Extraordinary Altruists Exhibit Enhanced Self-Other Overlap in Neural Responses to Distress

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Abstract

Shared neural representations during experienced and observed distress are hypothesized to reflect empathic neural simulation, which may support altruism. But the correspondence between real-world altruism and shared neural representations has not been directly tested, and empathy's role in promoting altruism toward strangers has been questioned. Here we show that individuals who have performed costly altruism (donating a kidney to a stranger; $n=25$) exhibit greater self-other overlap than matched controls ($n=27$) in neural representations of pain and threat (fearful anticipation) in anterior insula (AI) in an empathic pain paradigm. Altruists exhibited greater self-other correspondence in pain-related activation in left AI, highlighting that group-level overlap was supported by individual-level associations between empathic pain and first-hand pain. Altruists exhibited enhanced functional coupling of left AI with left mid-insula during empathic pain and threat. Results show that heightened neural instantiations of empathy correspond to real-world altruism and highlight limitations of self-report.

Keywords: altruism, empathy, neural simulation, non-directed living kidney donation

Does empathy promote altruism? Empathy is the suite of processes that enables an individual to perceive and understand others' distress, promoting the motivation to act on their behalf (de Waal, 2008). Empathy for pain entails recruiting neural processes that are equivalent to those recruited during the first-hand experience of pain (Rütgen et al., 2015) and such self-other mapping has been theorized to promote non-reciprocal altruism: voluntary, costly actions aimed at improving another's welfare (Ashar, Andrews-Hanna, Dimidjian, & Wager, 2017; Batson, 2010; de Waal, 2008; Preston & De Waal, 2002). But linking empathy unambiguously to altruism has proven challenging. Some argue that empathy may actually preclude altruism by biasing respondents away from distant or dissimilar others, and that empathy must be overridden by cognitively mediated compassion (Bloom, 2017). The difficulty of objectively measuring and operationalizing both empathy and altruism impedes clear conclusions. Empathic self-other mapping cannot be directly reported or observed through behavior, and genuinely costly altruism is impractical or unethical to reproduce in a laboratory. The aim of the present study was to test putative links between objectively measured empathy and costly real-world altruism by evaluating whether individuals who have voluntarily engaged in a stringently defined form of altruism (donation of a kidney to a stranger) exhibit spontaneous enhancements in self-other neural mapping of experienced and observed distress, including pain and threat (fearful anticipation).

The anterior insula (AI) is a neural region strongly implicated in empathy. Self-other mapping of pain can be observed in AI, which is active during both experienced and observed pain (Bernhardt & Singer, 2012; Fan, Duncan, de Greck, & Northoff, 2011; Lamm, Decety, & Singer, 2011; Rütgen et al., 2015; Singer et al., 2004; Zaki, Wager, Singer, Keysers, & Gazzola, 2016), particularly in response to close others or in-group members (Beckes, Coan, & Hasselmo,

2012; Hein, Silani, Preuschoff, Batson, & Singer, 2010), and has been implicated in affective empathy and non-reciprocal altruism more generally (Fan et al., 2011; Kanske, Bockler, Trautwein, & Singer, 2015; Patil et al., 2017; Tusche, Bockler, Kanske, Trautwein, & Singer, 2016). Only altruism for strangers can be unambiguously described as non-reciprocal; if empathy promotes non-reciprocal altruism, enhanced self-other neural mapping in AI and associated regions while viewing an anonymous stranger's pain may be observed in individuals who have engaged in costly altruism for strangers.

To test this hypothesis, we recruited a rare sample of individuals who had donated a kidney to a stranger and compared them with demographically matched control participants. Both groups underwent a pressure-pain paradigm and also watched as a stranger underwent an identical pain paradigm in real time. Altruistic kidney donation is a voluntary, extraordinarily costly form of altruism performed to benefit strangers, thereby satisfying stringent definitions of altruism (Batson, 2010; Clavien & Chapuisat, 2013; de Waal, 2008). Evaluating altruistic kidney donors circumvents ethical and practical considerations that preclude reproducing genuinely costly altruism in the laboratory and minimizes social desirability and norm-adherence motives that contaminate laboratory-elicited altruism (Eisenberg & Fabes, 1990). The study of this special population of extraordinary altruists therefore provides valuable insight into the basis of altruism, much as the study of other special populations has provided important insights into mechanisms underlying, for example, memory (LePort et al., 2012) and face processing (Russell, Duchaine, & Nakayama, 2009).

We hypothesized that enhanced group-level self–other mapping in AI and other affective pain regions would be observed in altruists relative to controls. Moreover, these group-level differences would be supported by increased self–other correspondence at the individual level

during two types of pain-related distress (defined as negative affect elicited in response to or anticipation of an aversive stimulus). The two types of distress examined here were threat (fearful anticipation following a cue that probabilistically predicted pressure pain in the ensuing trial) and pressure pain. In other words, not only would altruists show more overlap of activation during experienced and empathic pain, and during experienced and empathic threat, but also experience-based activation would be associated with empathic activation in altruists at the individual level. Functional connectivity of AI during empathic pain and threat was also examined given AI's role as a hub in an affective salience network (Bernhardt & Singer, 2012; Menon & Uddin, 2010) that may support empathically motivated altruism.

Methods

Participants

Fifty-seven participants, who included 29 altruistic kidney donors and 28 matched controls, took part in this study for monetary payment. Sample sizes were determined using fMRIPower (SPM Toolkit; Mumford & Nichols, 2008), specialized software used to determine power estimates for fMRI data, and pilot data from our previous study of altruist donors (Marsh et al., 2014). One altruist was unable to complete the task due to scanner malfunction. Additionally, three altruists and one control were excluded from analyses for movement exceeding 0.5 mm for at least 15% of the total number of task TRs. This resulted in a final sample of 25 altruistic kidney donors and 27 matched controls between 21 and 55 years old (see Table 1 for participant characteristics). Altruistic kidney donors were recruited using mailings and electronic advertisements through local and national transplant organizations. The sample of altruists was limited by the extreme rarity of this behavior (1,819 such donations in the United States through 2016 according to the Organ Procurement and Transplantation Network, 2017).

Because altruists were recruited from across North America, most altruists resided more than a two-hour drive from the university and were provided with airfare and up to two nights' lodging. All altruists had donated a kidney to a stranger unknown to them personally at the time they decided to donate. Nineteen altruists were non-directed donors for whom the recipient was anonymous at the time of donation. The remaining six directed their donations to a specific individual who was known to them at the time of donation but whose need for a kidney they had learned about through, for example, a flier or Internet posting. All donations were verified through independent sources, including transplant center records or media reports. Using data obtained from the Organ Procurement and Transplantation Network, which is administered by the United Network of Organ Sharing under contract with the U.S. Department of Health and Human Services, we confirmed that the altruists recruited for this study were representative of the national population of altruistic donors in terms of sex and race (exact ages are not available for the national sample). Healthy volunteers were recruited from the local community using fliers, online advertisements, and electronic participant databases including ResearchMatch. The present study was conducted three years after our prior neuroimaging studies (Marsh et al., 2014; Brethel-Haurwitz et al., 2017), and includes partially overlapping subject samples, with 12 altruists and 6 controls returning for this study.

