

8. A. G. Knudson Jr., *Proc. Natl. Acad. Sci. U.S.A.* **68**, 820 (1971).
9. M. Santarosa, A. Ashworth, *Biochim. Biophys. Acta* **1654**, 105 (2004).
10. C. J. Sherr, *Cell* **116**, 235 (2004).
11. M. S. Kumar et al., *Genes Dev.* **23**, 2700 (2009).
12. G. R. Bignell et al., *Nature* **463**, 893 (2010).
13. R. Beroukhi et al., *Nature* **463**, 899 (2010).
14. See supplementary materials on Science Online.
15. P. A. Futreal et al., *Nat. Rev. Cancer* **4**, 177 (2004).
16. S. A. Forbes et al., *Nucleic Acids Res.* **39** (Database issue), D945 (2011).
17. I. Bozic et al., *Proc. Natl. Acad. Sci. U.S.A.* **107**, 18545 (2010).
18. P. J. Paddison et al., *Nature* **428**, 427 (2004).
19. J. M. Silva et al., *Nat. Genet.* **37**, 1281 (2005).
20. M. R. Schlabach et al., *Science* **319**, 620 (2008).
21. A. Smogorzewska et al., *Cell* **129**, 289 (2007).
22. L. M. Zwemer et al., *Genome Biol.* **13**, 10.1186/gb-2012-13-2-r10 (2012).
23. A. H. Berger, A. G. Knudson, P. P. Pandolfi, *Nature* **476**, 163 (2011).
24. S. R. Payne, C. J. Kemp, *Carcinogenesis* **26**, 2031 (2005).
25. E. T. Sawey et al., *Cancer Cell* **19**, 347 (2011).
26. L. Zender et al., *Cell* **125**, 1253 (2006).

Acknowledgments: We thank S. Forbes, A. Futreal, and M. Stratton for generously providing the whole-genome sequencing data from the COSMIC database, and C. Shaw, D. MacPherson, M. Emanuele, C. Thoma, T. Westbrook, and members of the Elledge lab for helpful discussions and critical reading of this manuscript. Supported by grants from the National Human Genome Research Institute-funded Cancer Genome Atlas project (M.M.); NIH grant U54CA143798 (R.B.); NIH, Stand Up to Cancer, and the U.S. Department of Defense

(S.J.E.); Susan G. Komen for the Cure Foundation postdoctoral fellowship KG080087 (N.L.S.); American Cancer Society postdoctoral fellowship 116410-PF-09-078-01-MGO (Q.X.); and National Institute of General Medical Sciences Medical Scientist Training Program award T32GM07753 (C.H.M.). S.J.E. is an investigator of the Howard Hughes Medical Institute.

Supplementary Materials

www.sciencemag.org/cgi/content/full/science.1219580/DC1

Materials and Methods

Supplementary Text

Figs. S1 to S6

Tables S1 to S12

References (27–32)

24 January 2012; accepted 9 May 2012

Published online 24 May 2012;

10.1126/science.1219580

A Distinct Role of the Temporal-Parietal Junction in Predicting Socially Guided Decisions

R. McKell Carter,^{1,2,3} Daniel L. Bowling,^{1,2} Crystal Reeck,^{1,4} Scott A. Huettel^{1,3,4*}

To make adaptive decisions in a social context, humans must identify relevant agents in the environment, infer their underlying strategies and motivations, and predict their upcoming actions. We used functional magnetic resonance imaging, in conjunction with combinatorial multivariate pattern analysis, to predict human participants' subsequent decisions in an incentive-compatible poker game. We found that signals from the temporal-parietal junction provided unique information about the nature of the upcoming decision, and that information was specific to decisions against agents who were both social and relevant for future behavior.

By observing the choices and behavioral cues of others, individuals can learn about, and rapidly adapt their behavior to, dynamic environments (1, 2). Indeed, social information obtained by observing other agents' actions optimizes the learning of environmental contingencies (3). Mental state attribution is the lynchpin in this process, enabling individuals to decipher the motivations underlying the behavior of other agents and predict their upcoming actions (1, 4, 5). Different agents have different relevance for behavior, and failing to distinguish relevant from irrelevant agents may lead to following deceptive advice (6) or conforming with the attitudes or opinions of others (7, 8). Accordingly, some of the most striking examples of human social cognition reflect the differentiation between more and less important social partners: more heavily weighting the preferences of key players when making group decisions (9, 10), discriminating strategic actions from random behavior (11), and comparing oneself to more similar others (12).

