

## Oxytocin Tempers Calculated Greed but not Impulsive Defense in Predator-Prey Contests

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## Abstract

Human cooperation and competition is modulated by oxytocin, a hypothalamic neuropeptide that functions as both hormone and neurotransmitter. Oxytocin's functions can be captured in two explanatory yet largely contradictory frameworks: the fear-dampening (FD) hypothesis that oxytocin has anxiolytic effects and reduces fear-motivated action; and the social approach/avoidance (SAA) hypothesis that oxytocin increases cooperative approach and facilitates protection against aversive stimuli and threat. We tested derivations from both frameworks in a novel predator-prey contest game. Healthy males given oxytocin or placebo invested as predator to win their prey's endowment, or as prey to protect their endowment against predation. Neural activity was registered using 3T-MRI. In prey, (fear-motivated) investments were fast and conditioned on the amygdala. Inconsistent with FD, oxytocin did not modulate neural and behavioral responding in prey. In predators, (greed-motivated) investments were slower, and conditioned on the superior frontal gyrus. Consistent with SAA, oxytocin reduced predator investment, time to decide, and activation in superior frontal gyrus. Thus, whereas oxytocin does not incapacitate the impulsive ability to protect and defend oneself, it lowers the greedy and more calculated appetite for coming out ahead.

## Introduction

Human societies function, and their individuals prosper, when and because individuals extend trust and cooperate, control their greedy desires to appropriate other's wealth, and properly defend and protect themselves against predatory exploitation. Cumulating evidence from neurobiology and behavioral sciences suggests that human cooperation and competition is modulated by oxytocin, an evolutionary ancient neuropeptide that is produced in the human hypothalamus and functions as both hormone and neurotransmitter (Donaldson & Young, 2008; Ludwig & Leng, 2006; Carter et al., 2008; Meyer-Lindenberg, Domes, Kirsch, & Heinrichs, 2011; Bos, Panksepp, Bluthé, & Van Honk, 2012). Across mammalian species, oxytocin sustains pair bond formation and maintenance (Donaldson & Young, 2008; Carter et al., 2008). In humans, genetic polymorphism in the oxytocin receptor gene associates with generosity in humans (Roderigues, Saslow et al., 2009; Israel, Lerer et al., 2009), and intranasal administration of oxytocin appears to facilitate empathic responding and cooperation (Baumgartner, Heinrichs et al., 2008; Kosfeld, Heinrichs et al., 2005; Kirsch, Esslinger et al., 2005; Petrovic, Kalisch, Singer & Dolan, 2008; De Dreu, 2012a; De Dreu, Greer et al., 2010; Israel, Bornstein, & Weisel, 2013; Guastella, Mitchell, & Matthews, 2008). These and related findings have been captured in two largely competing frameworks, suggesting that oxytocin enables cooperation because (i) it mitigates the fear of being exploited and the concomitant need to protect oneself against predation, or (ii) it tempers the greedy desire to accumulate wealth at the expense of others. Below, we elaborate on the evidence and suspected mechanisms underlying these respective scenarios, and devise a novel predator/prey decision-making game to pit the competing hypotheses against each other.

The first perspective on the influence of oxytocin on human cooperation and competition rests on the fact that, upon its hypothalamic release, oxytocin targets the regions of the spinal cord that regulate the parasympathetic branch of the autonomic nervous system (Donaldson & Young, 2008; Ludwig & Leng, 2006). Oxytocin interacts with the hypothalamic-pituitary-adrenal axis to attenuate stress responses: it reduces cortisol levels after exposure to stressors, inhibits cardiovascular stress responses, and modulates neural circuitries involved in the processing of fear-related information (Carter et al., 2008; Meyer-Lindenberg et al., 2011; Bos et al., 2012). Accordingly, participants receiving intranasal oxytocin (versus placebo) showed reduced activation of the amygdala and attenuated coupling of the amygdala to brainstem centers responsible for autonomic and behavioral components of fear when processing fearful faces, (Kirsch et al., 2005; Petrovic et al., 2008; MacDonald & Feifel, 2014), were less fearful of being exploited, and more trusting of others (Baumgartner et al., 2008; Kosfeld et al., 2005; De Dreu et al., 2010). Together, these works converge on the fear-dampening (FD) hypothesis: Oxytocin dampens activation in the amygdala and its direct and indirect role in fear-responding, and thus enables humans to extend trust.

