Supporting Information

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SI Text

Neural Correlates of Inaccurate Inference. While our a priori interest was in the neural activity tracking with a perceivers' accurate inferences about social targets' affective states, our data also allowed for the opposite analysis. By using the relative accuracy of a perceiver for a given clip as a negative parametric regressor, we searched for activity tracking with inferential inaccuracy. This analysis produced 3 clusters of activity (see Table S2), 2 posterior clusters in the parietal and occipital cortex and 1 large cluster spanning the putamen and subgenual anterior cingulate cortex (sgACC). This last activation is of special interest, because these regions (among others) have been shown to track with many aspects of affective experience, including processing of reward and negative emotion, and autonomic control (1–3), and one might speculate that a negative correlation between activity here and accuracy could indicate that perceivers' inaccuracy may reflect their personal emotional reactivity to the stimulus videos, which could in turn impair their ability to attend to targets' affective cues.

That said, our a priori hypotheses in this study focused on the neural correlates of accuracy, not inaccuracy, and specifically concerned the specific neural systems known to be involved in MSA and SRs. As we had no specific predictions about the neural correlates of inaccuracy, we believe these results should be treated as exploratory, bearing in mind that any explanation we offer for them is necessarily speculative and post hoc. However, these findings may be valuable for future studies directed at further unpacking the cognitive and neural sources of interpersonal inaccuracy in a more focused manner.

Cross-Subject Coherence in Activation of Networks. Although our main analysis demonstrated that activity in both MSA- and SR-related brain regions tracked with interpersonal accuracy, it is possible that different subjects may have differentially recruited these systems to make accurate inferences. For example, some perceivers may rely more on sharing affective states with targets in making inferences, whereas other perceivers may rely more on cognitive appraisals of target cues.

To explore this possibility, we extracted each participant's accuracy-related beta weights from regions of interest pertaining to both MSA (the rostral and dorsal medial prefrontal cortex and the superior temporal sulcus) and SR (the right inferior parietal lobule and intraparietal sulcus, and bilateral premotor cortex). To quantify how much accuracy tracked with the engagement of each kind of system, we then averaged each participant's betas for the set of MSA regions and the set of SR-related regions. This allowed us to test 2 possibilities. On one hand, if some participants rely on MSA-related structures to make accurate judgments, while others depend on SR-related structures, then across participants we would not expect to observe significant correlations in between accuracy-related activity in these systems. On the other hand, if participants who engage one set of regions when making accurate inferences also engage the other set, then across participants we would expect to observe a significant correlation between accuracy-related activity in these systems.

The second possibility was borne out by the data: cross-participant correlation between accuracy-related activity in SR- and MSA-related regions was 0.57, significant at $P < 0.02$ (see Fig. S1). This suggests that MSA and SR-related brain regions are concurrently engaged to support accurate social inference.

ROIs from Previous Studies. To assess accuracy-related activity in brain areas previously identified as being involved in MSA and SRs, we used Pubmed and ISI Web of Knowledge-cited reference searches to find neuroimaging studies of SRs and MSA reporting activation in several a priori ROIs.

ROIs related to shared action representations included regions in the mirror neuron system (MNS) and cortical structures implicated SRs of pain, affective states, and touch. In searching for MNS activations, we entered the terms "action" AND "observation" AND "execution" AND "brain" OR "fMRI" into a Pubmed search, and also searched manually for citations in review papers (4–6), and references citing the first study of action observation and execution overlapping in the human MNS (7). MNS activations in the dorsal PMC and IPL were required to reflect a conjunction of activity elicited by both observation and execution of actions, including either goal-directed and intransitive movements or communicative gestures (i.e., hand signals or facial expressions), compared with control conditions not including biological motion.

For activations involved in SRs of affect and pain in the AI and ACC, we entered the terms "emotion" OR "pain" OR "disgust" AND "observation" AND "experience" AND "brain" OR "fMRI" into a Pubmed search, and also searched for studies citing well-known papers on SRs of pain (8, 9), disgust (10), and emotional facial expressions (11). Studies were required to include both the direct experience and observation of a sensory or emotional state (i.e., pain or disgust) or of posed emotional facial expressions.

To search for activation in regions thought to underlie SRs of nonpainful touch (bilateral SII), we entered the terms "action" AND "observation" AND "execution" AND "brain" OR "fMRI" into a Pubmed search and also manually searched for studies citing 2 well-known papers of SRs of touch (12, 13).

