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Alleyne P. Ross April 9, 2012

Reward Dependence: Personality and Neurological Correlates of Social Behavior

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Abstract

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The neural mechanisms of cooperative behavior have been studied from many angles. This study aimed to correlate personality measures with behavior, brain function, and brain structure during a simulation of genuine social interaction to increase our understanding of the mechanisms and individual variation of prosocial behavior. 185 individuals between the ages of 18 and 22 (mean=20.2) were scanned using fMRI while playing an economic decision making game with perceived human partners. Personality data were collected after the scan using the Temperament and Character Inventory. Behavioral results showed sexually dimorphic effects of personality on behavior in social economica decision making game. Using fMRI, both reward dependence and cooperativeness were shown to be correlated with amygdala activation in response to unreciprocated cooperation in females, while activation in the medial prefrontal cortex after a negative outcome was correlated with cooperativeness in males. Grey matter volume was correlated with cooperativeness in the dlPFC and right amygdala in males. Cooperativeness was also correlated with grey matter volume in the left insula extending into opercular cortex, in both males and females. Reward dependence was correlated with grey matter volume in the right amygdala in females. These results implicate the amygdala as a structure not only responsible for the affective response to negative social behavior, but also for increasing the saliency of negative social interactions, resulting in prosocial behavior to avoid negative situations. In addition, areas implicated in theory of mind and empathy, such as the mPFC and insula, were correlated with cooperativeness, but not reward dependence in males, showing differing neural mechanisms between the similar measurements. Finally, the lack of overlap in many of the conditions between males and females demonstrate sexual dimorphism in the neural mechanisms of cooperative behavior and possible different evolutionary constraints at work in males and females.

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"No man is an island, entire of itself; each is a piece of the continent, a part of the main."
--John Donne (1624)

Humans are highly social species, maintaining wide, complex networks comprised of both kin and nonrelated individuals. Cooperative behavior may have evolved to allow for the hunting of large game, alloparental care, and other necessities of human survival. No man is an island, and social interaction is inevitable. The ability to sustain interpersonal relationships allows humans to take advantage of these interactions and engage in mutually beneficial behavior.

Evolutionary origins of cooperative behavior

Cooperative behavior is seen in many forms in both human and animal societies. From vervet monkey alarm calls to worker ants, organisms seemingly sacrifice their own reproductive success for another individual. To explain this phenomenon, two well-known mechanisms have been proposed: kin selection and reciprocal altruism. The first, suggested by Darwin (1859) and expanded on by Hamilton (1964), among others, proposes that genetic traits in an individual that increase the fitness of its close relatives will be selected for, even though they may be disadvantageous to the individual. The second theory was initially proposed by Trivers (1971) and addresses the observation that nonrelated organisms will perform acts to help another individual at apparent cost to themselves.

In *On The Origin of Species* Darwin (1859) realized that natural selection could be applied to the family, not just an individual. Organisms can be assured that their genes will be passed on to the next generation if they adopt the strategy of doing what they can to ensure the reproductive success of their close relatives. Kin selection explains apparent acts of altruism, observed in many organisms. Hamilton (1964) proposed a mathematical solution to predict when kin selection would occur using r (relatedness coefficient), B (reproductive benefit gained by the

recipient), and C (reproductive cost to the actor). The equation rB>C predicts the likelihood of altruism occurring in both animal and robot populations (Waibel, Floreano, & Keller, 2011).

Kin selection underlies many behaviors seen in eusocial insect societies, such as ants. Among many species of ants, the queen is the sole reproducer. The eggs the queen lays are cared for and reared by their sterile older sisters. The female offspring of the queen have a surprisingly high relatedness coefficient, due to haplodiploidy (Queller & Strassmann, 1998). Haplodiploidy refers to the system by which the sex of offspring is determined in several insects and results in a higher proportion of females to males (Levitt, 1975) and a higher relatedness between sisters than offspring (Krebs & Davies, 1997).

E.O. Wilson has provided an amendment to this theory by stating that, while kin selection is important, evidence from social insect colonies points towards group selection, since the colony is often founded by unrelated individuals that work together. Haplodiploidy, Wilson claims, is only found in successful colonies and that the high relatedness coefficient cannot be what brings the insects together. He proposes a different equation for determining when altruism will occur: (rbk+be)>c where rbk is the benefit from collateral kin selection and be is the benefit from colony kin selection (Wilson, 2005).

While kin selection provides a compelling explanation for much of the cooperative behavior in the animal kingdom, there are cases where actors have zero or little genetic relation to the recipient of altruism. When a vervet monkey makes a warning call to alert others, not specifically relatives, that a predator is near, they are endangering their own reproductive success by exposing themselves to the predator. This behavior seems contradictory to what Darwin and Hamilton would have expected, based on the theories of natural selection and kin selection.

A simple explanation for this behavior, and others like it, was proposed by Trivers (Trivers, 1971). Designated reciprocal altruism, Trivers' theory proposes that even among

nonrelated organisms, altruism at the cost of the actor can evolve if the cost in the short run is outweighed by the long-term benefits. Trivers postulates that several criteria will determine if reciprocal altruism occurs: first, that individuals will have long lifetime to increase the likelihood that any two individuals will encounter many opportunities for altruism; second, that there is a low dispersal rate of individuals to ensure that there will be repeated interactions between neighbors; third, that there is a degree of mutual dependence so individuals will be forced to rely on others for protection, food, etc.; fourth, that parental care occurs, although this is accounted for by kin selection, some situations are better explained by altruism, especially when there is a long period of parental care; fifth, where there is not a clear dominance hierarchy, so the more dominant animal does not automatically receive favors such as food sharing and these behaviors are performed in a more reciprocal manner; and sixth, that the species engages in combat during which dominance becomes a less important factor (Trivers, 1971). In order for reciprocal altruism to evolve and stabilize, individuals must be able to discriminate against non-reciprocators (Axelrod & Hamilton, 1981).

A well-documented example of reciprocal altruism in mammals is the vampire bat. Vampire bats (*Desmodus rotundus*) are known to regurgitate blood to feed offspring as well as nonrelated individuals that had been unsuccessful in hunting and are nearing minimum viable weight (Wilkinson, 1984). Wilkinson (1984) also showed that animals that received blood later donated significantly more than chance would predict to those that had shared with them, regardless of whether they had more blood to spare. This example of reciprocal altruism fulfills several of Trivers' postulates, including relatively long life span, low dispersal rate, mutual dependence, parental care, and lack of dominance hierarchy.

A genetic basis for altruistic behavior must exist in order for it to be an evolved trait. Studies by Rushton et al. (1986) have provided evidence that altruism is a genetically influenced.

Twin studies comparing altruistic and aggressive behavior found that altruistic tendencies were 60% heritable, a substantial portion. Possible determining factors include grey matter structure, white matter connectivity, and neocortex volume.

The social brain hypothesis was suggested by Dunbar as an explanation for the comparatively large brains of primates. He proposed that complicated social behavior, such as coalition-forming and reciprocal altruism, requires a larger brain, specifically neocortex, to mediate relationships between multiple partners (Dunbar, 1998). Evidence for this hypothesis has been found by correlating relative neocortex size (as a ratio of the whole brain) with group size (Dunbar, 1998). Ungulates present a difficulty to the social brain hypothesis, as they often live in large groups and have a small neocortex ratio (Shultz & Dunbar, 2006). However, Shultz and Dunbar (2006) have shown that among these groups, neocortex ratio can predict social complexity. If neurological differences affect social behavior and are variable by species, then variation within species must have been present and beneficial in order to have spread in the population. Thus, it is probable that individual difference in brain structure, and most likely function, will lead to deviations in social behavior.

Quantifying cooperative behavior

Many methods of quantitatively measuring altruism and cooperative behavior have been proposed. These methods include the public goods game, which measures resource pooling; ultimatum game, which measures fairness; dictator game, which measures altruism; and prisoner's dilemma game, which measures cooperativity (Axelrod & Hamilton, 1981).

