

Individual Differences in Loneliness Predict Neural Responses to Social Stimuli

John T. Cacioppo^{1,2}, Catherine J. Norris³, Jean Decety^{1,2}, George Monteleone¹, &
Howard Nusbaum^{1,2}

¹Center for Cognitive and Social Neuroscience, University of Chicago, Chicago, IL
60637

²Department of Psychology, University of Chicago, Chicago, IL 60637

³Department of Psychology, University of Wisconsin, Madison, WI 53706

All authors contributed to this work.

Loneliness is a debilitating psychological state that adversely affects the quality of life everyday for a large segment of the population¹. However, loneliness is not just a consequence of social isolation; it is a stable, heritable trait^{2,3} distinguishable from other personality factors such as extraversion, neuroticism, hostility, and negative affectivity that affects the way lonely people perceive and interact with others⁴. Here we show for the first time two very different patterns of neural activity that underlie this fundamental social problem. One set of brain regions, often associated with reward systems, is down-regulated in lonely people when viewing pleasant pictures involving people. Another set of brain regions, associated with visual attention and theory of mind, varies in response to unpleasant social pictures, indicating that lonely individuals are more attentive to social cues but think about this information in a more egocentric fashion than nonlonely individuals. These physiological results demonstrate how loneliness changes basic neural processing relevant to the rewards of positive social interactions and concerns about negative social interactions.

People are intensely social animals and a major function of the human brain is to support interactions with the social environment that are as adaptive and satisfying as their interactions with the physical environment⁵. Stable differences in the extent to which people achieve adaptive and satisfying social relationships manifest as individual differences in perceived social isolation or loneliness^{6,7}. Individual differences in loneliness influence how they attend to and perceive events in their everyday life⁸ and how they interact with others⁹. However much of this research depends on subjective reports and cannot directly indicate how much of this behavior is mediated by conscious consideration of these situations and how much stems from more ingrained responses. Here we use functional magnetic resonance imaging (fMRI) to investigate differences in the neural responses to social stimuli with emotional content, relative to matched nonsocial stimuli, in individuals differing in the extent to which they feel lonely and isolated.

Lonely individuals respond less positively to daily social interactions than nonlonely individuals¹⁰, raising the question of whether social stimuli in particular or emotional stimuli more generally have the same hedonic impact on lonely and nonlonely individuals. To address this question, we measured the activation of the region of ventral striatum, a deep brain structure in the basal ganglia, which has been associated with responses to hedonic reward¹¹, and rewarding aspects of social behavior such as cooperation in a prisoner's dilemma game¹², altruistic punishment¹³, and feelings of romantic passion¹⁴.

Twenty three female participants completed a picture viewing task while fMRI data were collected. Color pictures were chosen from the International Affective Picture System¹⁵ (IAPS) to vary on two dimensions: valence (negative, positive) and content (nonsocial, social). On each trial, participants viewed a picture for 6 sec and pressed one of three keys on a button box to indicate whether the picture was negative, neutral

or positive. All pictures were presented in a single block in an event-related design; intertrial intervals were jittered in order to allow for deconvolution of the hemodynamic response. Following the scanner protocol, participants viewed each picture and rated how positive and negative they felt about each using a 5 (negativity: 0 = not at all negative, 4 = extremely negative) x 5 (positivity: 0 = not at all positive, 4 = extremely positive) grid, and how arousing they found each using a 9-point arousal scale (1 = not at all arousing, 9 = extremely arousing). Finally, participants completed the UCLA Loneliness Scale.⁷ The fMRI data were subjected to whole-brain analyses.

Regression of individual differences in loneliness scores (see Figure 1) against neural activity in the ventral striatum measured using fMRI revealed the predicted covariation. As illustrated in Figure 1, nonlonely participants showed greater activation in the ventral striatum extending to the left amygdala and portions of the anterior thalamus than lonely participants ($r(21) = -.75, p < .001$). This region includes those areas previously associated with hedonic reward^{11,12} and romantic passion¹⁴. Analyses within condition indicated that the neural activation in the ventral striatum in response to pleasant social pictures was greater for nonlonely than lonely individuals ($r(21) = -.46, p < .03$), whereas the neural activation in the ventral striatum in response to pleasant nonsocial pictures was greater for lonely than nonlonely individuals ($r(21) = .69, p < .001$).