A key challenge for neural models of social cognition comes from the very ubiquity of social signals. Social signals in the natural environment are frequent, highly salient, and good predictors of needed future behavior. Information derived from social agents, therefore, might be processed by generalized neural systems that are geared toward identifying any important events in the environment rather than by specialized systems that carry information in specifically social contexts. This challenge and the difficulty in distinguishing its predictions from that of social cognition models lie at the heart of debates in the field (13, 14).

To explore the interaction of social agency with behavioral relevance, we used a simplified poker game (15) in which participants ($n = 18$) played against human and computer opponents (Fig. 1). The opponents alternated across eight functional runs, and the same real human opponent competed against all participants in an independent and incentive-compatible manner (Methods). The human and computer opponents were matched on overall decision probabilities so that differences in observed behavior and brain function could be attributed to perceived social agency.

In each trial, participants first viewed a picture of their opponent. Participants were then presented with either a high card that would win

if they chose to bet and were called or a low card, indicating that would lose if they chose to bet and were called. When the participant did bet, control of the game passed to the opponent who then decided to call or fold (i.e., bet by adding more money or fold by ceding the pot to the participant). Participants won money in this game when opponents bet on trials when they held high cards or folded on trials where the participant bet while holding a low card. Thus, participants maximized earnings in this game through bluffs that prevented the opponent from accurately guessing the card that was held. On average, participants bluffed 54% of the time (range from 29 to 73%), consistent with the equilibrium solution to this game (15). Participants' bluffing decisions were significantly influenced by their opponent's behavior on the previous trial [$t(17) = 8.8$, $P < 0.001$], with greater effects found for human compared with computer opponents [$t(17) = 2.3$, $P = 0.032$].

Our functional magnetic resonance imaging (fMRI) analyses used multivariate pattern analysis (MVPA) at the time of card presentation to predict the participant's subsequent decision, which occurred 6 s later in the trial. We conducted a combinatorial whole-brain analysis that allowed estimation of the unique information carried within local brain segments (16, 17). For every segment, we calculated the average increase or decrease in predictive performance when paired with other brain segments (Materials). We refer to this quantity as the unique combinatorial performance (UCP). A high UCP means that a region carries information that can predict future behavior beyond that obtained from other brain regions. A low UCP means that information within a region is largely redundant with that of other regions. Across both opponents, significant UCP was found in regions often associated with social cognition, including regions in both the dorsal and the medial prefrontal cortices (table S2).

A standard approach for establishing functional specificity in neuroscience research is subtraction, that is, statistical comparison of two conditions that differ only in one process of interest. However, activations identified by subtraction may not be unique to the process of interest

¹Center for Cognitive Neuroscience, Duke University, Durham, NC 27708, USA. ²Department of Neurobiology, Duke University, Durham, NC 27710, USA. ³Brain Imaging and Analysis Center, Duke University, Durham, NC 27710, USA. ⁴Department of Psychology and Neuroscience, Duke University, Durham, NC 27708, USA.

*To whom correspondence should be addressed. E-mail: scott.huettel@duke.edu

(Fig. 2C). In contexts like the current task, signals associated with selective attention and vigilance may be present in both social and nonsocial contexts but are more engaged when a social stimulus is present (18, 19). To remove these general cognitive effects, we regressed UCP for a human opponent against UCP for a computer opponent (Fig. 2B). Across regions, there was a robust correlation with a slope greater than one (slope = 1.4, $P = 0.016$). The general consistency of this

response—including for brain regions often described as constituting a social network—implies that the processes engaged during the performance of this task are greater for, but not specific to, social context.