The prisoner's dilemma game, named by Tucker (Rasmusen, 2001), has been used as a model of cooperation, altruism, and trust in humans. The prisoner's dilemma game is based on a hypothetical situation in which the player and partner have been caught by the police after committing a crime. They are each questioned separately and are offered the bargain that their

sentence will be lessoned if the player provides evidence against their partner. However, the partner is also being offered the same deal. If they choose to cooperate with each other, they will both receive a moderate prison sentence. If they both defect and give evidence against each other, they will both serve a long sentence. If the player defects and the partner cooperates, the player will walk free while the partner serves jail time. Likewise, if the partner defects and the player cooperates the partner will walk free and the player will serve jail time. This dilemma, common in interrogation, has been turned into an economic decision making game.

In the game, the player is given the choice to cooperate (C) or defect (D). Instead of years in prison, the payoff is given in monetary amounts. For our purposes, a situation in which both the player and partner choose to cooperate (CC outcome) results in a $2 payoff for each. If the player chooses to cooperate and the partner defects, (CD outcome) the player earns $0 and the partner earns $3. The opposite occurs if the player defects and the partner cooperates (DC outcome). If both players choose to defect (DD outcome), both receive $1 (figure 1). Various studies have used different paradigms including multiplayer, higher stakes, non-iterated, infinite rounds, and allowing communication (Axelrod, 1984).

Figure 1. Payoff matrix of prisoner's dilemma game used in this study.

The validity of the prisoner's dilemma game as model for social cooperation has been disputed since first used by Axelrod to explain the evolution of cooperation in 1981 (Robert, 1988). Due to the positive result for both players after a CC outcome and simultaneous choice, the PD game has been called a model of mutualism, rather than altruism. However, both of these complaints can be solved when one considers the truly logical approach to the game. During a completely rational, one shot game, both players should choose to defect, since that protects them from being exploited on by their partner and receiving $0. However, during an iterated game, there are multiple opportunities to build trust and cooperation, where both players sacrifice the most profitable option for cooperation. Based on similarities to genuine social interaction and the necessity of maintaining trust, the prisoner's dilemma game is a viable model for reciprocal altruism in humans.

Quantifying personality traits

The temperament and character inventory (TCI) was created with the intention of providing a categorical method for defining both temperaments, which are thought to be unchanging and heritable, and characters, which are learned and developed through life. Both reward dependence and cooperativeness are measured by this inventory, but each offers a different perspective on social behavior. The inventory is self-reported, with subjects answering 240 true/false questions.

Reward dependence (RD) is a measure of temperament. It describes the importance of social approval to an individual. People low in reward dependence are more likely to be socially withdrawn or uncooperative. Reward dependence may be heritable or involve unconscious biases in learning (C. Robert Cloninger, Svrakic, & Przybeck, 1993).

Cooperativeness is a measure of character, or a learned behavior. This character trait describes to what lengths a person is willing to help others, is empathetic, compassionate, and

helpful. People with low cooperativeness are usually socially intolerant, revengeful, and unhelpful (C. Robert Cloninger et al., 1993).

Neuroimaging

Functional magnetic resonance imaging (fMRI) has been used since 1991 to measure hemodynamic responses in the brain (Kwong et al., 1992). Blood-oxygen-level-dependant (BOLD) contrast is used to visualize blood flow throughout the brain. An increase in neural activity causes a change in the ratio of deoxygenated hemoglobin to oxygenated hemoglobin, which is detected by the fMRI scanner. This process produces a T2* weighted image, which has poor spatial resolution. The T1-weighted image is collected by measuring the rate at which protons align and spin after being exposed to a magnetic pulse at a specific radio frequency (Damadian, Goldsmith, & Minkoff, 1977). This MRI image shows the detailed, anatomical structure of the brain, but does not show any functional activation. The two images are then superimposed and co-registered to better identify the locations of changes in BOLD signal from the T2* images using the anatomically detailed T1 image (further discussion in Methods section). Although BOLD signal should not be confused with the actual firing of neurons, several studies have shown similarities in function between areas implicated by fMRI and lesion studies (Gaillard et al., 2006; Menon & Desmond, 2001; Saygin, 2007).

Voxel-based morphometry (VBM) is a method to measure grey matter volume using the T1 weighted MRI image. A voxel is a volumetric pixel that represents a value in 3D space. The images are first registered to a standard brain and smoothed to allow for comparison between subjects (Ashburner & Friston, 2000). Grey matter density is then compared across subjects (Ashburner & Friston, 2000). Neuroanatomical features are highly heritable, as demonstrated in twin studies (Wright, Sham, Murray, Weinberger, & Bullmore, 2002).

Cooperative behavior could be motivated by the rewarding feeling of doing good for others or the negative feeling from non-cooperative behavior. How either of these motivations are processed in the brain is of interest to this study and can be illuminated when one considers the neural response to other rewarding or negative stimuli.

Using fMRI and VBM, several brain structures have been implicated in reward processing. These structures include the medial orbitofrontal cortex (mOFC), amygdala, and nucleus accumbens (NAc), which are activated by rewards such as sexual activity and food (McClure, York, & Montague, 2004). Social rewards, such as beautiful faces (Aharon et al., 2001) and cooperation (Rilling et al., 2002), have been shown to activate these same areas. The argument for a reward system in the brain was put forth by Olds and Milner in 1954, who suggested that dopaminergic projections from the ventral tegmental area (VTA) project to the NAc and prefrontal cortex, based on their experiments using electrical self-stimulation (Spanagel & Weiss, 1999). Since then, the process of coding rewards has been shown to be more complicated than previously thought and includes, among other areas, the hypothalamus, as well as GABAergic and glutamate neurons, and the opioid system (Satoshi, 2010).

The amygdala and insula relate to various aspects of negative social interaction. The amygdala is activated in response to fear and mistrust in social situations (Amaral, 2003). Engell et al. showed bilateral amygdala activation in response to untrustworthy faces during an fMRI study (Engell, Haxby, & Todorov, 2007). In addition, a region-of-interest analysis by Rilling et al. (Rilling, Goldsmith, et al., 2008) showed increased left amygdala activation in response to unreciprocated cooperation in the PD game. Together these experiments demonstrate the importance of the amygdala in mediating social situations. The insula is known to monitor the viscera and can be affected by situations ranging from gastrointestinal pain to social rejection (Derbyshire, 2003; Eisenberger, Lieberman, & Williams, 2003). Other studies have shown an

increase in insula activation during the rejection of unfair offers in the ultimatum game (Sanfey, Rilling, Aronson, Nystrom, & Cohen, 2003). The insula and amygdala work together to produce a negative affective response to unreciprocated cooperation.

Previous research

No studies have looked at how reward dependence affects behavior or functional activation in the prisoner's dilemma game. Tost et al. (2010) found that amygdala grey matter volume was negatively correlated with reward dependence in a co-ed sample, but not when divided by sex. Another study, by Lebreton et al. (2009) found reward dependence to be positively correlated with grey matter volume in the ventral striatum and mOFC in a male sample. These results must be further investigated and replicated in males and females separately, to compare possible differences in mechanisms establishing reward dependence.

Autism Spectrum Disorders (ASD) encompass a variety of syndromes primarily affecting social development (Association & DSM-IV, 2000). Although it has been shown to have genetic bases (Szatmari, 1999), it is puzzling that a trait so detrimental to reproductive success could have evolved and been maintained in the human population. People with ASD demonstrate significantly lower levels of reward dependence than the general population (Anckarsäter et al., 2006). These findings mandate further study into reward dependence and its neural mechanisms to better understand the evolution and deficits associated with ASD.

Aims and hypotheses

The aims and hypotheses of this paper are as follows:

Aim 1: Determine if cooperativeness is correlated with reward dependence to replicate the findings of Cloninger et al. (1993)

Hypothesis 1a: Cooperativeness, as defined by the TCI, will be positively correlated with reward dependence.