The alternative, social approach/avoidance (SAA) perspective on the influence of oxytocin on human cooperation and competition (Guastella et al., 2008; Kemp & Guastella, 2011; Striepens, Scheele, Kenrick & Hurlmann, 2012) rests on the well-established notion that human emotion and behavior is grounded in a tendency to approach positively valued and to avoid aversive, negatively valued states (Cardinal et al., 2002; Higgins, 1997; Roskes, Elliot, Nijstad, & De Dreu, 2013; Watson, Wiese, Vaidya, & Tellegen, 1999). It accordingly proposes that oxytocin (i) promotes approach-related exploration rather than exploitation (Kemp & Guastella, 2011, De Dreu, Baas et al., 2014), including pro-social behavior such as cooperation,

while (ii) allows to adaptively respond to aversive stimuli and threat by, for example, flight, seeking shelter or, if needed, lashing out to neutralize the threat (De Dreu, 2012b; Striepens et al., 2012).

That oxytocin drives pro-social approach fits studies showing that oxytocin increases trust and generosity (Baumgartner et al., 2008; Kosfeld et al., 2005; De Dreu et al., 2010; Chang, Barter, Ebitz, Watson & Platt, 2012), and studies showing that oxytocin up-regulates neural circuitries involved in empathic concern and reward processing (Donaldson & Young, 2008; Carter et al., 2008; Rilling et al., 2012; Skuse & Gallagher, 2005; Hurlemann, Patin et al., 2010). That oxytocin enables adaptive responding to threat contrasts with the FD hypothesis that oxytocin reduces fear and anxiety, yet resonates with work showing that oxytocin blunts attention to negative facial expressions in rhesus macaque (Parr, Modi, Sibert, & Young, 2013; Ebitz, Watson, & Platt, 2013) and, in humans, reduces the tendency to withdraw from angry faces (Hurlemann et al., 2010), potentiates startle reactivity to threat and facilitates protective (neural) responses to aversive stimuli, especially when unpredictable (Striepens et al., 2012; Grillon, Krimsky, Charney, Vytal, Ernst, & Cornwell, 2013). It also fits work showing that oxytocin motivates protective, competitive behavior when exchange partners are unfamiliar, potentially untrustworthy, and belonging to rivaling out-groups (De Dreu et al., 2010; Mikolajzak, Gross, Lane et al., 2010; De Dreu, Greer, Van Kleef, Shalvi & Handgraaf, 2011; Declerck, Bonne, & Kiyonari, 2010; Ten Velden, Baas, Shalvi, Kret & De Dreu, 2013).

Earlier analyses of oxytocin assumed that pro-social approach may be the result of lowered anxiety and reduced fear (e.g., Bartz et al., 2011), or used oxytocin-reduced amygdala activation in the face of threatening stimuli as evidence for pro-social approach (e.g., Kemp & Guastella, 2010; 2011). Here we disentangled fear-responding from pro-social approach

conceptually, and to illuminate the precise functions of oxytocin in social exchange problems, we tested derivations of the FD-hypothesis on the one hand, and the SAA-hypothesis on the other.

We did so using a newly developed, two-player Predator-Prey Game (PPG). The PPG is grounded in the economic theory of predation and economic growth (Carter & Anderson, 2001; Grossman, & Kim, 1996), and models the conflict between survival and preservation of the status quo on the one hand, and the drive towards appropriation and expansion on the other. In the PPG, one player (henceforth predator) has to decide how much to invest in predation ( $X$ ) out of a given endowment  $E$  (with  $0 \leq X \leq E$ ), while the other player (henceforth prey) simultaneously decides how much to invest in defense ( $Y$ ) out of an equal endowment  $E$  (with  $0 \leq Y \leq E$ ). If  $X > Y$  then the predator obtains all of  $E - Y$ ; added to the remaining endowment  $E - X$ , this leads to a total payoff for the predator of:  $2E - X - Y$ , while the prey is left with 0. If  $X \leq Y$  then the predator appropriates nothing, leading to a payoff of  $E - X$  for the predator and  $E - Y$  for the prey. The PPG is formally equivalent to a contest with as contest success function  $f = X^m / (X^m + Y^m)$ , where  $f$  is the probability that the predator wins,  $m \rightarrow \infty$  for  $X \neq Y$ , and  $f = 0$  if  $Y = X$  (Tullock, 1980).