Table 1

Participant Characteristics

	Altruists (<i>n</i> = 25)	Controls (<i>n</i> = 27)	<i>p</i>	Effect Size ^a
Male	9/16 (36.0%)	13/14 (48.2%)	.376	0.12
White	23/2 (92.0%)	22/5 (81.5%)	.267	0.15
Right	24/1 (96.0%)	25/2 (92.6%)	.599	0.07
Household Income $\geq$ \$60,000	19 (76.0%)	24 (92.3%)	.109	0.22
Education $\geq$ Four-Year Degree	17 (68.0%)	24 (88.9%)	.065	0.26
Age <i>M</i> (95% CI)	41.92 [38.04-45.80]	38.89 [35.38-41.40]	.229	0.34 [-0.21-0.88]
IQ <i>M</i> (95% CI)	108.28 [103.40-113.16]	111.22 [106.96-115.48]	.375	0.25 [-0.30-0.79]

Note: One control subject did not report household income. For age and IQ, 95% confidence intervals are given in brackets.

^aEffect sizes for gender, race, handedness, income, and education are ϕ s; effect sizes for age and IQ are *ds*.

Exclusion criteria for all participants included current use of psychotropic medication, history of head injury or neurological illness, IQ < 80 (as assessed using the Kaufman Brief Intelligence Test - Second Edition (Kaufman & Kaufman, 2004)), and pregnancy or other contraindications to safe MRI scanning, including metal fragments or implants. Thorough screening of psychopathology was also conducted, in order to ensure group matching on potentially relevant psychological variables. Participants were excluded if they scored above clinical cutoffs for Global Severity, Positive Symptom Distress, or Positive Symptom Total on the Symptom Checklist - 90 (SCL-90; Derogatis & Unger, 2010), due to scores on the Somatization, Obsessive-Compulsive, Depression, Anxiety, Paranoid Ideation, or Psychoticism subscales. If totals reflected elevated scores on the Interpersonal Sensitivity or Hostility subscales, participants were not excluded. Additionally, given the nature of the task, participants were excluded if they reported a pain disorder or hearing difficulties. Controls were excluded if they reported having ever volunteered to donate an organ to any individual (not including consenting to become a deceased organ donor), or if they expressed interest in potentially doing so. Specifically, all controls were asked during initial screening if they would be interested in

receiving additional information from the Washington Regional Transplant Center about becoming a living organ donor, and 27 potential controls that answered yes to this question were excluded solely for this reason. All study procedures were approved by the Institutional Review Board at Georgetown University in Washington, DC, and all participants provided written informed consent before testing.

Procedures

All interested volunteers initially completed a 90-minute online survey assessing exclusion and inclusion criteria, demographic variables, and several self-report questionnaires including the Interpersonal Reactivity Index (IRI; Davis, 1983). The IRI is a 28-item questionnaire that measures both total self-reported empathy and four subscales: empathic concern, perspective taking, fantasy scale, and personal distress. Eligible volunteers were then screened by telephone to confirm eligibility. Researchers coordinated altruists' travel to and lodging at Georgetown University to enable on-site neuroimaging and cognitive testing. On-site testing included the Empathy for Pain Scale (EPS; Giummarra et al., 2014), which is a self-report questionnaire measuring empathy specific to pain through 12 emotion constructs across four contexts in which pain may be observed, resulting in three subscales: empathic concern, affective distress, and vicarious pain. To ensure groups were matched, eligible controls completed laboratory screening that included assessments of IQ, income, education, psychological history, medication use, and MRI compatibility before MRI scanning. After confirmation of eligibility, controls completed neurocognitive tasks and MRI scanning in a final visit.

During the calibration procedure and the fMRI task (see Neuroimaging Task), participants received painful pressure stimulation to their right thumbnail. Pneumatic pressure was administered remotely by an MRI-safe device connected to a laptop computer with software

programmed to consistently administer a selected pressure level at intervals and durations matching the task structure. When pressure was administered, a circular plastic plunger with an 2 cm diameter rubber surface made contact with the right thumbnail of the participant or confederate, whose thumb was positioned in a clear plastic tube to keep it in place throughout the task (see Figure 1a). Pressure of a rectangular waveform was administered for 6 seconds.

Two live video feeds allowed each participant to observe both the hand of the confederate and their own hand during the task (Figure 1a). A video camera positioned next to the confederate in the MRI console room captured video of the confederate's hand. Each participant was briefly introduced to the confederate in this set-up, so that it was apparent to the participant that the video feed would in fact be live. An MRI-safe video camera positioned adjacent to the scanner was adjusted for each participant to capture an equivalent view of the participant's own right hand receiving painful stimulation. The video feed was switched between these two cameras depending on the run of the task.

Figure 1. Empathic pain task. (a) Participants viewed continuous live video feeds of the hand of the study partner (confederate), then their own hand, in separate runs. (b) Variable anticipation

periods were followed by the administration or omission of painful pressure stimulation to the right thumbnail. An audio cue at the beginning of the anticipation period indicated whether the trial was safe or had the potential for pain. A second audio cue indicated whether or not painful pressure was administered.

Neuroimaging Task

Participants completed three runs of the pain task, each lasting 12 minutes and 18 seconds, during fMRI scanning. In the first two runs, participants observed a “study partner,” and in the third run they experienced the task themselves (Figure 1a). The study partner was a female confederate whom participants were briefly introduced to immediately prior to the scan. Two confederates participated over the course of the study, balanced between the two groups. The second run of the task began with a prompt to encourage increased empathizing with the study partner and is not reported here, in order to limit the current analyses to group differences in baseline responses to the observation of pain in another person relative to the first-hand experience of pain. The effect of the empathy prompt will be reported in a separate manuscript.

Each run was composed of 30 trials, with each trial made up of a variable anticipation period, the administration or omission of painful pressure stimulation, and a variable rest period (Figure 1b). Half of the trials were safe trials, in which participants knew that there would be no thumb pressure, while the other half of the trials had the potential for thumb pressure, and thus served as threat trials, resulting in 15 threat trials and 15 safe trials within each block. Pressure was omitted on one third of these potentially painful trials in order to keep the administration of pain probabilistic rather than deterministic, which is important to elicit fearful anticipation (Sylvers, Lilienfeld, & LaPrairie, 2011), resulting in 10 pain trials and 20 no pain trials within each block. Throughout each trial, participants viewed continuous live video feeds of either the

confederate's hand in the first and second runs, or their own hand in the third run. Audio cues via MRI-safe headphones indicated the trial structure, with a first sound indicating at the start of each trial whether it was a safe trial or had the potential for painful pressure, and a second sound after the anticipation period indicating whether or not pressure was currently being administered. Participants were trained in the meaning of the various audio cues prior to the scan, reminded of the cue meanings once in the scanner, and quizzed on their comprehension prior to the first run. Participants' ability to hear the audio cues and differentiate them from scanner noise was confirmed during a localizer scan prior to the first run.