Hypothesis 1b: Sex differences in reward dependence will be apparent, with females displaying more reward dependence and cooperativeness.

Aim 2: Determine if self-reported emotional state is correlated with personality measures.

Hypothesis 2a: Subjects with high reward dependence will, as player 1, self-report more disappointment and anger with unreciprocated cooperation and more happiness when cooperation is reciprocated.

Hypothesis 2b: Subjects with high cooperativeness will, as player 1, self-report more happiness after reciprocated cooperation.

Aim 3: Determine if cooperativeness and reward dependence can predict behavior in the Prisoner's Dilemma game.

Hypothesis 3a: Reward dependence will be positively correlated with probability of reciprocating cooperation as player 2. As player 1, reward dependence will also be positively correlated to probability of C after CC and DC.

Hypothesis 3b: Cooperativeness will be positively correlated with probability of C after CC, DC, CD, and DD.

Aim 4: Determine if variance in reward dependence affects brain function

Hypothesis 4a: Subjects with high reward dependence will show increased ventral striatum and mOFC activation in response to reciprocated cooperation (CC).

Hypothesis 4b: Subjects with high reward dependence will show increased anterior insula and left amygdala activation in response to CD outcomes as player 1.

Aim 5: Determine if variance in reward dependence affects brain structure.

Hypothesis 5a: Whole brain VBM will find grey matter volume in the amygdala to be negatively correlated with reward dependence, while grey matter in the mOFC and striatum will be positively correlated with reward dependence

Methods

Subjects

101 men and 84 women between the ages of 18 and 22 (mean = 20.2). were recruited from Emory University. 59 subjects were excluded from the functional neuroimaging analysis due to excessive motion (45), missing data (11), or not having an outcome of interest (3), but all 185 subjects were included in the behavioral, personality, and structural analysis. Subjects were asked to fill out a medical survey and were excluded if they reported a history of head trauma, seizures, any psychiatric or neurological disorder, substance abuse, hypertension, cardiovascular disease, or diabetes. Subjects who reported having used medications with known psychoactive effects within the last 12 months were also excluded. Studies were conducted between the hours of 9 AM and 6 PM across the entire year. All subjects gave informed consent and the study was approved by the Emory University Institutional Review Board.

Behavioral procedures

Subjects completed a computer tutorial on the Prisoner's Dilemma game and a short quiz to evaluate their understanding of the game. If any question was answered incorrectly, the correct answer was explained to the subject and, if necessary, the subject would go through the tutorial again. They then played two rounds with the button box they would use in the scanner to familiarize themselves with its operation.

As part of the larger study, one-third of subjects were administered intranasal oxytocin, one-third vasopressin, and one-third a placebo. Data was collected and analyzed from all subjects, regardless of drug group. The study was double blind, so I was unable to control for drug group. Temperature, heart rate, and blood pressure were monitored both pre-drug administration and 20 minutes after.

Subjects were briefly introduced to two sex-matched confederates who they were told they would be playing the game with. Confederates were not matched on race, but previous analyses showed no difference in outcomes as a function of race (Rilling, DeMarco, Hackett, Thompson, Ditzen, Patel, & Pagnoni, 2012a). A total of 42 different confederates were used (14 male, 28 female).

Task procedure

Once subjects were situated in the scanner, a visual display informed them with which partner they were about to play. Subjects played four sessions of 30 rounds of the prisoner's dilemma game. Subjects were told they were playing the human confederates they had just met for two of these rounds and a computer partner for the other two. In actuality, the subjects were always playing a computer algorithm. Subjects were compensated with two-thirds of their total earnings across all four sessions.

For both partner types (human and computer) subjects played as either player 1 or player 2 in the first session and in the second session the roles were reversed. They then would play the second partner type. The order of human and computer rounds was counterbalenced between subjects to remove order bias, so if the order had been player 1 with human partner (H1), player 2 with human partner (H2), player 1 with computer partner (C1), then player 2 with computer partner (C2), the second subject would look like this: C1, C2, H1, H2.

When the subject was playing as player 1, the computer algorithm would reciprocate defection 90% of the time and cooperation at 67% of the time. When the subject was playing as player 2, the computer played a forgiving tit for tat strategy that began with cooperation and always reciprocated cooperation from the previous round. Following mutual defection the algorithm cooperated 33% of the time. Following unreciprocated cooperation it cooperated 10% of the time, but never after two sequential DC outcomes.

After each session subjects were asked to rate their emotional response to each type of outcome on a scale of 1 to 7. Six emotional states were assessed: afraid, angry, happy, guilty, relief, and disappointed.

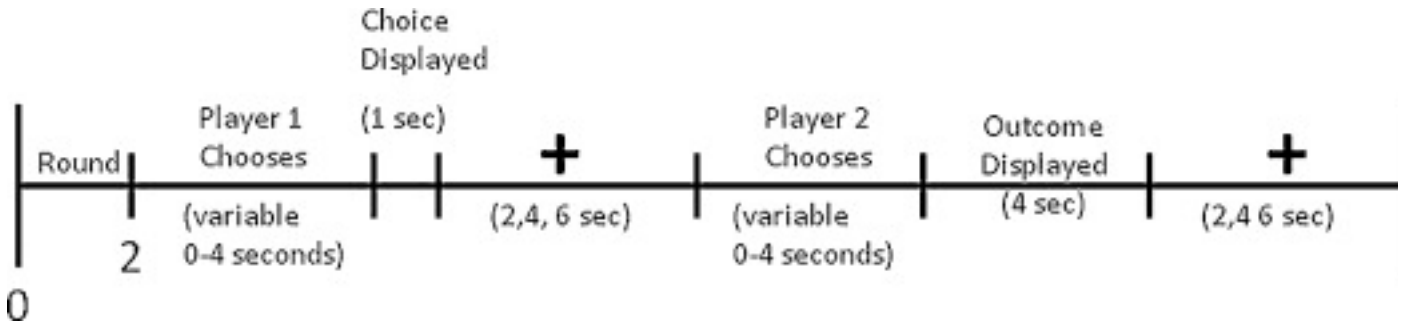


Figure 2. Prisoner's dilemma game timeline. Courtesy of Rilling et al. 2012

Personality data procedure

Subjects returned for personality testing within two weeks of initial scan and completed the Temperament and Character Inventory, along with several other personality inventories, solitarily on a computer at the direction of a research associate. Scores were computed using a computer algorithm.

Behavioral analysis

In order to account for variation in the denominator of the behavioral probability, outcome probabilities were weighted correcting for continuity and variance. Continuity was corrected for by weighing each observation by the inverse variance of the cooperation probability. For example: p * (1 - p) / #CC outcomes, where p is the probability of cooperating after a CC outcome. Variance was increased by adding two prior counts, one negative and one positive, to each outcome before dividing by total number of C choices to arrive at the probability of cooperation. For self-reported emotional score, subjects who fell more than three standard deviations from the mean were excluded (n=4).

Correlations were made using a two-tailed bivariate t-test in SPSS.

MRI image acquisition:

Imaging was conducted on a Siemens Trio 3T MRI scanner with a padded head restraint to minimize subject motion. A T1-weighted MPRAGE anatomical scan (TR= 2300 ms, TE = 4 ms, matrix = 256x256, FOV=256, slice thickness = 1.00 mm, gap = 0 mm) and a functional scan were acquired. Functional data was acquired with an EPI sequence of the following parameters: TR = 2000 ms, TE = 28 ms, matrix = 64 x 64, FOV = 192 mm, slice thickness = 3.0 mm, and 32 axial slices.

fMRI image analysis

All image analysis and preprocessing was conducted with Brain Voyager QX (version 2.0.8) software (Brain Innovation, Maastricht, The Netherlands). Functional images were realigned by six-parameter 3-D motion correction. Functional images were co-registered with their high-resolution 3-D anatomical scan. Images were normalized into Talairach space (Talairach and Tournoux 1988). Images were smoothed at 8-mm FWHM. A separate general linear model was defined for each subject for the four second epoch when the outcome was revealed to both players. Two regressors were defined for each subject: CC and CD. Each regressor was convolved with a standardized model of the hemodynamic response. For each subject the CD-CC contrasts of parameter estimates of interest were computed at every voxel of the brain. Covariate analysis for reward dependence and cooperativeness were conducted using random effects ANCOVA. The resulting correlation maps were thresholded at an uncorrected p value less than 0.005, with a 10 voxel spatial extent threshold. All data is from player 1 sessions.

