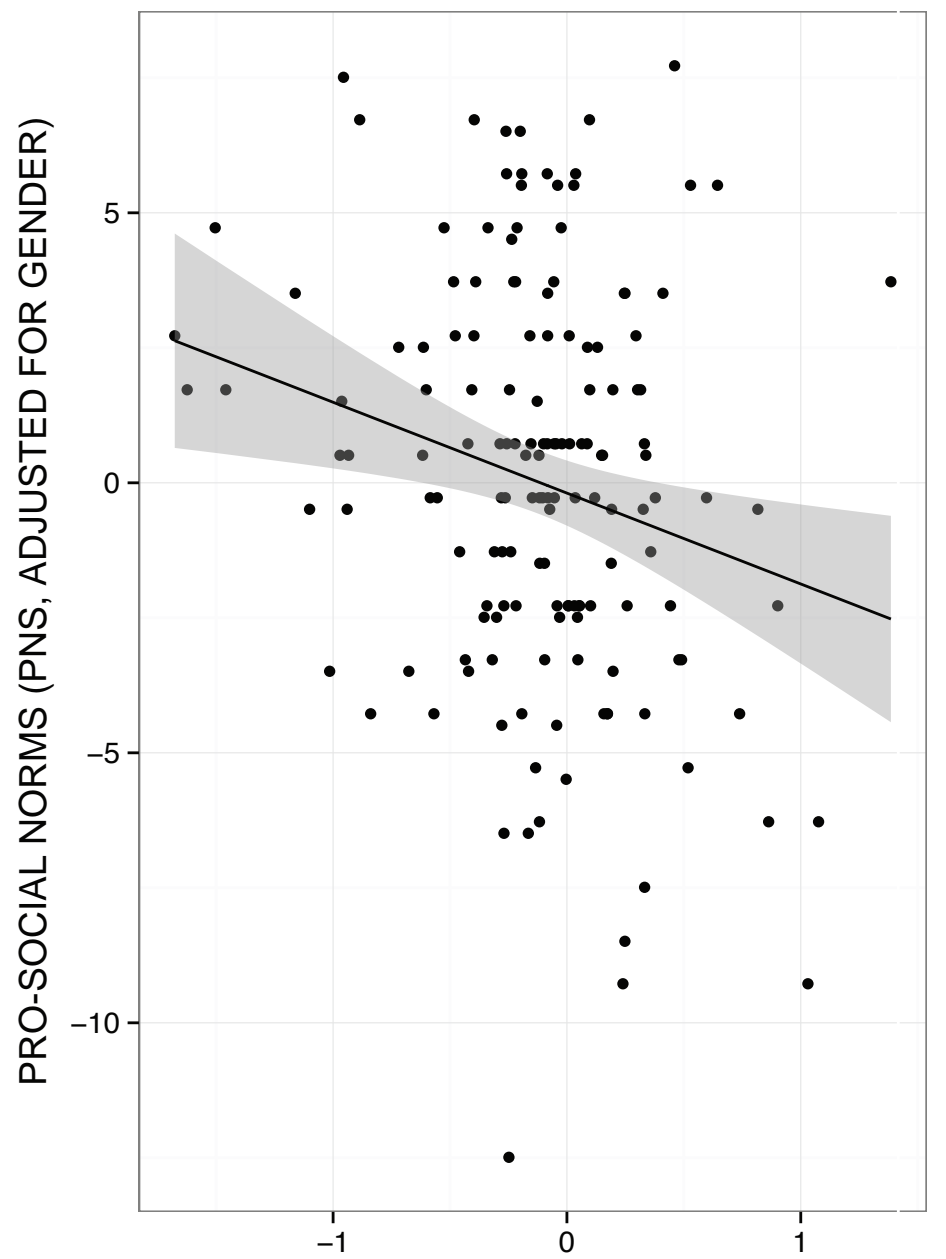
 EMPATHIC ACCURACY-RELATED **RIGHT TPJ** ACTIVATION

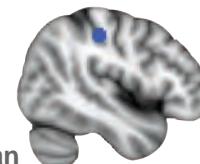
C)



 EMPATHIC ACCURACY-RELATED **RIGHT STS** ACTIVATION

D)