To quantify whether any local brain regions carried distinctly social information, we defined a metric of social bias (Fig. 2D) by using the normalized residual distance from the whole-brain regression line shown in Fig. 2B (Methods). A

region with a positive social bias has a greater UCP against the human opponent than against the computer opponent. One region, the temporal-parietal junction (TPJ), exhibited an extreme social bias that was five standard deviations higher than the mean of all other brain segments (Fig. 2E). The gap between the social bias found in the TPJ and that found in the second-most-biased region was greater than the range of variation throughout the remainder of the brain. This in-

Fig. 1. A single-card poker game. Each trial begins with a picture of the opponent (i.e., a photograph of the human opponent or a computer). The participant's card is revealed, and they then decide whether to bet (B) or fold (F). Buttons then appear, with left/right position randomized across trials, and the participant indicates his or her response. If the participant chooses to fold, the trial ends. If the participant chooses to bet on the card, control passes to the opponent, who has 3 s to decide whether or not to match the participant's bet or fold. Predictions are made by using fMRI data associated with the time period highlighted in green.

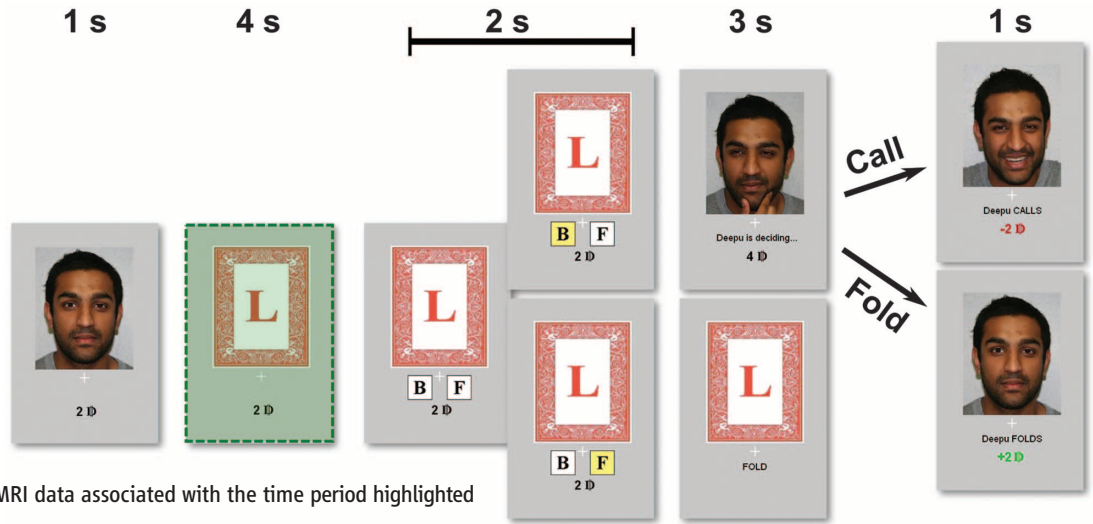
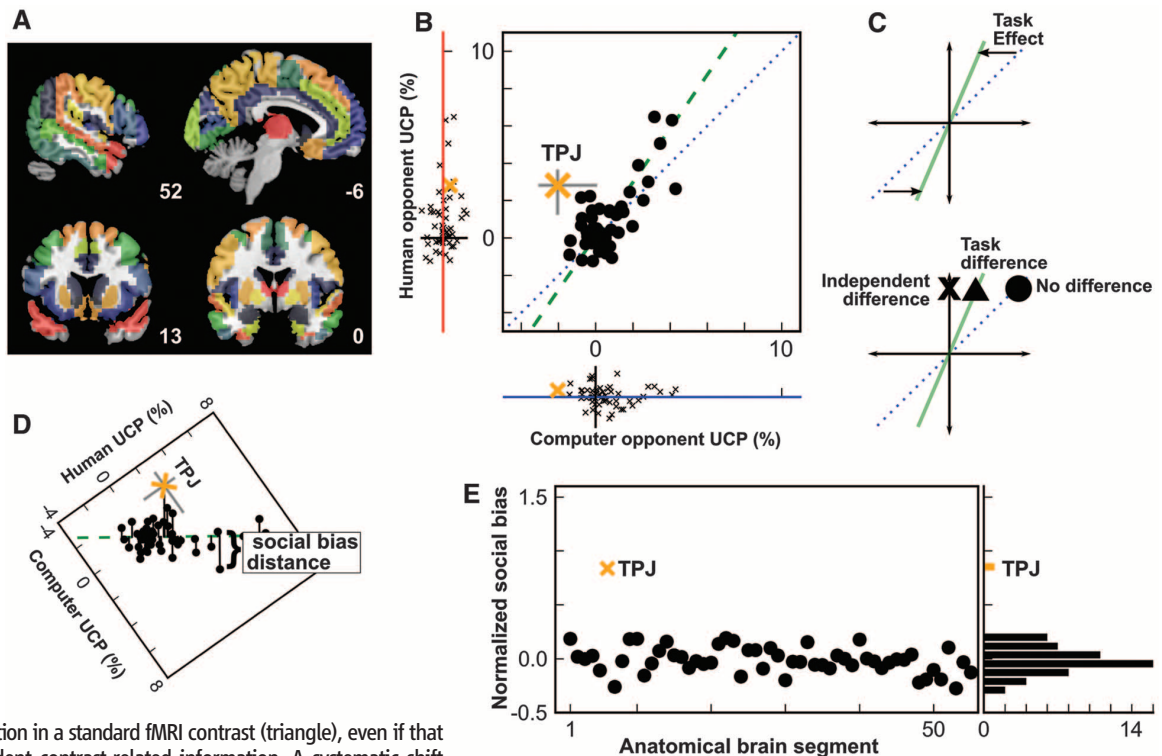