In the PPG, the predator's decision not to invest reflects cooperation because it is collectively beneficial; any amount invested reflects the greedy desire to accumulate personal wealth by subordinating the prey. Vice versa, the prey's decision not to invest reflects trust and is collectively beneficial; any amount invested reflects fear of being exploited and concomitant defensive aggression (Camerer, 2003; Coombs, 1973). Presumably because detecting opportunities and acquiring gains is less essential and less basic to survival than detecting threat and preventing loss (Delgado, Schotter, Ozbay, & Phelps, 2008; De Martino, Camerer, & Adolphs, 2010), animal studies show that predatory greed is relatively slow, goal-directed, and controlled by brain circuitries centered on prefrontal cortex. Defensive aggression in prey is

faster, more relying on sensorimotor links, and conditioned on fear-signaling in amygdala-centered networks (Albert, Walsh, & Jonik, 1993; Siegel, Roeling, Gregg, & Kruk, 1999; Nelson, & Trainor, 2007; Choi & Kim, 2010). Along similar lines, human decision making geared at the inconsiderate accumulation of wealth rests on brain circuitries involved in impulse control, such as the superior frontal gyrus (Polosan et al., 2011; Chaminade, Marchant, Kilner, & Frith, 2012; Kruschwitz et al., 2012; Fahrenfort, Van Winden, Pelloux, Stallen & Ridderinkhof, 2012), whereas decisions geared at protection and defense are strongly amygdala-dependent (Baumgartner et al., 2008; Rilling et al., 2012; Delgado et al., 2008; De Martino et al., 2010).

Whereas we know that oxytocin shapes the neural circuitries and behavioral tendencies in cooperation and competition, precise predictions as to what oxytocin does starkly differ depending on the FD versus SAA hypothesis. SAA predicts that among predators, oxytocin promotes prosocial approach and tempers calculated greed, as reflected in reduced prefrontal activity as well as reduced predator investments. Among prey, oxytocin enables fear-driven defensive aggression, as reflected in maintained or even increased amygdala activity as well as maintained or intensified investments. By contrast, FD predicts that among prey, oxytocin dampens the fear of being exploited and mitigates defensive aggression, as reflected in reduced amygdala activity as well as reduced defensive investments; Among predators, no such effect will be observed.

## **Materials and Methods**

**Overview.** Predictions derived from FD and SAA were tested with the PPG in a double-blind, placebo controlled cross-over design. Twenty-seven males without neurological or psychiatric history and not using drugs or prescription-based medication participated in two sessions of 1.5 hours, with one week in between. They received instructions for the PPG and self-

administered intranasally 24 IU oxytocin (3 puffs per nostril) or placebo (containing all carrier ingredients except for the neuropeptide; see below). Because oxytocin effects on brain and behavior emerge approximately 35min after administration (e.g., De Dreu, Greer et al., 2010; Kosfeld et al., 2005; also see Baumgartner et al., 2008; Kirsch et al., 2005), we ensured a 30min gap before participants were placed in the scanner and made 6 blocks of 5 investments as predator and 6 blocks of 5 investments as prey. Role alternated between blocks, and starting role was randomly determined. Per trial (see Fig 1), a randomly generated prompt (range 0-10) was given; participants moved up or down by button presses to indicate desired investment. A trial ended by providing feedback about the protagonist's investment and the resulting payoff. BOLD-MRI was recorded using a 3T Philips Achieva TX MRI scanner.

***Participant Recruitment and Test Medication.*** The experiment was approved by the Psychology Ethics Committee of the University of Amsterdam, and complied with American Psychological Association guidelines, and the Helsinki Protocols. Male participants ( $M=25.31$  years) were recruited via an on-line recruiting system and offered a monetary reward of €60 for participating in a neuro-imaging study on the effects of medication on test scores and decision-making. Participants were informed about the medication provided only after both test sessions were over and informal debriefing revealed no indication that participants knew they received oxytocin or placebo. Exclusion criteria were significant neurological or psychiatric history, prescription-based medication, smoking more than five cigarettes per day, and drug or alcohol abuse. Eligible participants were assigned to a session and instructed to refrain from smoking or drinking (except water) for 2 hours before the experiment. They were promised a €60 show-up fee for two separate MRI-sessions each lasting approximately 1.5 hours, and that during each session they could earn up extra money during decision making (i.e., across the two sessions

three predator and three prey decision trials would be randomly selected and paid out, for a maximal total extra earning of €87 ( $= 3 \cdot 19 + 3 \cdot 10$ ). For each session they provided written informed consent.