These differences in the activation of the ventral striatum were observed even though lonely and nonlonely participants rated the social and nonsocial pictures equally positively. The results suggest that for non-lonely individuals, another person in a positive circumstance carries with it additional hedonic value than a nonsocial stimulus (e.g., a stack of money) that is rated as equally pleasant, whereas for lonely individuals the reverse is the case (see Table 1 & Supplementary Materials). Such differences in the rewarding qualities of others may help explain prior findings such as daily uplifts –

most of which involve other people –having less impact on lonely than nonlonely individuals¹⁶. These data are also consistent with a growing literature indicating that social reward coopts the appetitive system¹²⁻¹⁴.

The outcome of social interactions also provides a basis for developing attitudes about another person, and the ventral striatum appears to play an important role in the process of impression formation¹⁷. Having a prior impression of another person, on the other hand, is associated with lower ventral striatum activity during a social interaction¹⁸. In the present study, when faced with pleasant social stimuli, lonely people show reduced ventral striatum activity, indeed reduced activity over a wide region of the limbic system that plays a role in affective learning. This reduction may reflect the hypoactivation of this system, relative to non-lonely, based on prior experience regarding the relatively less rewarding outcomes of positive social interaction. It also may indicate that lonely individuals bring to new social encounters a stronger prior impression of what the individual will be like, whereas nonlonely individuals are less biased by a priori beliefs when forming impressions of new acquaintances.

As summarized in Table 2, the regression analyses for the pleasant pictures also revealed nonlonely, compared to lonely, participants showed greater activation in the left fusiform gyrus ($r(21) = -.68, p < .001$) and left anterior insula ($r(21) = -.68, p < .001$). Lonely, compared to lonely, participants, on the other hand, showed greater activation in the right medial frontal gyrus ($r(21) = .67, p < .001$). Follow-up analyses of the right medial frontal gyrus, left anterior insula and left fusiform gyrus revealed the associations between loneliness and neural activation in these regions were limited to the pleasant pictures of objects rather than people.

Lonely individuals also have been characterized as having poor social skills¹⁹. Two lines of evidence indicate this difference is attributable to social information

processing rather than to social skills knowledge per se. First, lonely and nonlonely individuals score similarly on tests of social skills knowledge²⁰, and lonely individuals are more rather than less attentive to social information²⁰. Second, when loneliness is experimentally manipulated, and hence social skills knowledge is held constant, participants in the lonely condition score more poorly on measures of social skills than participants in the nonlonely condition⁴. The visual cortex and the temporo-parietal junction (TPJ) were therefore of interest, the former because of its sensitivity to motivated visual information processing²¹ and the latter because it is involved in reasoning about the contents of other people's minds²² and agency²³. Saxe and Kanwisher²², for instance, measured neural activation in the TPJ using fMRI while the participants responded to five different kinds of stories: false belief stories, false photograph stories, desires, inanimate descriptions, and physical people. Only the false belief test requires a person to think about the mental contents of another person to perform the task correctly, and the false belief story led to a larger increase in the average percent signal change in the right and left TPJ than any other story.

The regression relating individual differences in the BOLD activation for the unpleasant social minus unpleasant nonsocial contrast from scores on the UCLA loneliness scale revealed greater activation of left and right visual cortex in lonely than nonlonely participants ($r(21) = .83$ and $.69$, respectively, $p < .001$), whereas nonlonely participants showed greater activation of the left ($r(21) = -.58$, $p < .01$) and right ($r(21) = -.57$, $p < .01$) regions of the temporo-parietal junction (TPJ) than lonely individuals (Figure 1). Follow-up analyses within condition indicated that the neural activation in the left and right visual cortices in response to unpleasant social pictures tended to be greater for lonely than nonlonely individuals ($r(21) = .35$ and $.39$, respectively, $ps < .10$), whereas neural activation in the left and right visual cortices in response to unpleasant nonsocial pictures was unrelated to individual differences in loneliness ($r(21) = -.06$ & $-.10$, respectively, $ps > .50$). Similar analyses for the TPJ regions

indicated that the neural activation in response to unpleasant social pictures tended to be greater for nonlonely than lonely individuals ($r_s(21) = -.47$ & $-.46$, respectively for left and right TPJ, $ps < .05$), whereas the neural activation in bilateral regions of the TPJ in response to unpleasant nonsocial pictures were unrelated to individual differences in loneliness ($r_s(21) = .29$ & $.25$, respectively, $ps > .15$). Finally, studies of theory of mind have been most reliably associated with activation of the right TPJ¹⁹. As illustrated in Figure 2, lonely and nonlonely participants showed increased activation of the right TPJ when viewing unpleasant pictures people rather than objects, but this increase was greater in nonlonely than lonely individuals.