Fig. 2. TPJ plays a distinct role in predicting social decisions. (A) Whole-brain fMRI data was segmented into 55 bilateral anatomical regions, as described in Materials. (B) UCP for a human opponent was regressed against UCP for a computer opponent, across regions (green dashed line, slope = 1.4). For the range reported here, negative values of UCP correspond to a return to chance levels and not negatively predictive models. (C) The slope of the regression line in (B) is consistent with a general task effect (top), such that social contexts tend to engage task-related regions across the brain more than similar nonsocial contexts. A region that was highly engaged by the task might exhibit activation in a standard fMRI contrast (triangle), even if that region carried no independent contrast-related information. A systematic shift away from the regression line (x) would be necessary to show an independent effect in a region. (D) Social bias was defined by the residual difference (social minus nonsocial) in predictive power from the whole-brain regression line. (E) The magnitude of social bias in each region (normalized by the variance estimates for



each segment's UCP), sorted by UCP against the human opponent. Only one region, the TPJ, contributed significantly more UCP against a human opponent than against a computer opponent, independent of the overall task effect.

dependent contribution of the TPJ was robust to multiple forms of correction for brain segment characteristics (figs. S5 and S6) and to Bonferroni correction for multiple comparisons (Materials).

These findings identify a unique and independent role for the TPJ in representing information predictive of behavioral actions during social interactions. To rule out any potential biasing effects of this particular segmentation approach, which defined segments of the brain according to prior anatomical and functional divisions, we repeated all analyses by using random, voxel-based segmentations of the brain (Materials). Voxel-based UCP metrics were then calculated by using the median UCP across the different segmentations (fig. S7). The analysis replicated both previous findings: a nonspecific overall increase in UCP against human compared with computer opponents (slope of 1.4, across all gray matter voxels) but strong social bias in the TPJ (fig. S7D). Moreover, the specificity of TPJ was maintained when extending analyses to combinations of three regions (figs. S9 and S10).

We next evaluated how the subjective behavioral relevance of each opponent modulated information within the TPJ. After completion of the scanning session, participants indicated whether the human or the computer was a better opponent. The social bias found in TPJ was present only for participants who judged the human opponent to be superior (Fig. 3A); again, its bias was more than five standard deviations from the mean normalized residual (Fig. 3B). Conversely, no social bias was observed in TPJ for those who judged the computer opponent as superior to the human [$t(6) = 1.3$, $P = 0.26$; difference between groups: $t(16) = 2.6$, $P = 0.02$].