Participants self-administered a single intranasal dose of 24 IU oxytocin (Syntocinon-Spray, Novartis; 3 puffs per nostril, each with 4 IU oxytocin, with 2min interval between puffs) or placebo. To avoid any subjective effects (for example, olfactory effects) other than those caused by oxytocin, the placebo contained all the active ingredients except for the neuropeptide. The placebo was manufactured by Stichting Apothekers Haarlemse Ziekenhuizen (SAHZ) in coordination with the pharmacy at the Amsterdam Medical Centre (AMC), adhering to the European Union guidelines on Good Manufacturing Practice (GMP) and Good Clinical Practice (GCP). The placebo was produced using the exact same recipes and procedures used by Novartis Inc. to produce the carrier of Syntocinon – the synthetic analogue of oxytocin. Placebos were delivered in the same bottles as Syntocinon. In short, participants were ignorant about what treatment they received and the only difference between the placebo and treatment was the absence versus presence of the active neuropeptide

***Experimental Procedures and Materials.*** Experimental sessions were conducted between noon and 4PM and participants were tested individually. Upon arrival, participants were escorted to a private cubicle where they read and signed an informed consent form. They read the instructions for the predator-prey game, and answered a series of quiz questions to verify whether they accurately understood the decision making task and consequences. (Because past work on oxytocin revealed no effects on mood or changes therein (e.g., Kosfeld et al., 2005) a mood measure was not included here or in the post-experiment debrief). Experimenters verified responses and provided the participant with test-medication (double-blind) and instructions.

Following self-administration, the experimenter prepared the participant for neuroimaging. The time between neuropeptide administration and entrance into the scanner was fixed at 30 minutes.

Participants received a booklet with instructions for the Predator-Prey Game (labeled Investment Task), containing several examples of investments and their consequences to both predator (labeled Role A) and prey (labeled Role B), and several questions to probe understanding of the game structure and decision consequences. Neutral labeling was used throughout. We introduced a group-version in which participants represented themselves and two others (further ignored), and an individual version in which participants represented themselves only. In each of the two *f*MRI sessions, participants played 6 x 5 trials as predator and 6 x 5 trials as prey. For each trial, participants received a prompt, randomly generated between 0 (indicating no investment) and 10 (indicating investment of the entire endowment) and used a button-press to adjust the given number up or down to indicate their desired investment. Subsequently, they received feedback about their protagonist's investment, and were shown the respective payoffs to oneself and to the protagonist (who was randomly chosen on each trial from a pool of 150 predator [prey] investments, see below). This completed one trial. Data for one participant were discarded because of answers to quiz questions indicated failure to understand the payoff structure.

Trial feedback during the experiment was real and the “no deception policy” was explicitly stated on several occasions during the recruitment and instruction phase. For each trial that participants in the MRI-scanner played (henceforth “scanner participant) s/he was paired to a matching trial that was played by a randomly selected subject in an independent behavioral experiment (henceforth “non-scanner participant”). This behavioral experiment involved a 2 (Order: Predator Role first/second) x 2 (Role: Predator vs. Prey) factorial, with the second factor

within-participants. Fifteen students served as “non-scanner participants.” They were invited to a study on investment decisions and arrived in the laboratory in groups of 2 to 4, where they provided informed consent, and were placed in individual, soundproof cubicles preventing them from seeing and/or communicating with others. After participants were seated, the experimenter handed them instructions that were identical to those given to the scanner-participants. Non-scanner participants made 10 decisions as predator, denoted as Role A (or prey, denoted as Role B), followed by 10 decisions as prey, denoted as Role B (or predator, denoted as Role A). For each investment decision, non-scanner participants were reminded that actual pay was at stake, in that out of the 10 trials they played in Role A (and later or earlier in Role B), one trial would be randomly chosen to be matched with a randomly chosen investment decision of their counterpart (i.e., the investment decision made by the matched scanner-participant). For each decision, participants entered a number between 0 (no investment) and 10 (their entire endowment), and they indicated how confident they were their investment was sufficient to settle the game in their favor (both 1=not at all, to 5=very much; not analyzed).

The 15 non-scanner participants in the behavioral experiment thus produced 15 x 10 trials = 150 prey investments, and 15 x 10 trials = 150 predator investments. In line with the results from the *fMRI* experiment (see below) average investments across the 10 trials were higher than theoretically predicted and higher among prey than predator ( $M = 5.953$ ,  $SD = 1.782$  versus  $M = 4.953$ ,  $SD = 1.821$ ;  $F(1, 14) = 6.76$ ,  $p = 0.021$ ). These 150 predator and 150 prey decisions generated in this behavioral experiment provided the pool of trials from which we randomly chose one on each trial and for each scanner-participant to provide actual feedback to the decision made by the scanner-participant. Thus, the scanner-participant played a trial as predator (prey), and feedback was given based on a randomly chosen investment decision made by a non-scanner

participant in the role of prey (predator). We verified that, in the *f*MRI study, there were no inadvertent effects of Treatment on the investments from the randomly chosen (non-scanner) protagonists,  $F(1, 26) < 1$ . This indicates that our procedures provided scanner-participants in oxytocin and placebo conditions with similar “tough” protagonists, and rules out the possibility that results from the *f*MRI experiment were (partially) due to differences in feedback provided.