Structural data analysis

Structural data were analyzed with FSL-VBM, a voxel-based morphometry style analysis (Ashburner 2000, Good 2001) carried out with FSL tools (Smith 2004). First, structural images were brain-extracted using BET (Smith 2002). Next, tissue-type segmentation was carried out

using FAST4 (Zhang 2001). The resulting grey-matter partial volume images were then aligned to MNI152 standard space using the affine registration tool FLIRT (Jenkinson 2001, 2002). The resulting images were averaged to create a study-specific template, to which the native grey matter images were then non-linearly re-registered. The registered partial volume images were then modulated (to correct for local expansion or contraction) by dividing by the Jacobian of the warp field. The modulated segmentated images were then smoothed with an isotropic Gaussian kernel with a sigma of 2 mm. Finally, voxelwise GLM for correlation to either reward dependence or cooperativeness were applied using permutation-based non-parametric testing. The resulting maps were visualized in FSL-VIEW and thresholded at a p value less than 0.05 and a spatial extent threshold equivalent to the 10 voxel threshold of the functional neuroimaging data.

Results

Personality results

As expected, reward dependence was highly correlated with cooperativeness in both the male and female sample (r=0.479 p<0.0001, males; r=0.614 p>0.0001, females). Unlike other studies (Cloninger et al., 1993), there was no significant difference between males and females in reward dependence or cooperativeness score (p=0.110, reward dependence; p=0.236, cooperativeness, two-tailed t-test). However, there was a non-significant trend of males scoring lower in reward dependence than females.

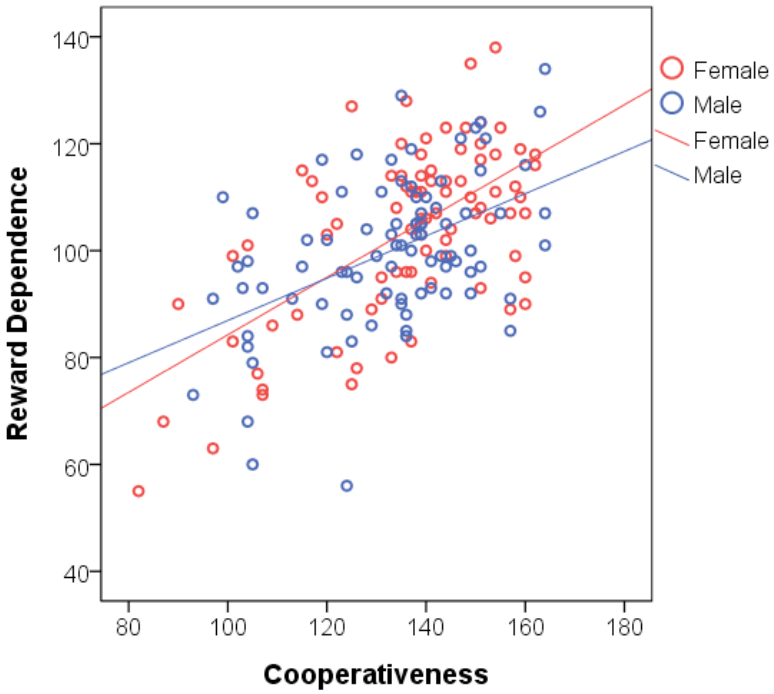


Figure 3. Reward dependence is correlated with cooperativeness with no significant difference between males and females (r=0.479 p<0.0001, males; r=0.614 p>0.0001, females). Bivariate t-test, n=101 (males) and 84 (females).

Emotional results

As hypothesized, reward dependence in both males and females was correlated with self-reported happiness after a CC outcome (p=0.016, r=0.236; p=0.008, r=0.271) as player 1 (figure 4a). Cooperativeness was also correlated with happiness after a CC outcome in females, but not in males (p=0.009, r=0.265) as player 1 (figure 4b). Disappointment and anger were not correlated with either measure as player 1.

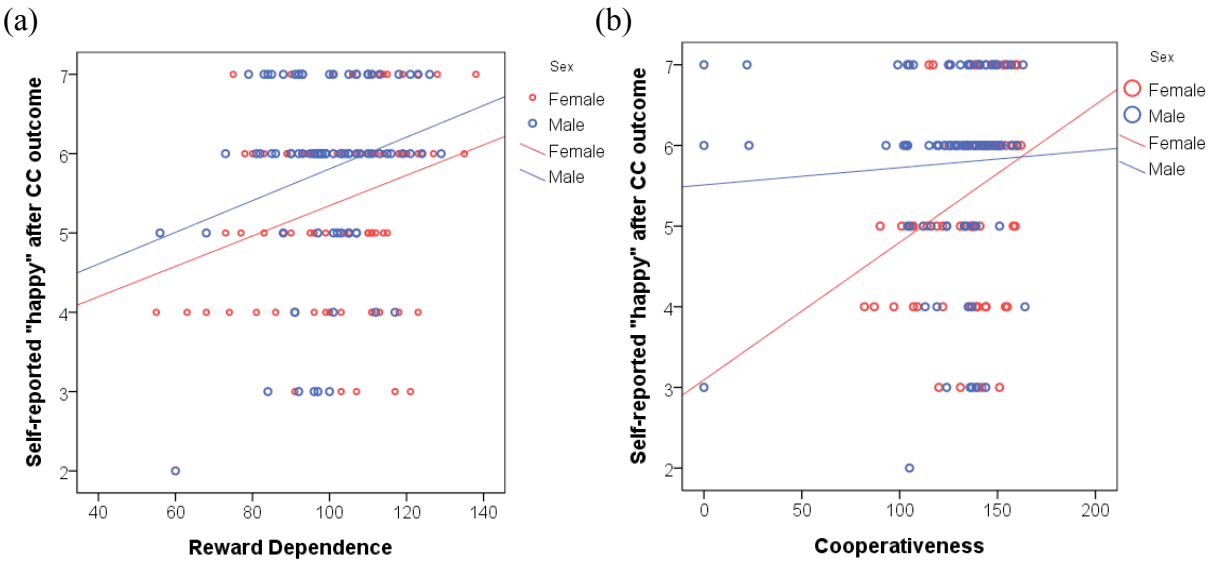


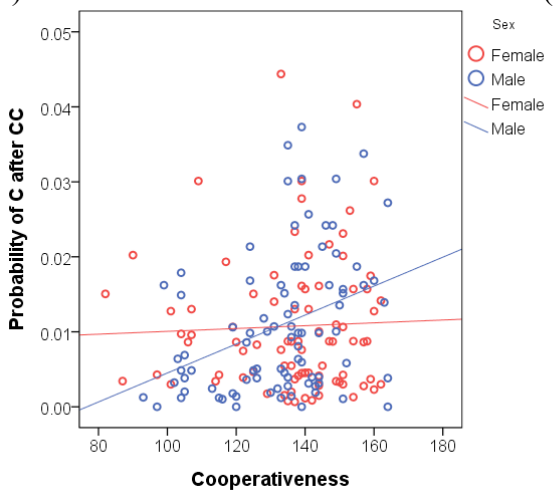
Figure 4. (a) Reward dependence is positively correlated with self-reported happiness after a CC outcome in both males and females (p=0.016, r=0.236; p=0.008, r=0.271). (b) Cooperativeness is positively correlated with self-reported happiness after a CC outcome in females (p=0.009, r=0.265), but not in males. Bivariate t-test, n=101 (males) and 84 (females).