The observed differences in neural activation in the visual cortices during the presentation of unpleasant social pictures suggests increased visual processing and thus is consistent with Gardner et al.'s²⁰ social monitoring theory, which posits that discrepancies between desired and perceived social connection lead to increased monitoring of the environment for social cues and opportunities to connect with others. In the research by Gardner and colleagues²⁰, participants were instructed to form an impression of a person based on excerpts they read from a (hypothetical) person's daily diary. Contrary to a social skills deficit model of loneliness, lonely individuals showed greater incidental social memory than nonlonely individuals. Results from the current study, in which participants were exposed to pleasant and unpleasant pictures of people and objects, indicates that attentional (social monitoring) rather than solely memorial mechanisms contributed to their results.

In the present study, evidence of greater attentional processing was found for unpleasant but not for pleasant stimuli, whereas in prior research lonely individuals showed heightened incidental social memory regardless of the valence of the behavioral description they read in the diary²⁰. However, the positive, neutral, and negative behavioral events in the prior research described the *same* individuals about whom the

participants were developing an overall impression. Given the interdependence of the behavioral stimuli and the negativity bias in impression formation, it is possible the social context in the prior studies was more similar to the unpleasant than pleasant pictures in the current study. We do not wish to overinterpret the absence of a significant association between loneliness and neural activation of the visual cortices in the pleasant social minus pleasant nonsocial contrast, however. Replication with a larger sample size would help clarify this issue.

Lonely individuals have been characterized as having poor social skills, yet behavioral and neuroimaging results suggest lonely individuals may be more rather than less attentive to social information—and perhaps also think differently about this information. The finding that lonely individuals show less neural activation in the right and left TPJ than nonlonely individuals despite showing more activation in the visual cortices suggests that lonely individuals attend more to other people but think less or less deeply about the mental states of these individuals. Together, these results are consistent with the notion that, at least in stressful circumstances, lonely individuals adopt a relatively egocentric perspective on other individuals²³. Consistent with this reasoning, higher levels of loneliness have been associated with poorer performance on a nonverbal perception task when the task involved forming an impression of the other person²⁴.

The regression analyses for the unpleasant pictures further revealed nonlonely participants showed greater activation in the right caudate ($r(21) = -.67, p < .001$) and right inferior frontal gyrus ($r(21) = -.58, p < .03$) (see Table 2). Follow-up analyses indicated the neural activation in response to unpleasant social pictures tended to be greater in the caudate and right inferior frontal gyrus for nonlonely than lonely individuals ($r_s(21) = -.41$ & $-.48$, respectively, $p_s < .06$ & $.02$, respectively), whereas the neural activation in both of these areas in response to unpleasant nonsocial pictures

tended to be greater for lonely than nonlonely individuals ($r_s(21) = .40$ and $.49$, respectively for the caudate and inferior frontal gyrus, $p_s < .06$). Loneliness was unrelated to activation in the right inferior frontal gyrus in response to unpleasant nonsocial pictures.

The right caudate was the only region to be predicted by loneliness in response to pleasant and unpleasant social stimuli after controlling for the neural responses to equally emotional nonsocial stimuli. The neural activation of the caudate has been shown to be involved not only in reward-based learning²⁵ but in incentive-based learning more generally²⁶. The reduction in neural response in the caudate observed for lonely individuals may reflect the down-regulation of this system, relative to non-lonely, based on prior experience regarding the relatively less rewarding outcomes of positive social interaction. It may also reflect a reduced ability by lonely individuals to learn from their social encounters.