After both the behavioral experiment and the scanner-experiment were completed, we determined actual earnings by non-scanner and scanner-participants (range €0 – €8, with  $M = €5$  for non-scanner participants, and €0 – €33, with  $M = €19$  for scanner participants). Participants received their participation fee and earnings by bank transfer; the acting administrator was unaware of the fact that the money was earned in a decision making experiment. Accordingly, at any point deception was avoided and participant pay was private and conditioned on their performance.

***NeuroImage Acquisition.*** Scanning was performed on a 3T Philips Achieva TX MRI scanner using a 32-channel head-coil. Each subject participated in two scanning sessions, one for the placebo and one for the oxytocin condition. Each session consisted of six blocks of the predator-prey game during which functional data were acquired using a gradient-echo, echo-planar pulse sequence (TR = 2000 ms, TE = 27.63 ms, FA = 76.1°, 280 volumes, FOV = 192<sup>2</sup> mm, matrix size = 64<sup>2</sup>, 38 ascending slices, slice thickness = 3 mm, slice gap = 0.3 mm) covering the whole brain. We also recorded a 3DT1 recording in one of the sessions (3D T1 TFE, TR = 8.2 ms, TE = 3.8 ms, FA = 8°, FOV = 256<sup>2</sup> mm, matrix size = 256<sup>2</sup>, 160 slices, slice thickness = 1 mm). During acquisition we also recorded respiration and the pulse oximetry signal and the breath-rate of the subject. Stimuli were back-projected onto a screen that was viewed through a mirror attached to the head-coil.

FEAT (fMRI Expert Analysis Tool) version 4.1, part of FSL [Oxford Centre for Functional MRI of the Brain (FMRIB) Software Library; [www.fmrib.ox.ac.uk/fsl](http://www.fmrib.ox.ac.uk/fsl)] was used to analyze the fMRI data (Woolrich et al., 2009; Smith, Jenkinson et al., 2004). Preprocessing steps included slice-time correction, motion correction, high-pass filtering in the temporal domain ( $\sigma = 100$  s), spatially filtered (5mm) and pre-whitening (Woolrich et al., 2009). Apart from the modeled condition we also included, in the GLM, nuisance variables for movement (6 parameters), the pulse oximetry signal (1 parameter) and respiration (2 parameters). The respiration parameters were modeled using the PhLEM toolbox (Versteynen & Deshpande, 2011).

Structural images were co-registered to the functional images and transformed to MNI standard space (Montreal Neurological Institute) using FLIRT (FMRIB's Linear Image Registration Tool; FSL) and FNIRT (FMRIB's Linear Image Registration Tool). The resulting normalization parameters were applied to the functional images. We excluded between 1 and 4 blocks of 8 subjects and removed 2 subjects completely because of excessive head movement. Given past work on oxytocin showing differential effects on left and right amygdala (Baumgartner et al., 2008; Rilling et al., 2012), and decision making research indicating bilateral activation in the superior frontal gyrus (Polosan et al., 2011; Chaminade et al., 2012, Kruschwitz et al., 2012), subcortical ROIs (left and right amygdala) were segmented per individual using FIRST (Patenaude, Smith, Kennedy, & Jenkinson, 2011) and the cortical ROI (bilateral superior frontal gyrus) were generated on the basis of the Harvard-Oxford atlas included in FSL (Woolrich et al., 2009). The normalized predictor estimates were extracted from each region of interest (weighted for the probabilistic Harvard-Oxford atlas), per subject, per condition, and averaged over voxels. The resulting values were analyzed using SPSS.