Behavioral results

As hypothesized, cooperativeness in males was correlated with probability of continuing cooperation after a CC outcome as player 1 (p=<.0001, r=0.353) (figure 5a). Also in males, reward dependence was negatively correlated with probability of cooperating after a DD outcome as player 1 (p=.015, r=-.238) (figure 5b). In females reward dependence was correlated

with probability to return to cooperation after DC outcome (p=0.021 r=0.222) (figure 5c). Neither reward dependence nor cooperativeness was correlated with total number of C choices in males or females as player 1 or 2. In addition, neither personality measure had any correlation with probability of reciprocating cooperation as player 2.

(a)



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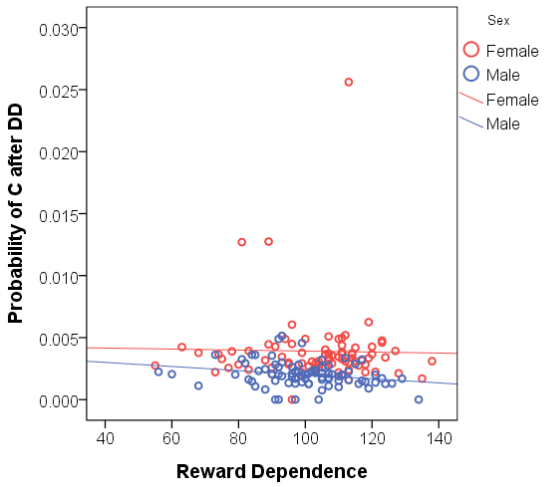

(c)

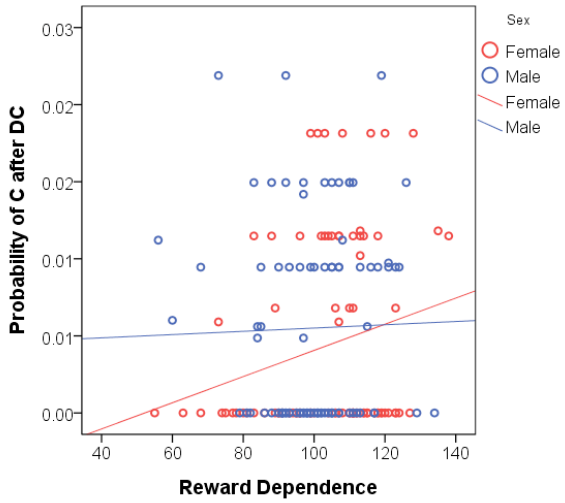

Figure 5. (a) Cooperativeness is positively correlated with probability of cooperating after a CC outcome as player 1 in males (p=<.0001, r=0.353), but not females. (b) Reward dependence is negatively correlated with probability of cooperating after a DD outcome in males (p=.015, r=-.238) , but not females. (c) Reward dependence is positively correlated with cooperating after a DC outcome in females (p=0.021 r=0.222), but not males. Bivariate t-test, n=101 (males) and 84 (females).

Functional neuroimaging results

In males, reward dependence was not correlated with any of the hypothesized areas. Exploratory whole brain analysis in males showed that reward dependence was correlated with greater activation in the left superior temporal sulcus (p=0.00007, r=-0.472) after a CD than a CC outcome as player 1. As hypothesized, reward dependence was correlated with activation in the left amygdala for females after a CD outcome rather than a CC outcome (p=.000175, r=0.462). Further whole brain analyses showed that reward dependence was negatively correlated with activation in the right superior frontal gyrus (p=.000254, r=-0.452) and positively correlated with left mOFC (p=.000442, r=0.436), and the left inferior frontal sulcus (p=.000355, r=0.443) after a CD than CC outcome as player 1.

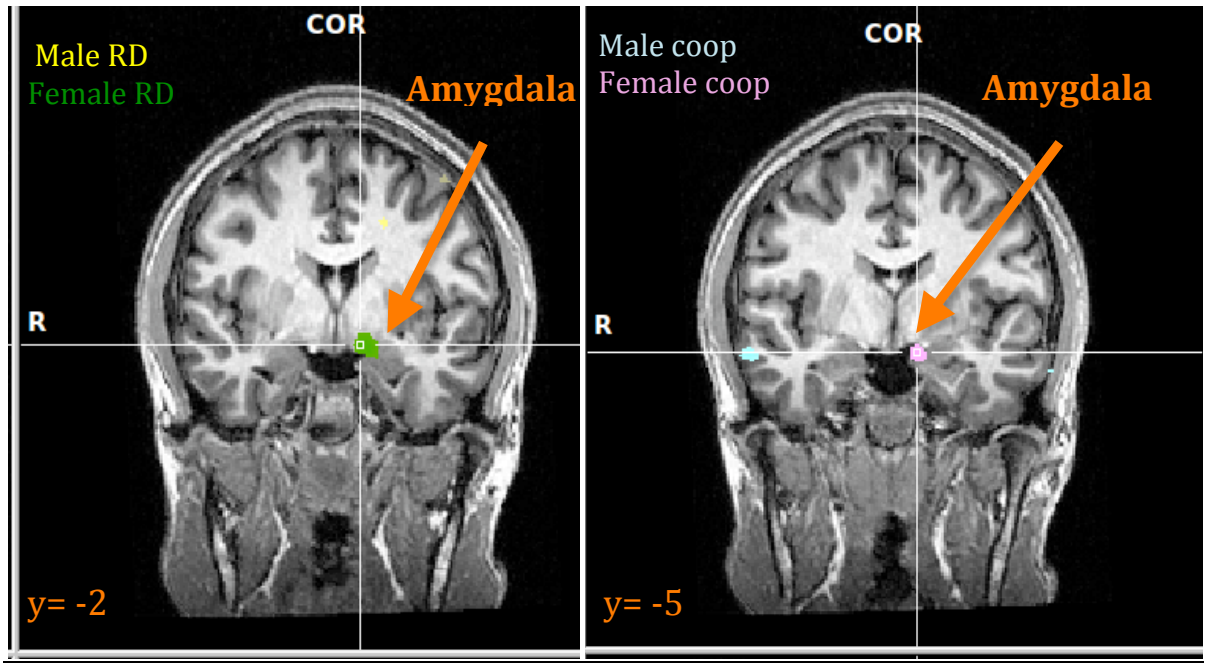

Figure 6. (a) CD-CC contrast as player 1 beta values correlated with reward dependence. Positive male correlation is in yellow and positive female correlation is in green. Arrow is pointing to the left amygdala. Image is thresholded at p<0.005. Corrected for multiple comparisons. n=65 (males) and 61 (females). (b) CD-CC contrast beta values correlated with cooperativeness. Negative male correlation is in light blue and positive female correlation is in pink. Arrow is pointing to the left amygdala. Image is thresholded at p<0.005. Corrected for multiple comparisons. n=65 (males) and 61 (females)

In males, cooperativeness was correlated with activation in the right middle temporal gyrus (p=0.000642, r=-0.412), right precentral gyrus (p=0.000401, r=-0.4262), and left medial prefrontal cortex (p=.000319, r=-0.4326) after a CD than CC outcome as player 1. In females, cooperativeness was negatively correlated with activation in the right subparietal sulcus (p=.00183, r=-0.390) and positively correlated with activation in the left amygdala (p=.00025, r=0.452) and ventral lateral prefrontal cortex (p=.00140, r=0.399) after a CD than CC outcome as player 1.