For comparison, we also plotted UCP for the medial prefrontal cortex (MPFC) and medial posterior cortex (MPC), a network of anatomical regions that, along with the TPJ, have been linked

to aspects of social cognition (20–23). None of these regions exhibited a significant social bias. These results were robust to neural segmentation method selection, with analyses using random voxel-based neural segmentation producing very similar results (fig. S8). Our findings indicate the MPFC and MPC contribute similarly to predicting future behavior in both our social and nonsocial settings, suggesting that they support computations that are critical for social cognition but also applied in at least some nonsocial settings (24, 25).

Our results point to a specific role for TPJ within the social cognition network and demonstrate the unique sensitivity of this region to perceived behavioral relevance of other agents. The TPJ stands out as a contributor of unique and independent social information, even compared with other regions considered to be recruited by social cognition (Figs. 2 and 3). This finding indicates a potential reconciliation for the opposing perspectives that have been proffered for TPJ function: mental inference (26) and orienting to salient external stimuli (14, 27). Responses in the TPJ during social cognition tasks may reflect the nexus of these two operations—that is, interacting with an opponent whose internal states can be modeled (i.e., another human) and whose behavior is also relevant for guiding one's future actions. This interpretation is consistent with demonstrations that TPJ is activated when inferring an adviser's motives when the advice is relevant for an upcoming decision (6) or on potentially highly rewarding trials when implementing an advanced strategy during an interactive choice game (28). However, the present results demonstrate that the TPJ is not generally recruited by external social stimuli but specifically contributes to choice deliberation when modeling the behavioral and cognitive tendencies of a social agent. Accordingly, when others are of lower status (29) or not considered relevant for future behavior,

as in the case of dehumanization (30), the TPJ may be disengaged. The sensitivity of TPJ to both social context and perceived relevance highlights a critical role for this region in coordinating behavior in a dynamic, social environment and demonstrates the capacity of behavioral relevance to modify neural signals.

References and Notes

1. D. Lee, *Nat. Neurosci.* **11**, 404 (2008).
2. E. Danchin, L.-A. Giraldeau, T. J. Valone, R. H. Wagner, *Science* **305**, 487 (2004).
3. L. Rendell *et al.*, *Science* **328**, 208 (2010).
4. T. E. J. Behrens, L. T. Hunt, M. F. S. Rushworth, *Science* **324**, 1160 (2009).
5. A. Olsson, K. N. Ochsner, *Trends Cogn. Sci.* **12**, 65 (2008).
6. T. E. J. Behrens, L. T. Hunt, M. W. Woolrich, M. F. S. Rushworth, *Nature* **456**, 245 (2008).
7. S. E. Asch, *Sci. Am.* **193**, 31 (1955).
8. R. M. Raafat, N. Chater, C. Frith, *Trends Cogn. Sci.* **13**, 420 (2009).
9. T. Kameda, Y. Ohtsubo, M. Takezawa, *J. Pers. Soc. Psychol.* **73**, 296 (1997).
10. S. Bonaccio, R. Dalal, *Organ. Behav. Hum. Decis. Process.* **101**, 127 (2006).
11. W. Yoshida, B. Seymour, K. J. Friston, R. J. Dolan, *J. Neurosci.* **30**, 10744 (2010).
12. L. Festinger, *Hum. Relat.* **7**, 117 (1954).
13. J. P. Mitchell, *Cereb. Cortex* **18**, 262 (2008).
14. M. Corbetta, G. Patel, G. L. Shulman, *Neuron* **58**, 306 (2008).
15. A. Rapoport, I. Erev, E. V. Abraham, D. E. Olson, *Organ. Behav. Hum. Decis. Process.* **69**, 31 (1997).
16. A. N. Hampton, J. P. O'Doherty, *Proc. Natl. Acad. Sci. U.S.A.* **104**, 1377 (2007).
17. J. A. Clithero, R. M. Carter, S. A. Huettel, *Neuroimage* **45**, 1329 (2009).
18. C. C. Goren, M. Sarty, P. Y. Wu, *Pediatrics* **56**, 544 (1975).
19. T. Ro, C. Russell, N. Lavie, *Psychol. Sci.* **12**, 94 (2001).
20. S.-J. Blakemore *et al.*, *Cereb. Cortex* **13**, 837 (2003).
21. D. Tankersley, C. J. Stowe, S. A. Huettel, *Nat. Neurosci.* **10**, 150 (2007).
22. P. C. Fletcher *et al.*, *Cognition* **57**, 109 (1995).
23. J. P. Mitchell, J. Schirmer, D. L. Ames, D. T. Gilbert, *J. Cogn. Neurosci.* **23**, 857 (2011).
24. F. Heider, M. Simmel, *Am. J. Psychol.* **57**, 243 (1944).
25. S. Krach *et al.*, *PLoS ONE* **3**, e2597 (2008).
26. R. Saxe, N. Kanwisher, *Neuroimage* **19**, 1835 (2003).
27. J. Decety, C. Lamm, *Neuroscientist* **13**, 580 (2007).
28. M. A. Bhatt, L. Lohrenz, C. F. Camerer, P. R. Montague, *Proc. Natl. Acad. Sci. U.S.A.* **107**, 19720 (2010).
29. S. V. Shepherd, R. O. Deaner, M. L. Platt, *Curr. Biol.* **16**, R119 (2006).
30. L. T. Harris, S. T. Fiske, *Eur. Rev. Soc. Psychol.* **20**, 192 (2009).