In sum, social interactions are replete with opportunities for trust, understanding, hope, support, and cooperation just as they are full of opportunities for treachery, mistrust, betrayal, and conflict. Loneliness operates in part by shaping what people expect and think about other people. Lonely individuals seek to fulfill unmet needs but generally are less forgiving of minor hassles and transgressions than nonlonely individuals. The results raise new questions about the role of the ventral striatum, TPJ, and caudate in differences in social cognition between lonely and nonlonely individuals, and about the brain mechanisms that enable skillful social interactions.

Methods

Participants. Twenty-three female University of Chicago undergraduates participated in the study. All were right-handed, had normal or corrected-to-normal vision, and were not currently seeking treatment for affective disorders. Participants were required to

either have completed a previous fMRI study or to undergo an fMRI simulation session prior to their participation. Participants gave informed written consent before the experiment in accordance with the University of Chicago Health Sciences Institutional Review Board and were compensated for their time at the rate of \$20/hour. Participants completed four tasks in the scanner; the picture viewing task was included to test the current hypotheses.

Loneliness. Loneliness was measured using the UCLA Loneliness Scale (Version 3)⁷, which consists of 20 items measuring general loneliness and degree of satisfaction with one's social relationships. An example statement is, "How often do you feel that there is no one you can turn to?" Participants are instructed that the statements describe how people sometimes feel, and that for each statement they should indicate how often they feel the way described by the statement (1 = never, 2 = rarely, 3 = sometimes, 4 = always). The range of possible scores is 20-80, with higher scores signifying greater loneliness. After reverse scoring appropriate items, the UCLA loneliness score is calculated by summing the scores of all items. Russell⁷ reported internal consistency (coefficient α) ranging from .89 to .94 and test-retest over one year period of $r = .73$. The concurrent and discriminant validity of the UCLA Loneliness Scale are also provided by Russell⁷.

Task. Participants viewed pictures that varied in their emotional (i.e., negative/unpleasant, positive/pleasant) and social (i.e., nonsocial, social) content. Pictures were chosen from the International Affective Picture System¹⁵ based on normative ratings for females such that normative arousal and extremity (i.e., distance from the midpoint of the normative valence scale) did not differ across the four sets. The target pictures were embedded in neutral filler pictures.

Each picture was presented for 6 s. Intertrial intervals, consisting of a white crosshairs on a black background, were jittered to allow for deconvolution of the

hemodynamic response and ranged from 1.5 – 29 s in duration. Participants were asked simply to view each picture for the entire duration that it was presented and to make a categorical judgment regarding the valence of each picture by using their right hand to press one of three buttons on a response box to indicate whether it was negative (index finger), neutral (middle finger), or positive (ring finger). Pictures were presented in one of two pre-determined random orders that were counterbalanced across subjects. No effects for order of presentation were found, so this factor is not discussed further.

Following the scanner protocol, participants viewed each picture and rated how positive and negative they felt about each using a 5 (negativity: 0 = not at all negative, 4 = extremely negative) x 5 (positivity: 0 = not at all positive, 4 = extremely positive) grid, and how arousing they found each using a 9-point arousal scale (1 = not at all arousing, 9 - extremely arousing).

Data acquisition. A PC was used to present stimuli and to record participants' responses. Visual stimuli were presented using binocular goggles mounted on the head coil approximately two inches above the participant's eyes. Button-press responses were made on an fMRI-compatible response box.

Imaging was performed on a 3T GE Signa scanner (GE Medical Systems, Milwaukee, WI) with a standard quadrature GE head coil. High-resolution volumetric T1-weighted spoiled gradient-recalled (SPGR) images were obtained for each subject in 124 1.5-mm sagittal slices with 10° flip angle and 24 cm field of view (FOV) for use as anatomical images. Functional images were acquired using a gradient-echo spiral-in/out pulse sequence²⁷ with 33 contiguous 5-mm coronal slices in an interleaved order spanning the whole brain (TR = 2.5 s, TE = 26 ms, flip angle = 77°, FOV = 22 cm; 64 x 64 matrix size, fat suppressed).

Data analysis. Spiral-in and spiral-out images were reconstructed first separately and then combined using a weighted-average algorithm that maximizes signal-to-noise ratio while reducing signal loss^{27,28}. Further image processing was performed using AFNI software. For each subject, motion detection and correction were undertaken using a six-parameter, rigid-body transformation. Functional images were temporally smoothed using a low-pass filter consisting of a 3-point Hamming window; and were spatially smoothed using a 5 mm full-width at half-maximum (FWHM) Gaussian filter.