For activations of the MPFC and TPJ related to MSA, we entered the terms "social cognition" OR "mental state attribution" OR "mentalizing" AND "fMRI" OR "brain" into a Pubmed search and also manually searched through reference sections in several recent reviews of mental state attribution. For inclusion in subsequent analyses, studies were required to contain an experimental condition in which perceivers made explicit judgments about targets' internal states from pictures, cartoons, or vignettes. Contrasts were included if they compared these judgments to nonsocial judgments of similar stimuli. To interrogate accuracy-related activity in an area of rostral MPFC previously associated with MSA, we took advantage of a recent meta-analysis of BA 10, which aggregated results from 23 studies (26 contrasts) of "mentalizing," or MSA (14).

Results from these searches, using these criteria, yielded at least 2 papers with relevant activation points for each ROI and an average of 6.18 papers per region.

Euclidian distances of each mean peak coordinate and the analogous peak from the current results were then calculated (for listings of studies used for each ROI, mean coordinates for each ROI gathered from these studies, and calculations of distance between each ROI taken from previous studies and the relevant ROI in the current study; see Table S3). Because the AI, ACC, TPJ, and SII were not found in our whole-brain parametric analysis (even at a relaxed threshold of $P < 0.01$, $k = 5$ voxels), it was impossible to spatially compare ROIs in those areas defined from previous studies with these parametric results.

For further analysis, a sphere with a radius of 6 mm was defined around each peak gathered from previous studies. For each ROI, we then extracted beta values from our accuracy-related analyses for each subject and used 1-sample t tests to examine whether these beta values were reliably >0; in other words, we explored whether activity in each MSA and SR-related ROI culled from previous studies tracked with accuracy. Betas were averaged over a priori small volumes of interest, and as such we used a threshold of $P < 0.05$ to determine significance. Because we had an a priori hypothesis that activity in MSA and SR-related regions extracted from previous studies would be positively, and not negatively, related to accuracy, significance was determined by using 1-tailed tests. Results of these analyses are described in *Results* and *Discussion* (7–12, 14–45).

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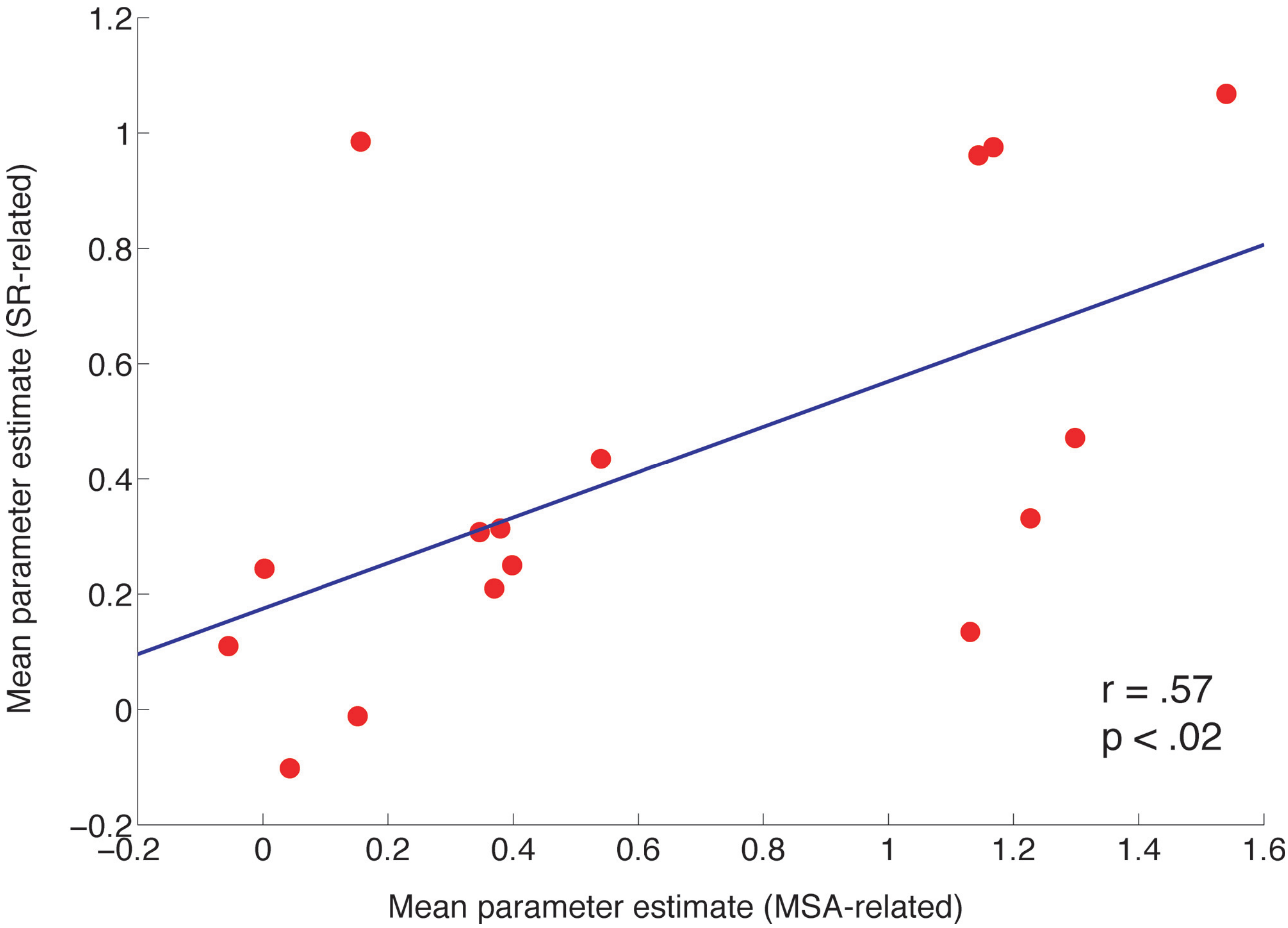