## Analyses and Results

Making the standard assumption of rational selfish behavior, with an endowment of 10 (euro) per trial, the following mixed strategies for predator (with probability of investing  $X$  denoted by  $p(X)$ ) and prey (with probability of investing  $Y$  denoted by  $p(Y)$ ) define a unique Nash equilibrium for PPG: Predator:  $p(X = 1) = 2/45$ ,  $p(X) = p(X - 1)[(12 - X)/(10 - X)]$  for  $2 \leq X \leq 6$ ,  $p(X = 0) = 1 - [p(X = 1) + \dots + p(X = 6)] = 0.4$ , and  $p(X) = 0$  for  $X \geq 7$ ; Prey:  $p(Y) = 1/(10 - Y)$  for  $0 \leq Y \leq 5$ ,  $p(Y = 6) = 1 - [p(Y = 0) + \dots + p(Y = 5)] = 0.15$ , and  $p(Y) = 0$  for  $Y \geq 7$ . In the PPG it is collectively irrational and wasteful to invest in either predation or defense, because the money involved is lost for both predator and prey. Nevertheless, it is individually rational to invest, as indicated by the Nash-equilibrium. On average, prey is expected to invest 3.38 per trial and predator 2.62. This can be broken down into a prediction for *aggression frequency* (expected number of trials per block in which an investment is made; range 0 - 5) which equals 3 for predator and 4.5 for prey, and a prediction for *force of aggression* (expected investment across five trials, with no-investment excluded; range 1 - 10) which equals 4.36 for predator and 3.75 for prey.

Neither Session (whether placebo was given first or second) nor Trial Block interacted with Treatment and Role (all  $F < 2.7$ , all  $p > 0.18$ ) and we proceeded by collapsing investment decisions across these factors. Figure 2 shows the distribution of investment choices for predator and prey. In line with game-theoretical predictions, we find that participants do invest, that investments are spread, and that prey clearly invests more than predator. Unlike these game-theoretical predictions, but fitting regular findings in experimental contests (Abbink, 2012), both

predator and prey overinvest: the spread of investment levels frequently exceeds 6, which should never occur theoretically. These results are suggestive for not fully rational but impulsive behavior. Our treatment effect findings, discussed next, are supportive in this respect.

Figure 2 suggests that predators under oxytocin opt for lower investment than predators given placebo, and that prey under oxytocin opt for higher investments than those given placebo. To test this, we first analyzed average investment across trials in a 2(Role: Predator/Prey) x 2(Treatment: Oxytocin/Placebo) within-subjects Analysis of Variance (ANOVA). This revealed no effect for treatment,  $F(1, 26) = 0.38, p = 0.541, \text{partial } \eta^2 = 0.015$ , a main effect for Role,  $F(1, 26) = 36.03, p = 0.001, \text{partial } \eta^2 = 0.581$ , and a marginally significant interaction among Role and Treatment,  $F(1, 26) = 3.48, p = 0.074, \text{partial } \eta^2 = 0.118$ . Means and standard deviations are shown in Table 1. Fitting SAA, oxytocin somewhat reduced overall investment in predators, directional  $t(26) = 1.50, p = 0.073, \text{partial } \eta^2 = 0.080$ . Oxytocin did not significantly increase investment among prey,  $t(26) = 0.87, p = 0.392, \text{partial } \eta^2 = 0.028$ .

A similar pattern of results was obtained when we analyzed force of aggression (average investment across trials, with no-investment trials excluded; range 1 - 10). ANOVA revealed no Treatment effect,  $F(1, 26) = 0.20, p = 0.650, \text{partial } \eta^2 = 0.001$ , a significant Role effect,  $F(1, 26) = 37.31, p = 0.001, \text{partial } \eta^2 = 0.570$ , and a marginal Role x Treatment effect,  $F(1, 26) = 3.91, p = 0.059, \text{partial } \eta^2 = 0.11$ . Mean force patterned as predicted in SAA, and not in FD (see Figure 3A). Compared to placebo, oxytocin reduced force of aggression in predators, directional  $t(26) = 1.733, p = 0.048, \text{partial } \eta^2 = 0.056$ , and did not significantly increase force of aggression in prey, directional  $t(26) = 1.243, p = 0.12, \text{partial } \eta^2 = 0.056$ .

Figure 3B shows aggression frequency (average number of trials within blocks in which investments were made; range 0 - 5). A Role (Predator/Prey) x Treatment (Placebo/Oxytocin)

within-subjects ANOVA revealed no Treatment effect,  $F(1, 26) = 1.12, p = 0.300$ , partial  $\eta^2 = 0.041$ , and significant Role,  $F(1,26) = 10.48, p = 0.003$ , partial  $\eta^2 = 0.287$ , and Role x Treatment effects,  $F(1, 26) = 4.50, p = 0.044$ , partial  $\eta^2 = 0.148$ . Directional t-tests revealed that compared to placebo, oxytocin reduced aggression frequency among predators,  $t(26) = 2.035, p = 0.026$ , partial  $\eta^2 = 0.137$ , but did not reduce or increase aggression frequency in prey,  $t(26) = 0.53, p = 0.478$ , partial  $\eta^2 = 0.019$ . These results fit SAA and were not anticipated by FD.