Individual-subject analyses were conducted using a deconvolution analysis to generate impulse response functions (IRFs) of the BOLD signal on a voxel-wise basis²⁹. This approach produces an estimate of the hemodynamic response for each condition relative to a baseline state without a priori assumptions about the IRF. The deconvolution analysis uses a separate regressor for each time point of each condition, and fits these regressors using a linear least squares model to each time point of the hemodynamic response. Each of the four conditions (i.e., negative nonsocial, negative social, positive nonsocial, positive social) had seven regressors, one for each TR. Output from the deconvolution analysis conducted for each participant was converted to Talairach stereotaxic coordinate space³⁰ and interpolated to volumes with 3 mm³ voxels. Estimated signal intensity for the four TRs under the peak of the hemodynamic response (TRs 2-5) was averaged for each voxel in each condition for use in group analyses.

Whole brain voxel-wise regressions. For each subject, two contrasts were conducted for use in group-level analyses. The first contrast was calculated as the difference in percent signal change when viewing negative social versus negative nonsocial pictures; the second contrast was between positive social and positive nonsocial pictures. The ventricles, cerebellum, brainstem, and white matter were masked.

To examine the relationship between loneliness and patterns of neural activation to pictures that varied in emotional and social content, we conducted two whole-brain voxel-wise regression analyses predicting neural activation for each contrast from subjects' scores on the UCLA Loneliness Scale. The β_1 term from each regression at each voxel represents the relationship between loneliness and neural activation. Results from each whole brain regression were subjected to a cluster analysis, using an individual voxel threshold of $p < 0.05$, a minimum cluster connection radius of 5.2 and a cluster volume of 459 μL (corresponding to 48 active, contiguous voxels). Minimum cluster volume was determined using a Monte Carlo simulation with 10,000 iterations, and assuming some interdependence between voxels (5 mm FWHM).

1. Davis, J. A., & Smith, T. W. *General social surveys, 1972-1998: Cumulative codebook*. Chicago: National Opinion Research Center (1998).
2. Boomsma, D. I., Willemsen, G., Dolan, C. V., Hawkey, L. C., & Cacioppo, J. T. Genetic and environmental contributions to loneliness in adults: The Netherlands Twin Register Study. *Behavior Genetics*, **35**, 745-752 (2005).
3. McGuire, S., and Clifford, J. Genetic and environmental contributions to loneliness in children. *Psychological Science*, **11**, 487-491(2000).
4. Cacioppo, J. T., Hawkey, L. C., Ernst, J. M., Burleson, M., Berntson, G. G., Nouriani, B., & Spiegel, D. Loneliness within a nomological net: An evolutionary perspective. *Journal of Research in Personality*, **40**, 1054-1085 (2006).
5. Frith, C., & Wolpert, D. *The neuroscience of social interaction*. Oxford: Oxford University Press (2004).
6. Weiss, R. S. *Loneliness: The experience of emotional and social isolation*. Cambridge, MA: MIT Press (1973).

7. Russell, D. UCLA Loneliness Scale (Version 3): Reliability, validity, and factor structure. *Journal of Personality Assessment*, **66**, 20-40 (1996).
8. Hawkley, L. C., Burleson, M. H., Berntson, G. G., & Cacioppo, J. T. Loneliness in everyday life: Cardiovascular activity, psychosocial context, and health behaviors. *Journal of Personality & Social Psychology*, **85**, 105-120 (2003).
9. Rotenberg, K. Loneliness and interpersonal trust. *Journal of Social and Clinical Psychology*, **13**, 152–173 (1994).
10. Hawkley, L. C., Preacher, K. J., & Cacioppo, J. T. Multilevel modeling of social interactions and mood in lonely and socially connected individuals: The MacArthur social neuroscience studies. In A. D. Ong & M. van Dulmen (Eds.), *Oxford Handbook of Methods in Positive Psychology* (pp. 559-575). New York: Oxford University Press (2007).
11. Smith, K. S., & Berridge, K. C. The ventral pallidum and hedonic reward: Neurochemical maps of sucrose “liking” and food intake. *Journal of Neuroscience*, **25**, 8637-8649 (2005).
12. Rilling, J. K., Gutman, D. A., Zeh, T. R., Pagnoni, G., Berns, G. S., Kilts, C. D. A neural basis for social cooperation. *Neuron*, **35**, 395-405 (2002).
13. De Quervain, D., Fischbacher, U., Treyer, V., Schellhammer, M., Schnyder, U., Buck, A., & Fehr, E. The neural basis of altruistic punishment. *Science*, **305**, 1254-1258 (2004).
14. Aron, A., Fisher, H., Mashek, D. J., Strong, G., Li, H., & Brown, L. L. Reward motivation and emotion systems associated with early-stage intense romantic love. *Journal of Neurophysiology*, **94**, 327-337 (2005).