Immediately prior to scanning, all participants were guided through a calibration procedure to determine the level of pressure to be administered during the scan, such that subjective pain perceptions were equivalent across participants. All participants were calibrated to receive pain that was subjectively "slightly intense" corresponding to a rating of 13.5 on the 21-point Gracely Box Scale (Gracely & Kwilosz, 1988), which was selected to be moderately painful but not harmful. Following explanation of the Gracely Box Scale and the calibration procedure, increasing pressure levels were administered, beginning with 5 psi and increasing by increments of 5 psi until participants gave a rating of 13.5. Ascending pressure was continued until a rating higher than 13.5 was given, then descending pressure in increments of 5 psi was administered until participants gave a rating lower than 13.5. If different, the lower of the two pressure levels rated 13.5 was selected as the "slightly intense" pressure level. The pressure selected during the calibration procedure was checked in the scanner immediately prior to the run in which participants received pressure themselves. Several participants in each group (8 altruists and 10 controls, $\chi^2(1) = 0.15$, $p = .703$, $\phi = 0.05$) rated the pressure selected during calibration more highly than 13.5 once in the scanner, resulting in a re-calibration procedure in which

descending pressure in increments of 5 psi was tested until participants gave a rating of 13.5. This re-calibrated lower pressure was then the pressure administered to the participant during the scan. Because altruists selected significantly higher objective pressure for their subjectively calibrated “slightly intense,” $t(50) = 3.97, p < .001, d = 1.10$, 95% confidence interval (CI) for the effect size = [0.51, 1.68] (Figure S1b), final pressure level was included as a covariate in analyses of experienced pain and threat. The confederate always received 15 psi of pressure, which was selected to be clearly visible over the live video feed and within the range of slightly intense pain for both groups.

Subjective ratings of pain experience were collected during and after scanning. Following each run, participants were asked to rate pain intensity on a 1 (no pain) to 7 (extreme pain) scale. For Run 1, this was their perception of the study partner’s pain level, while for run 3 this was their rating of their own pain experience. After the scan, participants filled out a questionnaire in which they rated how fearful/anxious and unpleasant their experiences during the anticipation and pain portions of the task were, respectively, on a 1 (not at all) to 7 (extremely) scale. They also answered the same questions regarding the experience of their study partner. Importantly, despite significantly different objective pressure stimulation levels selected as “slightly intense” by altruists and controls (Figure S1b), subjective experiences of threat and pain were equivalent between the two groups. There were no group differences in subjective ratings of threat or pain, during or after the scan, for the participant’s first-hand experience or their perception of the study partner’s experience, all $p > .05$ (Table 2). Across all participants, cues indicating that pain may follow were rated as more fear and anxiety-inducing than safety cues, $t(50) = 12.55, p < .001, d = 2.38$, supporting the interpretation that this anticipation epoch induced fearful anticipation, and thumbnail stimulation was rated as more unpleasant than the omission of thumbnail stimulation,

$t(50) = 13.02, p < .001, d = 2.41$. Threat of pain, $t(50) = 14.04, p < .001, d = 2.64$, and the experience of thumbnail stimulation, $t(50) = 12.02, p < .001, d = 2.22$, were also rated negatively for the study partner, relative to the safety trials and omission of stimulation.

Table 2

Ratings of Intensity of Subjective Pain, Pain Unpleasantness, and Fear by Group

Rating	Condition	Altruists	Controls	<i>p</i>	<i>d</i>
Pain	Self	4.48 [4.00-4.96]	4.30 [3.81-4.79]	.603	0.15 [-0.40-0.69]
	Other	4.08 [3.66-4.50]	3.93 [3.62-4.24]	.564	0.16 [-0.38-0.71]
Unpleasantness	Self Pain	3.60 [3.06-4.14]	3.85 [3.32-4.38]	.527	0.18 [-0.37-0.73]
	Self No Pain	1.16 [1.01-1.31]	1.27 [1.01-1.53]	.476	0.20 [-0.35-0.75]
	Other Pain	3.84 [3.34-4.34]	3.81 [3.20-4.42]	.936	0.02 [-0.53-0.57]
	Other No Pain	1.44 [1.03-1.85]	1.12 [0.99-1.25]	.137	0.42 [-0.13-0.98]
Fear	Self Threat	3.36 [2.76-3.96]	3.65 [3.20-4.10]	.442	0.22 [-0.33-0.77]
	Self No Threat	1.16 [1.01-1.31]	1.15 [1.01-1.29]	.953	0.02 [-0.53-0.57]
	Other Threat	3.48 [2.94-4.02]	3.92 [3.47-4.37]	.222	0.35 [-0.21-0.90]
	Other No Threat	1.12 [0.99-1.25]	1.23 [1.03-1.43]	.367	0.25 [-0.30-0.80]

Note. 95% CIs are reported for means and *d* statistics. This pattern of results is the same when controlling for objective pain level.

Participants also rated their perception of connectedness to others on the Inclusion of Other in the Self Scale (Aron, Aron, & Smollan, 1992). Connectedness was rated by selecting one of seven diagrams of overlapping circles representing perceived connectedness to the other individual, from 1 (separate and distant circles, representing lowest degree of connectedness) to 7 (completely overlapping circles, representing highest degree of connectedness). Relationships rated included immediate family, extended family, friend, acquaintance, stranger, and study partner from the empathic pain task. Data from one control were missing for the experience questionnaire and one altruist did not complete the Inclusion of Other in the Self Scale.

All reported statistical tests were two-sided. Correlations between behavioral variables and neural activation in AI ROIs are reported in Table S1. Only significant correlations surviving correction for multiple comparisons via the Benjamini-Hochberg method of controlling the false

discovery rate ($Q < .05$) are reported are reported here. For additional details on neuroimaging acquisition and analysis, see the Supplemental Material.