In addition to investments, we analyzed decision latency. If indeed greed-driven investments among predators are more calculated whereas fear-driven investments among prey are relatively impulsive, the former should take more time (Rand, Greene, & Nowak, 2012). Furthermore, FD implies that oxytocin slows down decision-making among prey because it reduces impulsive fear; SAA, on the other hand, implies that oxytocin accelerates decision-making among predators because it promotes pro-social approach and tempers calculated greed. We analyzed decision time averaged across trials in a 2(Role: Predator/Prey) x 2(Treatment: Oxytocin/Placebo) ANOVA (observed latencies are shown because log-transformation reduced skewness but did not affect results). This revealed a Treatment x Role interaction,  $F(1, 26) = 4.26, p = 0.049$ , partial  $\eta^2 = 0.141$ . Directional t-tests show that predators took less time when given oxytocin rather than placebo,  $t(26) = 1.749, p = 0.046$ , partial  $\eta^2 = 0.105$  (see Table 1, and Figure 3C); correlational analyses revealed that shorter decision latency tended to associate with frequency of predator attack ( $r = -0.304, p = 0.12$ , versus  $r = -0.254, p = 0.202$ ), but these relationships were not significant. Prey decision latencies were not influenced by treatment,  $t(26) = 0.16, p = 0.782$ , partial  $\eta^2 = 0.003$ ; and correlational analyses revealed that decision latency did not associate with reduced frequency of prey defense ( $r = -0.002, p = 0.991$ , and  $r = -0.206, p = 0.31$ ). Results fit with SAA, although they could have been stronger.

Finally, we considered neural activity in (left and right) amygdala and (bilateral) superior frontal gyrus regions of interest (ROIs) during and collapsed across investment decisions. Figure 4A shows right amygdala activation as a function of Treatment x Role,  $F(1, 26) = 6.35$ ,  $p = 0.018$ , partial  $\eta^2 = 0.196$ . Oxytocin compared to placebo dampened amygdala in predators,  $t(26) = 2.48$ ,  $p = 0.020$ , partial  $\eta^2 = 0.202$ , but not in prey,  $t(26) = 0.01$ ,  $p = 0.99$ , partial  $\eta^2 = 0.008$ . This interaction effect was replicated in the left amygdala,  $F(1, 26) = 5.92$ ,  $p = 0.022$ , partial  $\eta^2 = 0.185$ : Oxytocin compared to placebo reduced amygdala activity in predators ( $M = -0.161$  vs.  $M = 0.257$ ;  $t(26) = 2.57$ ,  $p = 0.016$ , partial  $\eta^2 = 0.192$ ), but not in prey ( $M = 0.197$  vs.  $M = 0.116$ ;  $t(26) = 0.41$ ,  $p = 0.646$ , partial  $\eta^2 = 0.002$ ). These results fail to confirm the FD prediction that oxytocin dampens amygdala among prey; maintained amygdala activation is consistent with SAA. Dampened amygdala among predators given oxytocin was anticipated by neither hypothesis.

Figure 4B shows activation in the superior frontal gyrus time-locked to investment decisions. Although Role, and Role x Treatment effects were not significant, both  $F(1, 26) < 2.64$ ,  $ps > 0.12$ , the effect for oxytocin was,  $F(1, 26) = 13.71$ ,  $p = 0.001$ , partial  $\eta^2 = 0.345$ . As can be seen in Figure 4B, oxytocin compared to placebo reduced activation in the superior frontal gyrus. Figure 4B also shows that this effect of oxytocin was particularly pronounced in predators,  $t(26) = 4.096$ ,  $p = 0.001$ , partial  $\eta^2 = 0.392$  (in prey,  $t(26) = 2.29$ ,  $p = 0.030$ , partial  $\eta^2 = 0.168$ ). This effect is consistent with the SAA prediction of tempered calculated greed, and is not anticipated in FD.