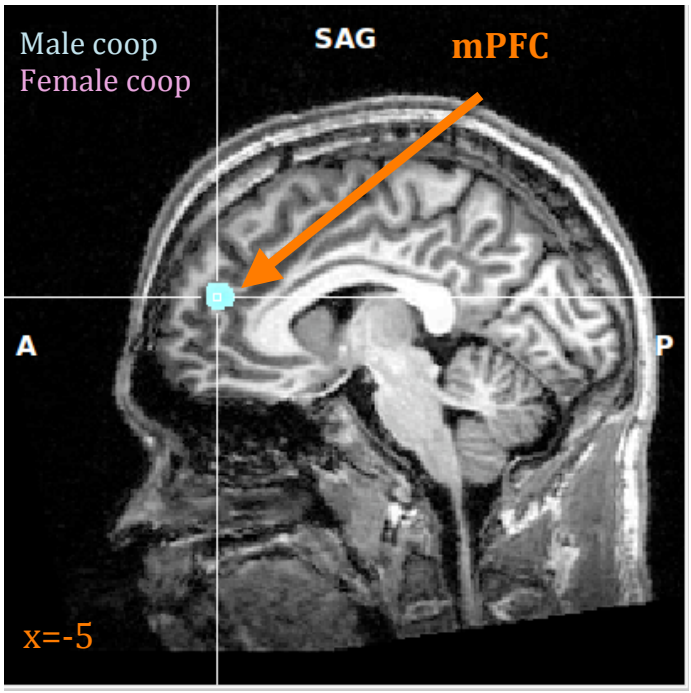

Figure 7. CD-CC contrast as player 1 beta values correlated with cooperativeness. Negative male correlation is in light blue. Arrow is pointing to the medial prefrontal cortex. Image is thresholded at p<0.005. Corrected for multiple comparisons. n=65 (males) and 61 (females)

Structural neuroimaging results

Total grey matter volume and total brain volume were negatively correlated with reward dependence in females, but not males (p<0.0001, r=-0.378). Cooperativeness was not correlated with total grey matter volume or total brain volume in males or females.

Reward dependence was not correlated with grey matter volume in males at a p-value of less than 0.05, except for the brain stem. However, in females reward dependence was positively

correlated with bilateral grey matter volume in the amygdala, hippocampus, lateral hypothalamus, caudate nucleus, and anterior cingulate cortex in females (table 2).

In males, cooperativeness was correlated with grey matter volume in the left insula (figure 10), left dorsal lateral prefrontal cortex (figure 8), and right amygdala (figure 9) (table 2). In females, cooperativeness was correlated with GMV in the mOFC, right hippocampus, and opercular cortex (figure 10) (table 2).

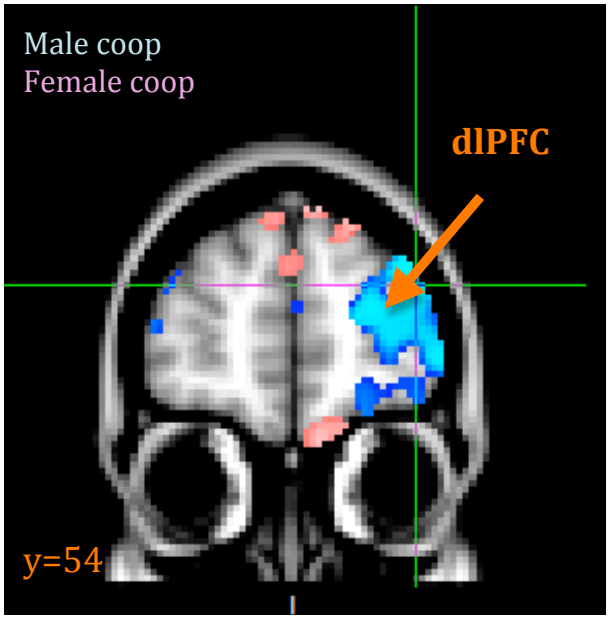

Figure 8: GMV correlated with cooperativeness. Positive male correlation in blue and positive female correlation in pink. Arrow is pointing to the dorsolateral prefrontal cortex. Image is thresholded at $p<0.05$. Uncorrected for multiple comparisons. n= 101 (males) and 85 (females).

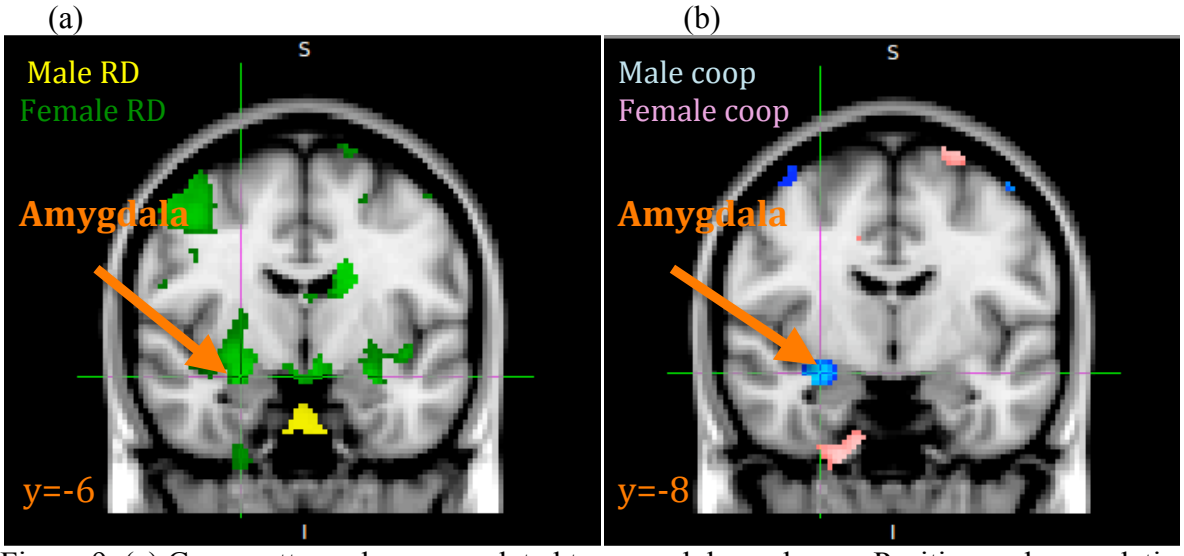

Figure 9. (a) Grey matter volume correlated to reward dependence. Positive male correlation in yellow and positive female correlation in green. Arrow is pointing to the right amygdala. Image is thresholded at $p<0.05$. Uncorrected for multiple comparisons. n= 101 (males) and 85 (females). (b) Grey matter volume correlated to cooperativeness. Positive male correlation in blue and positive female correlation in pink. Arrow is pointing to the right amygdala. Image is thresholded at $p<0.05$. Uncorrected for multiple comparisons. n= 101 (males) and 85 (females).

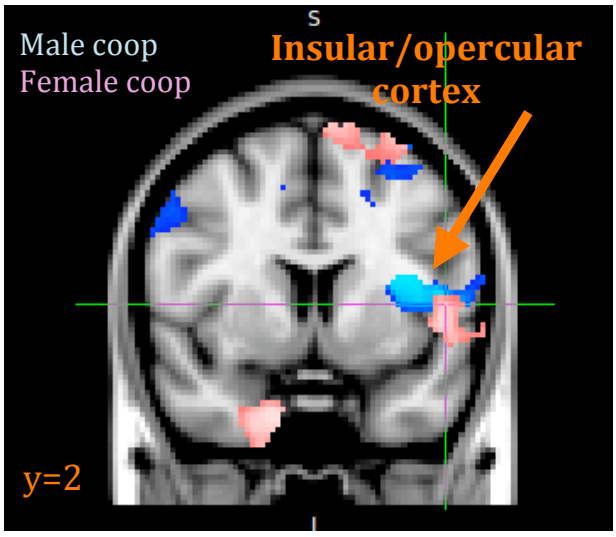

Figure 10. Grey matter volume correlated with cooperativeness. Male positive correlation in blue and female positive correlation in pink. Arrow is pointing towards overlap in the left opercular and insular cortex. Image is thresholded at $p<0.05$. Uncorrected for multiple comparisons. n= 101 (males) and 85 (females).