Results

First, whole-brain conjunction analyses were conducted to compare activation for experienced and empathic pain. Individuals who have engaged in costly altruism for a stranger spontaneously exhibited greater self-other conjunction in bilateral AI while observing an anonymous stranger's pain, such that increased activation in bilateral AI emerged during both experienced and observed pain, $p < .05_{\text{corrected}}$. Both altruists and controls exhibited overlap in bilateral inferior parietal cortex and right AI, but only altruists exhibited overlap in left AI (Figure 2a). In altruists only, conjunctions were also observed in putamen, thalamus, dorsomedial prefrontal cortex, and middle cingulate cortex (Table S2). A similar pattern was observed for distinct epochs of experienced and empathic threat, during which conjunction in bilateral AI, as well as dorsomedial prefrontal cortex was found in altruists, whereas conjunction in controls was limited to right AI, right caudate, and left inferior parietal lobule, $p < .05_{\text{corrected}}$ (Figure 2a, Table S3). Reinforcing that these group differences reflect specifically empathic processes, differences in self-other mapping across groups emerged despite comparable activation for experienced pain and threat across groups (Figure S1, Tables S4 & S5). Examining activation levels in AI ROIs for experienced and empathic pain and threat, no group differences were found, even when controlling for objective pain level, all $p > .05$, all $d < 0.48$ (Figure S2). There were also no significant differences within any condition in whole-brain group contrasts.

Figure 2. Empathic pain and threat conjunction and covariation results. Whole-brain statistical maps (a) show the conjunction of neural activation for experienced and empathic pain and the conjunction of neural activation for experienced and empathic threat, separately for each group ($z = 0$). A whole-brain clusterwise corrected threshold $p < .05$ at uncorrected voxelwise threshold of $p = .001$ was applied to the statistical maps. The scatterplot (b) shows the relationship between activations in the left AI region of interest for experienced pain and empathic pain. Standardized residuals and lines of best fit are plotted, controlling for objective pain level. Shading represents 95% confidence intervals.

Mean parameter estimates were extracted for ROIs in bilateral AI to examine individual-level correspondence in activation levels for experienced and empathic pain and threat. Partial correlations controlling for objective pain intensity confirmed group-level findings for experienced pain in left AI. In altruists, activation in left AI during first-hand pain experience was associated with activation in the identical region when observing an anonymous stranger experiencing pain, $r(22) = .57$ [95% CI: .22-.79], $p = .004$, while no similar relationship was

observed in controls, $r(24) = -.15 [-.51-.25]$, $p = .456$ (Figure 2b); these correlations differed significantly in magnitude, $z = 2.64$, $p = .008$. This effect was phenomenologically specific, in that left AI activation during pain experience was not associated with left AI activation for empathic threat in altruists, $r(22) = -.23 [-.58-.19]$, $p = .286$. Neither altruists, $r(22) = .19 [-.23-.55]$, $p = .380$, nor controls, $r(24) = .22 [-.18-.56]$, $p = .291$, exhibited self-other covariation in right AI. Parallel partial correlations during threat were also examined. Here, no self-other covariation was observed in altruists' left AI, $r(22) = .29 [-.13-.62]$, $p = .168$, or right AI, $r(22) = .01 [-.40-.41]$, $p = .965$. The same was true for controls in both left AI, $r(24) = -.02 [-.40-.37]$, $p = .932$, and right AI, $r(24) = .30 [-.10-.62]$, $p = .137$. Pain self-other conjunction and covariation results hold when repeated in two control analyses: when excluding directed altruistic donors and when including education and income levels as covariates. However, threat self-other conjunction results are less robust¹.

Given the insula's theorized role as a hub of a neural network critical in processing the salience of internal and external stimuli (Bernhardt & Singer, 2012; Craig, 2009; Lamm & Singer, 2010; Menon & Uddin, 2010), and the observed differences between altruists and controls in self-other mapping in left AI for the neural processing of pain and threat, group differences in functional connectivity between a left AI seed and *a priori* regions of interest were examined. During both empathic pain and empathic threat, altruists exhibited greater functional connectivity than controls between left AI and left mid-insula, $p < .05_{\text{corrected}}$ (Table S6). During empathic threat, at a less stringent voxelwise cluster-forming threshold of $p = .005$, altruists also exhibited greater functional connectivity between left AI and left amygdala. Repeating the two sets of control analyses, in which functional connectivity results were examined in a reduced sample of altruists and with education and income covariates, revealed mixed results². Altruists'

greater functional connectivity between left AI and left mid-insula during empathic pain persisted in the reduced sample but not following the inclusion of demographic covariates. In contrast, altruists' greater functional connectivity between left AI and left mid-insula and left amygdala during empathic threat persisted with demographic covariates but not in the reduced sample.

Altruists' enhanced self-other neural conjunction for a stranger's distress may reflect increased subjective valuation of the welfare of strangers (Vekaria, Brethel-Haurwitz, Cardinale, Stoycos, & Marsh, 2017). Consistent with this, altruists reported higher inclusion of other in the self (a measure that corresponds to feelings of connectedness) with the study partner, $t(48) = 2.16, p = .036, d = 0.61$ [95% CI: 0.04-1.18], and, at a trend level, strangers in general, $t(48) = 2.00, p = .051, d = 0.57$ [0.00-1.13]. Altruists and controls' reported connectedness with objectively closer relationships did not differ, all $p > .05, d < 0.28$ (Figure S3). Inclusion of rated connectedness with the specific anonymous stranger experiencing pain in this study as a covariate in whole-brain self-other conjunction analysis of the threat condition eliminated self-other conjunction in right AI in altruists. By comparison, if rated connectedness with immediate family was instead added as a covariate in this conjunction analysis, bilateral AI self-other conjunction for threat in altruists was maintained. Feelings of connectedness with a stranger in distress may therefore partially mediate altruists' empathic responsiveness, particularly during the experience of threat.

In light of ongoing debates about the value of empathy in promoting concern and altruism (Bloom, 2017), we investigated the relationship between self-reported empathy and outcome variables. Despite altruists and controls exhibiting objectively measurable differences in empathic responding in this paradigm, they did not differ in self-reported total or subscale

general empathy, including empathic concern, all $p > .05$, $d < 0.44$. Altruists and controls also did not differ on any subscale of self-reported empathy for pain, all $p > .05$, $d < 0.48$. In altruists only, both general empathic concern, $r(22) = .60$ [95% CI: .26-.81], $p = .002$, and empathic concern specifically for pain, $r(22) = .58$ [.23-.80], $p = .003$, were associated with ratings of connectedness with strangers. Neither measure of self-reported empathic concern was associated with neural measures of empathy in either group, as indexed by activation in AI ROIs during empathic pain or threat, when controlling for multiple comparisons (Table S1). Thus—unlike measures of empathy at the neural level—neither self-report measure corresponded to real-world altruism, reinforcing the need for caution when interpreting self-report measures of empathy (Eisenberg & Fabes, 1990).