Acknowledgments: The authors thank P. Kragel and J. Pearson for assistance with analyses; D. Murty for assistance with data collection; and N. Clement, L. Harris, K. LaBar, M. Platt, V. Venkatraman, K. Watson, and A. Winecoff for comments on the manuscript. This project was supported by National Institute of Mental Health (NIMH) grant R01-70685, NIMH R01-86712, and National Institute of Neurological Disorders and Stroke P01-41328. R.M.C. was supported by 5T32-NS051156-04. C.R. was supported by an NSF Graduate Research Fellowship. S.A.H. was supported by an Incubator Award from the Duke Institute for Brain Sciences.

Supplementary Materials

www.sciencemag.org/cgi/content/full/337/6090/109/DC1

Materials and Methods

Supplementary Text

Figs. S1 to S11

Tables S1 to S5

References (31–60)

26 January 2012; accepted 21 May 2012

10.1126/science.1219681

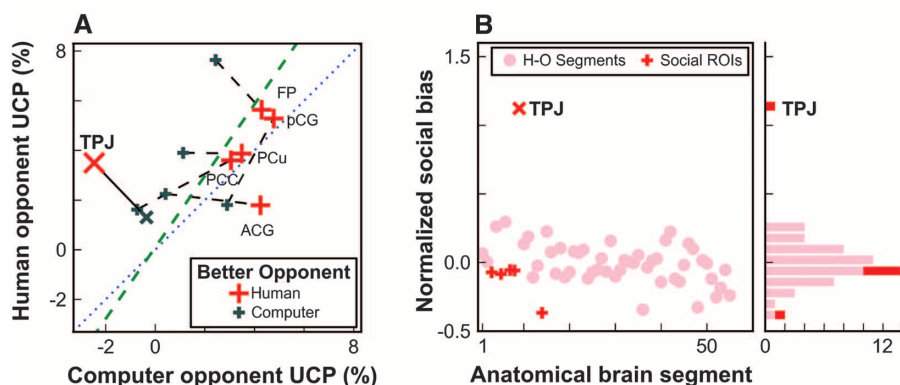


Fig. 3. Social bias in the TPJ depends on the participant's evaluation of the opponent. **(A)** The social bias observed in the TPJ was found only for those participants who considered the human to be a more informative opponent. Other putative social cognition regions do not show the same relationship with behavioral relevance (regions constituting MPFC: FP indicates frontal pole; pCG, paracingulate gyrus, and ACG, anterior cingulate gyrus; regions constituting MPC: PCC is posterior cingulate cortex and PCu, precuneus). **(B)** Social bias in all regions of interest (ROI); normalized by the variance estimates for each segment's UCP, sorted by UCP against the human opponent.