15. Lang, P. J., Bradley, M. M., & Cuthbert, B. N. *International affective picture system (IAPS): Digitized photographs, instruction manual and affective ratings*. Technical Report A-6. University of Florida, Gainesville, FL (1999).
16. Cacioppo, J. T., Ernst, J. M., Burleson, M. H., McClintock, M. K., Malarkey, W. B., Hawkley, L. C., Kowalewski, R. B., Paulsen, A., Hobson, J. A., Hugdahl, K., Spiegel, D., & Berntson, G. G. Lonely traits and concomitant physiological processes: The MacArthur Social Neuroscience Studies. *International Journal of Psychophysiology*, **35**, 143-154 (2000).
17. King-Casas, B., Tomlin, D., Anen, C., Camerer, C. F., Quartz, S. R., & Montague, P. R. Getting to know you: Reputation and trust in a two-person economic exchange. *Science*, **308**, 78-83 (2005).
18. Delgado, M. R., Miller, M. M., Inati, S., & Phelps, E. A. An fMRI study of reward-related probability learning. *Neuroimage*, **24**, 862-873 (2005).
19. DiTommaso, E., Brannen-McNulty, C., Ross, L., & Burgess, M. Attachment styles, social skills and loneliness in young adults. *Personality and Individual Differences*, **35**, 303-312 (2003).
20. Gardner, W. L., Pickett, C. L., Jeffries, V., & Knowles, M. On the outside looking in: Loneliness and social monitoring. *Personality and Social Psychology Bulletin*, **31**, 1549-1560 (2005).
21. Bradley, M. M., Sabatinelli, D., Lang, P. J., Fitzsimmons, J. R., King, W., & Desai, P. Activation of the visual cortex in motivated attention. *Behavioral Neuroscience*, **117**, 369-380 (2003).
22. Saxe, R., & Kanwisher, N. People thinking about thinking people: The role of the temporo-parietal junction in "theory of mind." *Neuroimage*, **19**, 1835-1842 (2003).

23. Decety, J., & Grezes, J. The power of simulation: Imagining one's own and other's behavior. *Brain Research*, **1079**, 4-14 (2006).
24. Pickett, C.L., & Gardner, W.L. The social monitoring system: Enhanced sensitivity to social cues as an adaptive response to social exclusion. In K. Williams, J. Forgas, and W. von Hippel (Eds.), *The social outcast: Ostracism, social exclusion, rejection, and bullying*. New York: Psychology Press (2005).
25. Galvan, A., Hare, T. A., Davidson, M., Spicer, J., Glover, G., & Casey, B. J. The role of the ventral frontostriatal circuitry in reward-based learning in humans. *Journal of Neuroscience*, **25**, 8650-8656 (2005).
26. Tricomi, E., Delgado, M. R., McCandliss, B. D., McClelland, J. L., & Fiez, J. A. Performance feedback drives caudate activation in a phonological learning task. *Journal of Cognitive Neuroscience*, **18**, 1029-1043 (2006).
27. Glover, G. H. & Law, C. S. Spiral-in/out BOLD fMRI for increased SNR and reduced susceptibility artifacts. *Magnetic Resonance in Medicine*, **46**, 515-522 (2001).
28. Preston, A. R., Thomason, M. E., Ochsner, K. N., Cooper, J. C., & Glover, G. H. Comparison of spiral-in/out and spiral-out BOLD fMRI at 1.5 and 3 T. *NeuroImage*, **21**, 291-301 (2004).
29. Ward, B. D. *Deconvolution Analysis of FMRI Time Series Data* (Technical Report). Milwaukee, Wisconsin: Biophysics Research Institute, Medical College of Wisconsin (2001).
30. Talairach, J., & Tournoux, P. *Co-Planar Stereotaxic Atlas of the Human Brain: 3D Proportional System: An Approach to Cerebral Imaging*. New York, New York: Georg Thieme Verlag (1988).