Discussion

The present findings directly link objectively measured empathy and altruism. Engagement in costly, non-reciprocal altruism for a stranger corresponded to spontaneous recruitment of shared neural representations while observing an anonymous stranger experiencing pain or threat. When altruists observed a stranger, activation in AI was more closely associated with activation during first-hand experience, particularly for pain. According to dominant models of empathy, shared representations of others' distress, including pain and fear, are key drivers of altruistic helping (Batson, 2010). Extensive evidence highlights that empathic pain reflects activation in affective components of the neural pain matrix that are also active during personal experiences of somatic pain, including bilateral AI (e.g., Corradi-Dell'Acqua, Hofstetter, & Vuilleumier, 2011; Lamm et al., 2011). That both experienced and empathic pain can be eliminated by placebo analgesia and reinstated using the opioid antagonist naltrexone supports the idea that both experienced and empathic pain rely on common

neurochemical circuits (Rütgen et al., 2015). The anterior portion of the insula in particular is thought to be involved in representing subjective unpleasantness (Craig, Chen, Bandy, & Reiman, 2000) and in integrating somatic and interoceptive information from middle and posterior insula (Craig, 2009). This ideally situates AI for processing both first-hand feelings and body states and similar states observed in others (Lamm & Singer, 2010). Further, AI is hypothesized to be critical for learning and predicting emotional states in social settings (Singer, Critchley, & Preuschoff, 2009) as a hub of a proposed salience network (Bernhardt & Singer, 2012; Menon & Uddin, 2010).

This study benefited from close matching of the first-hand experience of two distressing states—pain and threat—and the identical experiences observed in a stranger, allowing for a specific, direct test of self-other mapping. During experienced and empathic conditions, participants viewed nearly identical live video feeds of the right hand of the participant or confederate during painful pressure stimulation and anticipation of painful stimulation, within the same paradigm. Other studies have relied on secondary cues (e.g., Corradi-Dell’Acqua, Tusche, Vuilleumier, & Singer, 2016) to indicate whether pain was occurring, or photos of painful situations distinct from the participant experience (e.g., Krishnan et al., 2016; Lamm, Meltzoff, & Decety, 2010; Lamm, Nusbaum, Meltzoff, & Decety, 2007). While the current study aimed to match subjective experiences across groups, future investigations of empathic simulation in highly altruistic individuals could explore the effects of experienced and observed pain experiences of varying intensities, which could help to determine if the patterns observed here are specific to pain, which has been the focus of recent debate (Corradi-Dell’Acqua et al., 2016; Krishnan et al., 2016; Zaki et al., 2016). Functional activation findings for empathic pain were robust to control analyses. Less robust findings when examining empathic threat and in

analyses of functional connectivity possibly reflect the reduced statistical power of the control analyses, but highlight the need for further study. It will be particularly important to assess the generalizability of neural simulation across distress-related emotions and how the insula functions within a neural network to encode empathic distress.

Altruistic kidney donors were selected as a sample of extraordinary altruists meeting the most stringent definitions of human altruism. This allowed us to examine how altruism unconfounded by social desirability or norm adherence biases may be related to neural instantiations of empathy, and generalizability to individuals who engage in more normative and less costly prosocial behaviors may be limited (Brethel-Haurwitz et al., 2016). Whether enhanced empathic neural simulation would also be observed in other highly altruistic individuals (e.g., heroic rescuers) or the extent to which empathic neural simulation can be predicted by less extreme prosocial behaviors will be an important area for future research.

The present findings are bolstered by the use of multiple approaches to examining self-other neural mapping, including conjunction, covariation, and connectivity analyses of functional activation. While both empathic pain and threat elicited bilateral self-other overlap in AI in altruists, individual-level covariation was specific to left AI during empathic pain. Further evidence for the specific role AI may play during empathic threat and pain was highlighted by functional connectivity analyses, in which functional connections between this region and other areas of the insula, and perhaps the amygdala, may support altruists' enhanced empathic response to distress in strangers. This suggest that AI functions as part of an affective salience network (Bernhardt & Singer, 2012; Menon & Uddin, 2010) that may support altruists' enhanced responsiveness to others' distress (Marsh et al., 2014). That altruists, relative to controls, exhibit enhanced self-other mapping for strangers' distress—ordinarily observed only in response to

close others—supports the hypothesis that empathic biases against distant or dissimilar others can be overcome and that, ultimately, empathy can support the provision of costly altruism.

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Footnotes

¹The functional activation analyses and covariation analyses were repeated with the exclusion of 6 altruistic kidney donors who had donated to a specific stranger. In this reduced sample, altruists have significant bilateral self-other conjunction in AI for pain, and significant covariation between self and other pain activation in left AI, $r(16) = .49$ [95% CI: .03-.78], $p = .038$. However, in this reduced sample, altruists had significant self-other conjunction only in left AI (not in right AI) for threat. Functional activation analyses and covariation analyses were also repeated with education level and household income as binary covariates of no interest, given trends toward significant group differences in these demographic variables. In this analysis controlling for education and income, altruists still have significant bilateral self-other conjunction in AI for pain, and significant covariation between self and other pain activation in left AI, $r(20) = .59$ [.22-.81], $p = .004$. In controls, there was still only significant self-other conjunction for pain in right AI and no pain self-other covariation in left AI, $r(21) = -.16$ [-.54-.27], $p = .477$. However, with these demographic covariates, altruists no longer have self-other threat conjunction in either AI, while controls have a small but significant conjunction in right AI (2 voxels).

²The functional connectivity analyses were also repeated with the reduced altruist sample and the two demographic covariates noted above. With the reduced sample of altruists, there is still a significant group difference in which altruists have greater functional connectivity during empathic pain between left AI and left mid-insula, relative to controls. However, in this reduced sample, there is no group difference in functional connectivity with left AI during empathic threat, even at a less stringent voxelwise threshold of $p = .005$. With demographic covariates, there are no group differences in functional connectivity with left AI for empathic pain, except

for a significant cluster in left mid-insula at less stringent voxelwise threshold of $p = .005$. For empathic threat, altruists had significantly greater functional connectivity between left AI and left midinsula and between left AI and left amygdala, relative to controls, with education and income as covariates. At a less stringent voxelwise threshold of $p = .005$ there is also significantly greater functional connectivity with right amygdala for altruists during empathic threat, controlling for demographic covariates.

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Author Contributions

AAM developed study concept; AAM, KMBH, EMC, BW, and JWV designed research; KMBH, EMC, KMV, ELR, JWV, and AAM performed research; KMBH analyzed data; KMBH and AAM drafted the manuscript. All authors gave final approval for publication.