Discussion

The present study aimed to use two similar measurements of prosocial affinity and relate them separately to behavior, brain function, and brain structure in the PD game to investigate mechanisms of cooperative behavior and further our understanding of individual variation in social behavior. I hypothesized that a) reward dependence and cooperativeness would be positively correlated and that females would have higher scores on both measures, b) reward dependence and cooperativeness would be correlated with self-reported happiness after a CC outcome and reward dependence would be positively correlated with reported anger or disappointment after a CD outcome, c) reward dependence would be correlated with probability of C after CC and C after DC, while cooperativeness would be correlated with increased number of C choices, d) subjects with high reward dependence would show increased ventral striatum and mOFC activation in response to reciprocated cooperation and increased anterior insula and left amygdala activation in response to partner defection, e) grey matter volume in the amygdala would be negatively correlated with reward dependence, while grey matter in the mOFC and striatum would be positively correlated with reward dependence. The drugs administered as part of the larger study may have influenced the behavioral, emotional, and functional neuroimaging results, but did not influence the personality or structural neuroimaging data collected.

Personality

Reward dependence and cooperativeness were highly correlated (r=0.479, males; r=0.614, females), as previous studies had suggested. Despite our large sample size I did not find a significant sex based difference as Cloninger had observed (Cloninger, Przybeck, & Svrakic, 1991). This may have been due to the older population (43.9 years) or larger sample size (1,029) used in Cloninger's 1991 research. If age and generation do have an effect on the results of the TCI, it would be interesting as part of a much larger study to find trends predicting changes in

the TCI. The lack of significant difference between males and females suggest that there is no difference in the prosocial capacity of males and females. The imaging and structural results can further illuminate this hypothesis.

Emotional

The emotional data presents the similarities between the two personality types. Self-reported happiness after a CC outcome was correlated with reward dependence in males (r=0.236) and both reward dependence and cooperativeness in females (r=0.271; r=0.265). From this it can be deduced that, at the level of self-reflection, both personality measures had similar outcomes: an increase in happiness in response to mutual cooperation.

Behavioral

The behavioral results show that both reward dependence and cooperativeness are related to social behavior in the PD game. Cooperativeness was correlated with continuing cooperation (C after CC) in males (r=0.353), while reward dependence was negatively correlated with returning to cooperation after a DD outcome (r=-.238).

Reward dependence in females was correlated to returning to cooperation in females (C after DC in females, r=0.222). These data show the differences in the two personality traits, which although similar, have different motivations. Cooperativeness can be thought of as promoting cooperative behavior in general, while reward dependence is correlated with punishing your partner (D after DD) and returning to cooperation after they make up for it (C after DC). Reward dependence seems to be correlated with more complex social interactions like reward and punishment, which requires increased scrutiny of other's behavior.

The sexual dimorphism of these correlations is also interesting. In males, cooperativeness was highly correlated with the probability of continuing cooperation, while it

was not in females. This difference shows the importance of addressing each sex separately, since the effects of the personality measures differ between the two.

Functional neuroimaging

In males, reward dependence was not significantly correlated with any cortical activation at a threshold of .005. Cooperativeness was negatively correlated with activation in the mPFC in the contrast CD-CC (r=-0.412), meaning that it was positively correlated with activation in the contrast CC-CD (figure 7). The mPFC is an area implicated in theory of mind (Gobbini, Koralek, Bryan, Montgomery, & Haxby, 2010). Theory of mind (TOM), or the ability to attribute thoughts and motivation to others, is considered by many to be a uniquely human trait, though there is evidence of it occurring in other species (Penn & Povinelli, 2007). Children develop the ability to understand and predict what others know and do not know around age 4, but even before this age, some children are able to understand inconsistencies in gaze and the decoupling of pretend and reality (Frith & Frith, 2003). A PET study by Háppe et al. found that subjects with high functioning ASD had no activation in the mPFC when completing a TOM task, unlike normal controls (Happé et al., 1996). The correlation between cooperativeness and mPFC activation after a CC outcome in males may be a result of increased concern with other's state of mind and reasoning behind actions. Highly cooperative individuals are more likely to perpetuate cooperation in the PD game and may be more interested when their partner chooses to cooperate, using mental mind-reading to understand the motivations of their partner. Why TOM areas would be more active after a positive outcome than a negative outcome is a compelling question. Perhaps highly cooperative individuals are more familiar with cooperation and find it difficult to understand or project why others would choose not to cooperate. However, further analysis would be necessary to compare those who had DC outcomes and those who did not with activation in areas associated with TOM

In females, both reward dependence and cooperativeness were correlated with fMRI activation in the left amygdala in response to a CD outcome(r=0.462; r=0.452) (figure 6), which points towards a similar mechanism between the two measurements. The amygdala is known to be hypoactive in individuals with ASD (Schultz, 2005), so the increase in activation in response to socially challenging situations is not unexpected. The amygdala is thought to relate to the detection of emotional stimuli, as other studies have shown that the amygdala is responsible for facilitating attendance to emotional words and faces (Phelps, 2006). Our results show that, among prosocial females, the amygdala may be responsible for increasing the saliency and aversiveness of an outcome in which the subject's cooperation is not reciprocated. However, our behavioral results show that neither measure was correlated with the probability of cooperating after a CD outcome, so even if the amygdala is increasing the saliency of the outcome, the behavioral consequence is unknown. Future analyses could explore correlations of the functional response to DC outcomes and reward dependence, as we know that the behavioral probability of cooperating after a DC outcome is correlated with reward dependence.

Structural neuroimaging

Both total grey matter volume and whole brain volume were negatively correlated with reward dependence in females (r=-0.378, r=-0.378), but not in males. At first glance this finding is counterintuitive. Based on the social brain hypothesis, we would expect to find grey matter volume to be positively correlated with reward dependence, a measure of prosocial behavior. However, this measurement was of grey matter volume as a whole, not a ratio of neocortex to whole brain volume, as Dunbar has used (Dunbar 1998). In addition, it is probable that whole brain size drives grey matter volume, not the other way around. ASD is known to affect brain growth and causes a sharp increase in total brain volume during childhood. This difference in brain size between an autistic and normal sample remains until adulthood (Redcay &

Courchesne, 2005). Based on this research, it is not surprising that increased reward dependence is negatively correlated with grey matter volume and total brain volume.

In males, reward dependence was correlated with brainstem grey matter volume, but none of the hypothesized areas. It is difficult to say why reward dependence in males had no significant correlation with either grey matter volume or functional activation, especially since Lebreton et al. (2009) found significant correlation between GMV and reward dependence in several areas, including the mOFC and ventral striatum. Perhaps further research could address these concerns with a larger sample size or statistical analyses controlling for variation in background, age, and timing, since Lebreton's subjects were Finns between the ages of 33 and 35 and had completed the TCI several years before the MRI scans took place.

Cooperativeness in males was correlated with increased grey matter density in the dlPFC ($p=0.001$) (figure 8). The dlPFC is responsible for executive functions and cognitive control over emotional responses (McClure, Laibson, Loewenstein, & Cohen, 2004). Using the Ultimatum Game, Sanfey et al. (2003) showed activation in the dlPFC in response to the acceptance of unfair monetary offers. Since cooperativeness was correlated with continuing cooperation in males, we can hypothesize that the dlPFC is responsible for delaying the monetary reward of defection and promoting cooperative behavior. Increased grey matter volume in neocortical areas, like the dlPFC, allows for overriding immediate gratification in social situations and is correlated with cooperativeness. Such conclusions substantiate the social brain hypothesis within a human population, showing that highly heritable variation within a population can lead to prosocial behavior.