Supplementary Information accompanies the paper on www.nature.com/nature.

The authors would like to thank Robert Lyons, Carden Safran, John Scott Railton, J.S. Irick and Jia Hong Gao for their assistance. Support for this research was provided by NIMH Grant No. P50 MH72850, NIA Grant No. PO1 AG18911, and the John Templeton Foundation.

Competing Interests statement: The authors declare that they have no competing financial interests.

Authors' Contributions statement. All four authors contributed to the conceptualization of the study and the preparation of the manuscript. The second and fourth authors conducted and analyzed the study under the supervision of the remaining authors.

Address correspondence to John T. Cacioppo, Center for Cognitive and Social Neuroscience, University of Chicago, Chicago, IL 60637.

Figure 1. The relationship between participants' loneliness scores and differences in neural activation for Pleasant Social – Pleasant Nonsocial pictures. The 3-dimensional figure depicts the cluster of voxels showing an inverse relationship between loneliness and activation in the Pleasant Social – Pleasant Nonsocial contrast in the ventral striatum, extending to the left amygdala and portions of the anterior thalamus. The scatterplot demonstrates the individual datapoints contributing to the correlation: $r(21) = -.75, p < .001$. Estimated impulse response functions for nonlonely and lonely participants, using a median split for ease of interpretation, shows a crossover interaction for the relationship between loneliness and neural responses to pleasant social and pleasant nonsocial stimuli, such that nonlonely participants exhibit greater activation to pleasant pictures that contain social content and lonely participants exhibit greater activation to pleasant nonsocial pictures. This suggests that nonlonely individuals receive greater pleasure from social stimuli; whereas lonely participants prefer nonsocial stimuli.

Figure 2. Voxel-wise correlations between loneliness and neural activation for the Unpleasant Social – Unpleasant Nonsocial contrast. Two sets of correlations emerged from this analysis: first, bilateral areas of visual cortex exhibited a positive relationship between loneliness and neural activation for this contrast; and second, bilateral areas of the TPJ showed a negative relationship between loneliness and neural activation. This pattern of results suggests that although lonely individuals pay more attention to unpleasant social stimuli, nonlonely individuals think more about the mental states of people depicted in unpleasant social stimuli. Importantly, all participants tended to show an increase in activation of the right TPJ, the neural area most commonly associated with theory of mind and making judgments about others' mental states (see estimated IRFs for the right TPJ). Correlations for the left and right TPJ and the left and right visual cortex were: $r(21) = -.58, -.57, .83$ and $.69$, respectively, all $ps < .01$.

Table 1.

Mean normative ratings for target pictures. Superscripts that differ within a column indicate a significant difference in means at $p < .05$.

	Normative Arousal	Normative Valence	Normative Extremity
Unpleasant Nonsocial	5.79 ^a	2.65 ^a	2.35 ^a
Unpleasant Social	6.39 ^a	2.25 ^a	2.75 ^a
Pleasant Nonsocial	5.67 ^a	7.28 ^b	2.28 ^a
Pleasant Social	6.55 ^a	7.56 ^b	2.56 ^a

Table 2.

Neural regions exhibiting a significant relationship between loneliness and neural activation.

Region	BA	Volume	x	y	z	Mean Intensity
<i>Pleasant Social – Pleasant Nonsocial Pictures</i>						
Ventral striatum		24678	1	-5	2	-.012
Right medial frontal gyrus	6	702	10	-21	57	.011
Left fusiform gyrus		675	-31	-39	-12	-.015
Left anterior insula	13	513	-36	13	7	-.013
<i>Unpleasant Social – Unpleasant Nonsocial Pictures</i>						
Left visual cortex	17	891	-21	-80	16	.013
Right caudate & caudate body		810	15	2	16	-.011
Right inferior frontal gyrus	46	729	43	39	7	-.035
Left temporo-parietal junction	22, 39	513	-49	-54	22	-.016
Right temporo-parietal junction	22, 39	513	54	-57	17	-.017
Right visual cortex	19	459	27	-83	19	.020