Author Information

The authors declare no conflicts of interest. Correspondence and request for materials should be addressed to kbreth@sas.upenn.edu. Data and neuroimaging analysis scripts are available through the Open Science Framework: <https://osf.io/jyqa6/>

Supplementary Material

Extraordinary altruists exhibit enhanced self-other overlap in neural responses to distress

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Supplementary Material includes:

Supplementary Methods

Supplementary References

Figures S1-S3

Tables S1-S6

Supplementary Methods

Neuroimaging Acquisition

MR images were acquired with a 3T Siemens Tim Trio scanner (Siemens Medical Solutions) and a 12-channel phased-array head coil. Functional data were collected using a T2*-weighted echo-planar imaging sequence (46 3.0 mm transversal slices; 64×64 matrix; repetition time, 2,500 ms; echo time, 30 ms; field of view, 192 mm^2 ; $3.0 \times 3.0 \times 3.0 \text{ mm}$ voxels). The first four volumes of each functional run were excluded from analysis to account for magnet stabilization. High-resolution T1-weighted anatomical images were also acquired (3D Magnetization Prepared Rapid Acquisition Gradient Echo; 176 1.0-mm axial slices; field of view, 250 mm^2 ; repetition time, 1,900 ms; echo time, 2.52 ms; 246×256 matrix).

Analysis of Neuroimaging Data

Functional data were preprocessed and analyzed according to the general linear model, using Analysis of Functional NeuroImages (AFNI) (Cox, 1996). The three runs of the task were concatenated, despiked, motion-corrected, and spatially smoothed using a 6 mm full-width half maximum Gaussian filter. TRs with greater than 0.5 mm frame displacement were censored during preprocessing. Functional data were aligned to the anatomical grid, linearly transformed to a Talairach space template (the detailed TT_N27 template created from 27 scans of one individual), and masked with an extents mask to account for motion artifacts and to exclude voxels without valid data at every TR for every run, helping to control for false activations. Twelve regressors were created to model the anticipation and stimulation portions of each run, resulting in the following four regressors for each run: threat (cue indicates potential pain), no threat (safety cue), pain (stimulation), no pain (no stimulation). For each participant, contrasts were also calculated for pain (pain > no pain) and threat (threat > no threat) for each run. Rest

was modeled implicitly; baseline was modeled by a first-order function, and motion artifacts were modeled using the six estimated rigid-body motion parameters. Boxcar regressors representing the occurrence of each block type were convolved with a canonical hemodynamic response function, scaled to an amplitude of 1.

Group-level analyses were limited to a brain mask defined by voxels with functional activation shared by at least 50% of participants. Cluster size thresholds were calculated for a corrected clusterwise p threshold of .05, at uncorrected $p = .001$, for this group mask for each comparison using 10,000 Monte Carlo simulations conducted in conjunction with 3dttest++ (via the -Clustsim option) in AFNI (October 2016 AFNI version 16.3.03, using a nonparametric randomization approach to generate cluster size thresholds from the residuals of each t test to decrease risk of false positives (Cox, Chen, Glen, Reynolds, & Taylor, 2017), created in response to Eklund et al. (Eklund, Nichols, & Knutsson, 2016)). MNI coordinates of peak z statistics within significant clusters are reported. Region labels are reported according to the CA N27 ML atlas (Eickhoff et al., 2005) in AFNI. As noted above, final administered pressure stimulation level was included as a centered covariate in analyses of experienced pain and threat given the significant group difference, to examine group differences due to subjective experience rather than objective pressure stimulation level. The covariate was mean centered across all participants, so as to not artificially remove group differences in this variable.

In order to examine group differences in similarity of neural activation for experienced and empathic pain and threat, conservative conjunction-null analyses (Nichols, Brett, Andersson, Wager, & Poline, 2005) were conducted in which activation maps meeting statistical thresholds in each condition were compared, such that regions of conjunction indicated significant activation in both conditions independently, an approach that has been utilized in examining

similarity between *self* and *other* responses in empathic pain paradigms (e.g., Beckes et al., 2012). Specifically, a mask was created from a thresholded *self pain* > *self no pain* contrast with objective pain level as a covariate of no interest, and this mask was then applied to an *other pain* > *other no pain* contrast, as paired samples *t* tests within each group. Parallel contrasts were conducted for the threat conditions. Analyses were also conducted in which self-reported connectedness with the study partner and immediate family were separately included as covariates of no interest, centered across all participants, in contrasts at the *other* level. Following up on conjunction patterns observed at the group level, covariation analyses were conducted, in which the association between *self* and *other* activation levels in regions of interest were tested via partial correlation controlling for objective pain level, to determine if apparent self-other mapping at the group level in conjunction analyses were supported by individual-level correspondence in neural activation. Regions of interest (ROIs) in bilateral anterior insula (AI) were defined by 5 mm radius spheres centered at coordinates (left AI: $x = -40$, $y = 22$, $z = 0$; right AI: $x = 39$, $y = 23$, $z = -4$) derived from a functional meta-analysis of empathic pain studies (Lamm et al., 2011).

Generalized psychophysiological interaction (gPPI) functional connectivity analyses were conducted in SPM8 (Wellcome Trust Department of Cognitive Neurology) using the generalized PPI toolbox (McLaren, Ries, Xu, & Johnson, 2012). Functional images were slice-time corrected, realigned, coregistered to anatomical scans, normalized to $2.0 \times 2.0 \times 2.0$ mm voxel size in MNI space using parameters calculated during segmentation of anatomical scans, and smoothed using a 6 mm Gaussian kernel. Task-specific functional connectivity with left AI was estimated using gPPI analysis (McLaren et al., 2012). The AI seed region was the same ROI sphere used above. The *other* and *self* runs were processed separately, such that functional

connectivity in one run was not controlling for the other. A design matrix was created for each participant that included the stimulus time series for each of the four conditions (threat, no threat, pain, no pain) and six motion parameters, which were convolved with a hemodynamic response function to create psychological regressors. Within each condition, examining connectivity during threat experience was holding the other three conditions (no threat, pain, no pain) constant, and was thus specific to threat. Analogous contrasts were conducted for pain experience. Functional connectivity specific to the threat and pain conditions within the *other* run are the focus of the analyses reported here. Functional connectivity results were limited to a set of bilateral *a priori* ROIs for the two conditions (threat: amygdala, hypothalamus, periaqueductal gray, ventromedial prefrontal cortex, insula; pain: anterior cingulate cortex, periaqueductal gray, inferior parietal cortex, insula). All regions were defined using the AAL atlas (Tzourio-Mazoyer et al., 2002), except for the periaqueductal gray and hypothalamus. The periaqueductal gray was defined as two 5 mm radius spheres centered at the average coordinates for left and right activation ($x = \pm 4$, $y = -29$, $z = -12$) from a recent meta-analysis (Linnman, Moulton, Barmettler, Becerra, & Borsook, 2012). The hypothalamus ROI was defined using the Talairach Daemon label (Lancaster et al., 2000) in the WFU PickAtlas Tool (Maldjian, Laurienti, Kraft, & Burdette, 2003). The PickAtlas Tool was used to create all ROI masks. Nonparametric clusterwise inference was computed via the SnPM13 toolbox (<http://warwick.ac.uk/snpm>) in SPM8, at an FWE corrected threshold of $p = .05$ at an uncorrected $p = .001$, using 10,000 permutations. Reported results are from the output of these SnPM simulations. Independent samples t tests (altruists > controls) were conducted separately on the threat and pain contrasts to directly compare group differences in functional connectivity of the left AI during empathic threat and pain. MNI coordinates of peak t statistics within significant clusters are reported.