As previously discussed, the amygdala serves an important function in detecting salient emotional stimuli. The correlation between grey matter volume in the right amygdala and cooperativeness in males, as well as reward dependence in females ($p=0.008$; $p=0.012$)(figure 9),

is compelling for similar reasons as the functional activations; that is, the detection and modulation of emotional stimuli. Autism is associated with decreased grey matter in the amygdala in adults (Abell et al., 1999), strengthening our conclusion that amygdala volume is associated with prosocial behavior. I did not replicate the results of Tost et al. (2010), who found amygdala volume to be negatively correlated with reward dependence in a co-ed sample. However, because of the sexual dimorphism seen in our and other's results (Yamasue et al., 2008), it seems prudent to consider a sex stratified sample.

While the functional results in the amygdala were specific to females, the structural results are not sex specific. A larger amygdala was correlated with increased scores on the prosocial measures, regardless of sex. In addition, the functional results showed activation in the left amygdala, while the structural results showed correlation in the right amygdala. A meta-analysis of fMRI and PET studies showed that a majority of studies reported left amygdala activation during emotional tasks (Baas, Aleman, & Kahn, 2004), but a similar study using VBM has not been done. The laterality of the amygdala is questionable, although it may be sex based (Baas et al., 2004). Our results show a difference in laterality between functional activation and grey matter structure in the amygdala, but the precise meaning of this difference needs to be explored further. In addition, the functional role of the amygdala in promoting prosocial behavior in men should be investigated with region-of-interest analyses and different social paradigms.

While I did not find a correlation between mOFC volume and reward dependence in males or females, there was a correlation between cooperativeness and mOFC volume in males and females ($p=0.031$;$p=0.013$). As the mOFC is known to be involved in anticipating rewards, this can be seen as evidence that individuals high in cooperativeness are more attune to social

reward in general, perhaps leading to more wide-ranging compassion than the slightly more manipulative individuals that are high in reward dependence (Lebreton et al., 2009).

In both males and females, grey matter volume in the opercular and insular cortex was correlated with cooperativeness ($p=0.003$;$p=0.006$). A similar effect was found by Yamasue et al. (Yamasue et al., 2008) to be greater in females than males, although our results did not validate this. The insula is thought to monitor the viscera and is activated by both experiencing an emotion and viewing another experience the same emotion (Botvinick et al., 2005; Singer, Critchley, & Preuschoff, 2009). Because of these findings, the insula is thought to have a role in empathy. It stands to reason that individuals who are high in cooperativeness would have more grey matter devoted to areas associated with empathy.

One of the limitations of this study is the necessity to draw conclusions based on correlations alone, which do not imply causation. This is an inherent problem in human studies, as we cannot manipulate variables as easily as with other animal models. Similar studies, however, could be done on ASD patients, to further our understanding of the neural structures implicated here. Another limitation was effect of the drugs given to subjects as part of the larger study. The effects of oxytocin and vasopressin on behavior and functional activation have been shown in previous studies (Rilling et al., 2012). In men playing the prisoner's dilemma game, oxytocin increases amygdala and caudate nucleus activation in response to reciprocated cooperation and promotes cooperation following unreciprocation, while vasopressin promotes cooperation after a cooperative gesture by the partner (Rilling et al., 2012). Future analyses could account for this by using subjects who had received no treatment or a placebo.

I have shown the behaviors, functional activations, and structural differences associated with reward dependence and cooperativeness in both males and females. Evidence implicates the amygdala as having a role in detecting emotional saliency of a negative outcome in females,

while the mPFC is responsible for understanding the thoughts of the partner after a cooperative encounter in males. I have found some support for the social brain hypothesis in humans, as areas of the prefrontal cortex in males were correlated with our measures of prosocial behavior. Our results point to a lack of sexual dimorphism in the structural correlates of reward dependence and cooperativeness, while our functional results suggest a difference in processing mechanisms between males and females. This may be a result of different evolutionary pressures on males and females based on different social situations in a traditional hunter-gatherer society.

Cooperative behavior amongst humans is the result of many specialized mechanisms that evolved in a social context. By increasing our understanding of these mechanisms and the structures responsible for them, we can better understand human variation in social behavior.

Tables

Structure	Voxels	X	Y	Z	r	P-value
Male vs RD CD-CC						
Left STS	35	-52	-50	15	-0.472	.00007
Male vs Coop CD-CC						
Right middle temporal gyrus	20	69	-20	-15	-0.4124	.000642
Right precentral gyrus	53	62	-11	-9	-0.4262	.000401
Left mPFC	58	-4	46	18	-0.4326	.000319
Female vs RD CD-CC						
Right superior frontal gyrus	17	26	52	36	-0.452	.000254
Left medial amygdala	19	-10	-2	-9	0.462	.000175
Left OFC	17	-19	37	-18	0.436	.000442
Left inferior frontal sulcus	30	-40	-46	0	0.443	.000355
Female vs Coop CD-CC						
Subparietal sulcus	12	2	-44	48	-0.390	.00183
Left amygdala	10	-10	-8	-12	0.452	.00025
Left vlPFC	10	-46	40	-3	0.399	.00140

Table 1. fMRI Talairach table

Structure	Voxels	X	Y	Z	P-value
Male vs RD					
Brain-stem	31	2	-22	-40	0.02
Male vs Coop					
Left dlPFC	3371	-38	54	22	0.001
Left precentral gyrus	1980	-18	-18	78	0.004
ACC	1590	-14	16	32	0.012
Right frontal pole	928	42	36	40	0.001
Left insula	848	-32	2	14	0.003
Opercular cortex					
Right superior precentral gyrus	458	30	-18	56	0.019
Occipital cortex	296	8	-88	14	0.022
Right superior occipital cortex	279	22	-78	52	0.01
Right middle temporal gyrus	227	68	-44	6	0.01
Precuneous	222	-2	-56	68	0.028
Superior frontal gyrus	208	-16	16	70	0.025
Right anterior precentral gyrus	136	56	10	42	0.02
Right amygdala	134	30	-8	-14	0.008
Left posterior superior Temporal gyrus	42	-68	-22	2	0.034
Left OFC	37	-20	36	-10	0.031

Female vs RD					
Right amygdala	2038	26	-6	-16	0.012
Lateral hypothalamus					
Hippocampus					
Nucleus accumbens					
Right superior central sulcus	1068	54	-10	50	0.014
ACC	816	6	40	12	0.025
Left caudate	353	-14	-6	28	0.013
Medial BNST					
Left amygdala	333	-28	-8	-16	0.013
Right medial temporal pole	210	20	8	-40	0.037
Left postcentral gyrus	206	-24	-34	74	0.025
Right inferior frontal gyrus, pars triangularis	185	52	26	2	0.038
Right frontal pole	103	6	68	22	0.026
Brain stem	84	2	-16	-42	0.021
Anterior inferior temporal gyrus	64	42	2	-34	0.042
Left frontal pole	57	-10	50	-22	0.04
Right superior lateral temporal pole	45	60	8	-8	0.045
Left precentral gyrus	32	-26	-8	54	0.042
Female vs Coop					
Medial parietal cortex	1390	-30	-36	72	0.021
Posterior cingulate gyrus	788	0	-46	-2	0.005
Right hippocampus					
Right temporal pole	658	14	8	-36	0.009
Left insula	361	-48	12	-6	0.006
Opercular cortex					
OFC	266	6	40	-30	0.013
Superior frontal gyrus	236	-8	8	74	0.021
Left frontal pole	155	-36	40	42	0.017
Lateral occipital cortex	68	-38	-72	-4	0.024
Right superior frontal pole	67	10	48	52	0.02
Left precentral gyrus	60	-26	-8	74	0.025
Right inferior frontal pole	54	28	60	-16	0.03
Left Inferior frontal gyrus	41	-56	24	32	0.036
Superior parietal cortex	34	-34	-54	66	0.026

Table 2. VBM MNI table

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