Fig. S1. Scatter plot of between-subject correlations between activity tracking with empathic accuracy in MSA-related brain regions (*x* axis) and SR-related regions in the mirror neuron system (*y* axis).

Table S1. Brain regions tracking parametrically with empathic accuracy within participants

Region of activation	Laterality	Coordinates *x*	*y*	*z*	T score	Volume (vox)
Medial prefrontal cortex	M	−10	42	48	4.07	29
		−4	34	50	3.38	
Medial prefrontal cortex	R	10	54	14	3.58	22
Frontopolar gyrus	R	18	70	10	3.55	27
Dorsal premotor cortex/middle frontal gyrus	R	36	8	44	3.81	27
		32	18	46	3.3	
Dorsal premotor cortex/middle frontal gyrus	L	−34	8	45	4.25	71
Precentral gyrus	L	−22	−3	48	4.11	44
		30	−28	16	3.85	31
Postcentral gyrus	L	−24	−38	60	3.36	22
Inferior parietal lobule	R	60	−32	38	3.54	21
Inferior parietal lobule	R	50	−26	44	3.90	23
Intraparietal sulcus	R	30	−34	48	3.54	34
		36	−30	44	3.12	
Superior temporal sulcus	R	52	−10	−18	3.45	28
Middle occipital	L	−48	−76	12	4.36	35

Coordinates are in Montreal Neurological Institute (MNI) space. Local maxima are presented below main activation peaks. Voxels are 3 × 3 × 3 mm.

Table S2. Regions tracking parametrically with empathic inaccuracy within participants

Region of activation	Laterality	Coordinates			T score	Volume (vox)
		x	*y*	*z*		
Putamen/sgACC	R	16	20	−10	4.44	167
		26	20	−4	4.34	
		16	8	−8	4.01	
Posterior parietal cortex	R	54	−64	14	4.46	29
Dorsal occipital cortex	R	32	−76	24	4.15	27

Coordinates are in MNI space. Local maxima are presented below main activation peaks.

Table S3. Foci derived from previous studies used for the ROI analysis in the present study

Region	Studies used	Laterality	Coordinates (previous)			Coordinates (current)			Distance†	Accuracy-related parameter estimates	
			x	*y*	*z*	*x*	*y*	*z*		*t*	*p*
Accuracy related											
vMPFC	14*	M	8	53	10	12	53	10	4.33	2.77	<0.01
dMPFC	15–24	M	0	36	46	−4	34	50	4.24	2.51	0.01
PMC	25–27, 35–38	R	42	0	46	36	8	44	10.20	3.13	0.04
PMC	25–27, 35–38	L	−38	0	45	−34	10	45	10.77	2.79	<0.01
IPL	7, 25–27, 36–37, 39–40	R	47	−38	40	50	−26	44	13.00	2.56	0.01
Nonaccuracy related											
AI	8–9, 11, 26, 28–30, 41	R	37	18	0		N/A		N/A	−0.93	0.18
AI	8–9, 11, 26, 28–29, 39	L	−37	17	2		N/A		N/A	−0.80	0.22
ACC	8–10, 29–30, 44	M	4	17	32		N/A		N/A	0.20	0.43
TPJ	20, 31–32, 34	R	54	−54	21		N/A		N/A	−1.08	0.14
TPJ	20, 31–34, 45	L	−52	−59	21		N/A		N/A	−1.39	0.10
SII	42–43	R	59	−22	26		N/A		N/A	0.83	0.21
SII	12, 42	L	−59	−23	29		N/A		N/A	−0.85	0.20

Coordinates are in MNI space and represent the mean of foci reported in the studies listed.
*From a meta-analysis.
†Distance in mm from the similar activation focus identified in the whole-brain parametric analysis [listed in the Coordinates (current) column].