Two sets of follow-up control analyses were conducted in order to examine the robustness of our neural results: (1) repetition of analyses excluding 6 altruistic kidney donors who directed their donation to a specific stranger, (2) repetition of analyses in the full sample with the addition of household income and education as binary covariates of no interest, given trends toward group differences in these demographic variables (see Table 1). In the second set of analyses, covariates were mean centered across all participants and included at both the self and other levels of conjunction analyses. In the second set of control analyses, one control was excluded since income was not reported.

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Figure S1. Self pain and threat results and pressure stimulation levels. (a) Altruists and controls exhibited similar neural activation for *self pain* > *self no pain* and *self threat* > *self no threat*. $z = 0$. Whole-brain clusterwise corrected threshold $p < .05$ at uncorrected voxelwise threshold $p = .001$ (b) Final subjective “slightly intense” pain level selected by each group. Altruists selected a significantly higher pressure level than controls, $t(50) = 3.97$, $p < .001$, $d = 1.10$ [95% CI: 0.51-1.68]. Contours represent frequency distributions. Boxplots are displayed with dots representing means and outliers.

Figure S2. Parameter estimates for mean activation in left and right anterior insula (AI) ROIs.

Contours represent frequency distributions. Boxplots are displayed with dots representing means and outliers. Parameter estimates for pain and threat are relative to condition-specific baselines (pain > no pain, threat > no threat). There were no group differences in activation for any AI ROI, all $p > .05$, all $d < 0.48$. Across all participants, *self* pain resulted in higher activation than *other* pain in left AI, $t(51) = 2.39$, $p = .020$, $d = 0.41$, and right AI, $t(51) = 2.79$, $p = .007$, $d = 0.47$, and *self* threat resulted in higher activation than *other* threat in left AI, $t(51) = 3.11$, $p = .003$, $d = 0.59$, and right AI, $t(51) = 4.92$, $p < .001$, $d = 0.87$. However, pain activation was higher than threat activation for the *self* in left AI, $t(51) = 3.39$, $p = .001$, $d = 0.49$, and right AI, $t(51) = 2.20$, $p = .033$, $d = 0.37$, and pain activation was also higher than threat activation for *other* in left AI, $t(51) = 2.41$, $p = .020$, $d = 0.49$, and right AI, $t(51) = 3.71$, $p = .001$, $d = 0.69$.

Figure S3. Perceptions of connectedness as rated on the Inclusion of Other in the Self Scale.

Contours represent frequency distributions. Boxplots are displayed with dots representing means and outliers. Altruists rated greater connectedness for the study partner and strangers in general, both $p \leq .05$, both $d > 0.56$.

Table S1

Correlations between Connectedness, Self-Reported Empathy, and Activation in Bilateral Anterior Insula ROIs in Each Group

		IoS	IRI	EPS	L AI	R AI	L AI	R AI	L AI	R AI	L AI	R AI
		Study	Empathic	Empathic	Pain	Pain	Fear	Fear	Pain	Pain	Fear	Fear
		Partner	Concern	Concern	Self	Self	Self	Self	Other	Other	Other	Other
Altruists	IoS Stranger ^a	.70*** ^{†b}	.60*** [†]	.58*** [†]	-.18	-.20	-.23	.04	-.38	-.44*	.29	.28
	IoS Study Partner ^b		.23	.52*	.05	-.33	-.38	-.13	-.32	-.33	-.01	.32
	IRI Empathic Concern			.52**	.01	-.12	-.12	.01	-.16	-.20	.41*	.47*
	EPS Empathic Concern				-.25	-.35	-.37	-.19	-.23	-.36	.13	.31
	L AI Pain Self					.49*	.39	.24	.57*** [†]	.52**	-.23	.06
	R AI Pain Self						.27	.22	.38	.29	-.33	-.50*
	L AI Fear Self							.79*** [†]	.26	.46*	.28	-.12
	R AI Fear Self								.13	.40*	.21	-.02
	L AI Pain Other									.74*** [†]	-.19	.10
	R AI Pain Other										-.12	.14
	L AI Fear Other											.56*** [†]
Controls	IoS Stranger ^c	.78*** [†]	.18	.40*	.32	.22	.38	.38	-.02	.08	.30	.30
	IoS Study Partner		.34	.44*	.25	.26	.27	.31	-.13	.05	.37	.43*
	IRI Empathic Concern			.61*** [†]	-.15	.10	-.19	.02	.26	.50**	.20	.12
	EPS Empathic Concern				-.03	.07	-.10	-.08	.33	.36	.09	.13
	L AI Pain Self					.42*	.56*** [†]	.22	-.23	-.10	.04	.20
	R AI Pain Self						.11	.38*	.15	.21	.19	.31
	L AI Fear Self							.55*** [†]	-.29	-.11	-.02	.33
	R AI Fear Self								.07	.12	.28	.39*
	L AI Pain Other									.80*** [†]	.05	.01
	R AI Pain Other										.14	.16
	L AI Fear Other											.58*** [†]

Note. Altruist N = 25, Control N = 27, unless otherwise noted. ROI = region of interest. IoS = Inclusion of Other in Self. IRI = Interpersonal Reactivity Index. EPS = Empathy for Pain Scale. L = left. R = right. AI = anterior insula.

^aN = 24. ^bN = 23. ^cN = 26.

* $p < .05$. ** $p < .01$. [†] $Q < .05$ per Benjamini-Hochberg procedure for 66 tests within each group.

Table S2

Regions of Significant Activation for Other Pain > Other No Pain, Masked by Self Pain > Self No Pain, in Each Group

Altruists					
k ^a	Peak x	Peak y	Peak z	Peak z(24)	Peak Region
319	56	21	3	6.09	Right Inferior Frontal Gyrus
290	-62	-30	45	6.05	Left Inferior Parietal Lobule
286	66	-38	24	6.42	Right Supramarginal Gyrus
234	-49	-74	-4	6.76	Left Inferior Occipital Gyrus
150	50	-59	-5	6.20	Right Inferior Temporal Gyrus
46	-46	13	17	4.59	Left Inferior Frontal Gyrus
43	47	9	56	5.78	Right Middle Frontal Gyrus
42	-40	17	0	4.65	Left Insula
33	50	48	5	4.44	Right Middle Frontal Gyrus
28	-24	-65	-48	4.18	Left Cerebellum
27	31	-46	42	4.97	Right Inferior Parietal Lobule
21	-30	-16	-1	4.70	Left Putamen
17	8	9	52	4.94	Right Supplementary Motor Area
15	-11	-8	9	4.11	Left Thalamus
11	12	-8	12	3.82	Right Thalamus
10	-8	-24	37	4.03	Left Middle Cingulate Cortex
9	-24	1	-13	4.52	Left Putamen
Controls					
k ^b	Peak x	Peak y	Peak z	Peak z(26)	Peak Region
961	53	-68	-1	7.03	Right Middle Temporal Gyrus
715	-56	-24	41	6.33	Left Inferior Parietal Lobule
710	-46	-71	-1	6.77	Left Middle Occipital Gyrus
615	56	-21	37	6.37	Right Postcentral Gyrus
238	53	11	35	5.95	Right Precentral Gyrus
134	-4	-80	-41	4.77	Left Cerebellum
29	-53	10	28	5.44	Left Inferior Frontal Gyrus
26	43	2	-3	4.51	Right Insula
19	24	-54	63	4.45	Right Superior Parietal Lobule
15	12	-74	-44	5.63	Right Cerebellum

^aCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .001 = 8$ voxels

^bCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .001 = 10$ voxels

Table S3

Regions of Significant Activation for Other Threat > Other No Threat, Masked by Self Threat > Self No Threat, in Each Group

Altruists					
k ^a	Peak x	Peak y	Peak z	Peak z(24)	Peak Region
28	-30	23	-11	4.47	Left Inferior Frontal Gyrus
20	2	24	55	4.84	Left Supplementary Motor Area
19	-56	-47	25	4.72	Left Supramarginal Gyrus
18	34	-96	4	4.02	Right Middle Occipital Gyrus
16	31	26	-4	3.96	Right Insula
15	-20	-96	-3	3.73	Left Middle Occipital Gyrus
5	2	44	36	4.15	Left Superior Medial Gyrus
Controls					
k ^b	Peak x	Peak y	Peak z	Peak z(26)	Peak Region
16	50	24	3	4.31	Right Inferior Frontal Gyrus
14	-33	-96	1	3.92	Left Middle Occipital Gyrus
12	31	32	-5	3.64	Right Inferior Frontal Gyrus
10	-59	-21	30	3.92	Left Postcentral Gyrus
7	8	9	11	3.99	Right Caudate Nucleus
7	59	-47	25	3.90	Right Supramarginal Gyrus
4	-27	-87	-7	3.56	Left Inferior Occipital Gyrus
4	-33	-40	42	3.57	Left Inferior Parietal Lobule
4	-43	-45	56	4.05	Left Inferior Parietal Lobule

^aCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .001 = 5$ voxels

^bCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .001 = 4$ voxels

Table S4

Regions of Significant Activation for Self Pain > Self No Pain in Each Group

Altruists					
k ^a	Peak x	Peak y	Peak z	Peak z(23)	Peak Region
1557	-40	-2	-2	5.97	Left Insula
940	37	6	4	5.77	Right Insula
469	62	-34	34	5.88	Right Supramarginal Gyrus
351	28	-51	-26	5.34	Right Cerebellum
334	-1	8	42	5.64	Left Middle Cingulate Cortex
285	-30	-63	-25	5.22	Left Cerebellum
179	-4	25	-14	-4.33	Left Middle Orbital Gyrus
59	8	-32	65	-4.12	Right Paracentral Lobule
45	8	-13	-5	5.00	Right Thalamus
40	-14	-27	37	4.58	Left Middle Cingulate Cortex
36	-20	-71	-51	4.85	Left Cerebellum
32	34	-40	42	4.13	Right Supramarginal Gyrus
Controls					
k ^b	Peak x	Peak y	Peak z	Peak z(25)	Peak Region
1644	-53	-24	41	6.34	Left Inferior Parietal Lobule
1303	-59	-64	9	5.44	Left Middle Temporal Gyrus
1157	28	-88	-10	5.34	Right Inferior Occipital Gyrus
946	56	-26	20	6.30	Right Rolandic Operculum
736	53	15	10	6.08	Right Inferior Frontal Gyrus
376	5	8	35	5.16	Right Middle Cingulate Cortex
264	-56	20	-11	5.74	Left Temporal Pole
37	8	-32	69	-4.57	Right Paracentral Lobule
35	-33	43	15	4.11	Left Middle Frontal Gyrus

^aCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .001 = 27$ voxels^bCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .001 = 30$ voxels

Table S5

Regions of Significant Activation for Self Threat > Self No Threat in Each Group

Altruists					
k ^a	Peak x	Peak y	Peak z	Peak z(23)	Peak Region
836	18	12	11	5.25	Right Caudate Nucleus
359	-1	33	51	5.45	Left Superior Medial Gyrus
278	43	2	49	4.54	Right Precentral Gyrus
202	-30	-90	-3	4.71	Left Middle Occipital Gyrus
188	-56	-47	32	4.70	Left Supramarginal Gyrus
155	66	-44	28	4.73	Right Supramarginal Gyrus
126	28	-93	-3	5.41	Right Inferior Occipital Gyrus
101	-1	-54	-32	4.23	Cerebellar Vermis
74	-27	29	-4	4.81	Left Insula
47	-53	-58	8	4.55	Left Middle Temporal Gyrus
46	59	-46	1	4.42	Right Middle Temporal Gyrus
45	43	-64	-28	4.28	Right Cerebellum
Controls					
k ^b	Peak x	Peak y	Peak z	Peak z(25)	Peak Region
323	47	23	-11	5.44	Right Inferior Frontal Gyrus
290	-30	26	-8	5.07	Left Insula
260	-59	-21	37	4.97	Left Supramarginal Gyrus
220	2	18	55	4.63	Right Supplementary Motor Area
143	12	9	11	5.44	Right Caudate Nucleus
142	-24	-94	-6	4.62	Left Inferior Occipital Gyrus
131	53	-25	24	5.56	Right Rolandic Operculum
99	-8	8	0	5.52	Left Caudate Nucleus
59	43	5	46	4.67	Right Precentral Gyrus
52	-46	5	46	4.31	Left Precentral Gyrus
32	53	-27	-7	4.62	Right Middle Temporal Gyrus

^aCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .001 = 43$ voxels^bCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .001 = 29$ voxels

Table S6

Significant Functional Connectivity with Left AI for Altruists > Controls for Other Pain and Other Threat

Other Pain					
k ^a	Peak x	Peak y	Peak z	Peak <i>t</i> (50)	ROI
18 ^b	-38	14	0	3.88	Left Insula
11 ^b	-44	4	8	3.87	Left Insula
Other Threat					
k ^a	Peak x	Peak y	Peak z	Peak <i>t</i> (50)	ROI
14 ^b	-32	20	-12	4.08	Left Insula
9 ^c	-24	-2	-16	2.98	Left Amygdala

^a2mm³ voxels

^bCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .001 = 8$ voxels

^cCluster extent for clusterwise corrected threshold $p < .05$ at uncorrected $p = .005 = 3$ voxels