 EMPATHIC ACCURACY-RELATED **RIGHT IPL** ACTIVATION

**TABLE 1.** Summary of Regions with Activation Related to Empathic Accuracy.

	REGION	MAX INTENSITY (Z)	PEAK COORDINATES			VOLUME (mm)
			X	Y	Z	
ACTIVATION POSITIVELY RELATED TO EMPATHIC ACCURACY	Right Superior Temporal Sulcus	6.11	56	-14	0	1807
	Precuneus	5.6	-4	-62	22	1024
	Left Superior Temporal Sulcus	6.05	-58	-16	-8	1013
	Ventromedial Prefrontal Cortex	5.7	-2	56	-12	516
	Left Temporal Parietal Junction	5.47	-46	-56	26	485
	Dorsomedial Prefrontal Cortex	4.78	-8	40	52	373
	Right Temporal Parietal Junction	4.98	50	-60	26	280
ACTIVATION NEGATIVELY RELATED TO EMPATHIC ACCURACY	Right Superior Parietal Lobule	5.23	44	-44	54	1161
	Anterior Cingulate Cortex	5.14	4	22	36	862
	Right Dorsolateral Prefrontal Cortex	4.46	44	34	30	513
	Left Lateral Occipital Cortex	4.72	-20	-72	48	492
	Left Superior Parietal Lobule	4.47	-40	-46	48	357
	Right Lateral Occipital Cortex	4.27	16	-68	48	293
	Superior/Middle Frontal Gyrus	3.75	34	2	56	199
	Left Dorsolateral Prefrontal Cortex	4.01	-40	46	24	143
	Right Superior Parietal Lobule	3.87	10	-52	54	46

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## **Supplementary Material**

### **Supplementary Figure 1.** Gender Differences in Questionnaire Measures.

Females had greater self-reported empathic concern (A;  $t(156)=-3.93$ ,  $p<0.001$ ), perspective taking (B;  $t(156)=-2.47$ ,  $p=0.015$ ), and adherence to pro-social norms (C;  $t(156)=-2.19$ ,  $p=0.030$ ) than males. Error bars represent 95% CIs above and below the point estimates of the means (depicted as triangles). Raw data points are overlaid in gray.

**Supplementary Figure 2.** Relationship Between Empathic Accuracy and Questionnaire Measures. Empathic accuracy did not relate to empathic concern (A;  $t(149)=1.61$ ,  $p=0.109$ ), perspective taking (B;  $t(150)=1.41$ ,  $p=0.161$ ), or adherence to pro-social norms (C;  $t(152)=0.75$ ,  $p=0.453$ ). Precision envelopes represent 95% CIs above and below the point estimates. Data points are adjusted for effects of gender are overlaid in black.

## **Supplementary Methods**

### *Image Acquisition*

Images were acquired on a GE X750-3.0 Tesla MRI scanner with a 32-channel head coil. Anatomical scans consisted of a whole head 1.0 mm isotropic T1-weighted image acquired using an in-house MPnRAGE sequence (Kecskemeti et al., 2013). Three functional scan runs were acquired for the empathic accuracy paradigm using a gradient echo EPI sequence (64x64 in-plane resolution, 220mm FOV, TR/TE/Flip = 2000ms/20ms/60°, 36 slices, 4.5mm thick).

### *fMRI processing*

FMRI data processing was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.00, part of FSL (FMRIB's Software Library, [www.fmrib.ox.ac.uk/fsl](http://www.fmrib.ox.ac.uk/fsl)). The following pre-statistics processing was applied: motion correction using MCFLIRT (Jenkinson et al., 2002); non-brain removal using BET (Smith, 2002); spatial smoothing using a Gaussian kernel of FWHM 5mm; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with  $\sigma=50.0s$ ). While an average highpass filter of 136s was estimated across all subject's design matrices we did not want to risk the additional noise that would be added by less filtering, and used the standard setting (100s). The functional data from individual subjects were analyzed using a General Linear Model (GLM) in 3 levels, where the first level modeled within-run data using FILM prewhitening (Woolrich et al., 2001), the second level combined within-subject data from each trial using a fixed effects modeling approach, and the third level modeled data across subjects using the Flame1 mixed effects model estimation. In the first level each video was modeled as a separate block regressor, with length equal to the video duration, and each cue period was modeled as a block for the 3s duration; the fixation period was unmodeled and contributed to the baseline. All regressors were convolved with a double gamma hemodynamic response. Additional regressors of no interest were included to model 24 total motion-related parameters (the standard plus extended parameters, which include the squares, derivatives and squares of derivatives), trials during which participants did not make ratings, and the single trial that was excluded across all participants (as described above). To further



address motion, high motion time points (a framewise displacement (FD) measure larger than 0.9 mm; Siegel et al., 2014) were modeled out of the data with an individual regressor that consisted of all 0's and a single 1 for the TR of interest. Runs with more than 25% (77 TRs) of the data censored were omitted from analysis, leading to a total of 1 omitted run. On average 6 TRs were censored (interquartile range 0, 6).

Functional data were aligned to a group average anatomical space, which was created using Advanced Normalization Tools (ANTs; Avants et al., 2011). Image registration of the BOLD data to the study-specific group template was carried out using FSL in a two stage process where the Boundary Based Registration (BBR) approach (Greve and Fischl, 2009) was used to register the subject's time series data to their anatomical template and a 12DOF affine transformation was used to register the subject's anatomical to the group template using FLIRT (Jenkinson et al., 2002). ROIs were transformed from Montreal Neurological Institute (MNI) space to the group average space via a transformation matrix created using ANTS (a subset of ROIS are overlaid on results of the voxelwise analysis as red and blue masks, Figure 3).