Correlational analyses revealed no relationships between neural activity in amygdala or superior frontal gyrus on the one hand, and decision latency on the other (all  $-0.11 < r < 0.265$ , all  $ps > 0.190$ ). However, co-variance analyses (see also Figure 1) revealed a significant regression

of investment decisions in prey on right amygdala,  $\beta = 0.412$ ,  $t = 2.258$ ,  $p = 0.033$ ; no such relationship emerged for decision making in predators,  $\beta = 0.01$ ,  $t = 0.13$ ,  $p = 0.989$ . Oxytocin did not modulate these relations, all  $ps > 0.20$ . Across treatment conditions, predator investments were (marginally) correlated with superior frontal gyrus activation,  $\beta = -0.331$ ,  $t = -1.756$ ,  $p = 0.091$ ; no such relationship emerged in prey,  $\beta = -0.017$ ,  $t = -0.284$ ,  $p = 0.778$ . These correlations provide some initial evidence that while defensive aggression in prey is conditioned on the (right) amygdala, greed-driven aggression in predators is calculated and conditioned on the superior frontal gyrus.

### **Conclusions and Discussion**

Results showed that oxytocin modulates greed-driven predation and leaves unaffected fear-driven prey defense. Compared to placebo, oxytocin reduced investments among predators, reduced the time predators take to decide, and dampened activity in both amygdala and superior frontal gyrus. We conclude that predator investment is calculated, and that oxytocin reduces the greedy appetite to accumulate wealth at the expense of others. With regard to prey defense, we observed that oxytocin (compared to placebo) had little effect. Regardless of treatment, prey invested frequently and forcefully, did so relatively fast, and fear-driven prey defense was conditioned upon (right) amygdala. We conclude that prey defense is impulsive rather than calculated, and that oxytocin does not incapacitate such impulsive defense.

From earlier work we derived two largely competing predictions about the possible effects of oxytocin on cooperative and competitive decision making. The FD hypothesis is grounded in oxytocin's anxiolytic effects (Meyer-Lindenberg et al., 2011; Baumgartner et al., 2008; Kirsch et al., 2005) and implies effects of oxytocin especially in prey; the SAA hypothesis (Guastella et al., 2008; Kemp & Guastella, 2011; Striepens et al., 2012), in contrast, predicted

effects of oxytocin especially in predators. Results fit the latter prediction, and are difficult to reconcile with the FD hypothesis. Furthermore, results fit recent work by Rilling and colleagues (2012) who had participants given oxytocin or placebo making cooperation decisions in prisoner's dilemma games with partners who cooperated or who not cooperated. When partners responded with non-cooperation to participant's cooperation, and thus exploited them, oxytocin did neither increase nor decrease cooperation compared to placebo. As in the current study, oxytocin seems to have no impact on participants seeking to protect themselves against exploitation. Accordingly, we conclude that in social exchange problems oxytocin modulates cooperation and aggressive tendencies because it tempers (calculated) greed more than it mitigates (impulsive) fear of being exploited.

The fear-dampening hypothesis derived from oxytocin's anxiolytic effects (Carter, 2014; MacDonald & Feifel, 2014), and especially studies showing oxytocin dampens (amygdala) responding to threatening stimuli and fearful facial expressions (e.g., Kirsch et al., 2005; Petrovic et al., 2008; for a review see Meyer-Lindenberg, Kirsch, Domes, & Heinrichs, 2011). The current study allows for the possibility that oxytocin has such anxiolytic effects in these contexts yet highlights that these do not translate into reduced vigilance and readiness to aggress and defend oneself against predation. Accordingly, current results illustrate a broader point, namely that neural responses such as reduced activation in brain regions typically associated with vigilance and threat-detection (e.g., amygdala) not necessarily lead to reduced vigilance and threat-detection, let alone peaceful generosity and defenseless surrender. At best, we would argue, reduced fear-responding at the brain level permits but not necessarily leads to increased pro-social approach.

Although our findings fit the pro-social approach/inhibited avoidance hypothesis better than the fear-dampening hypothesis, effect sizes were sometimes small and replication studies would be welcome. New studies could address also whether current findings, obtained with a male sample, extend to female participants as well. Doing so would be important not only because relatively few administration studies include female participants, and recent work suggest oxytocin may have qualitatively different effects on cooperation and related brain circuitries in males compared to females (Rilling, DeMarco, Hackett, Chen, Gautam, et al., 2014). In addition, including females would enable the testing of specific predictions regarding sex differences in aggression (e.g., Archer & Coyne, 2005). An interesting hypothesis, grounded in evolutionary theory, is that female aggression, compared to male aggression, is constrained by the greater centrality of mothers' to offspring survival, and this resulted in a lower threshold for fear among women (Campbell, 2013). Work in economic decision making indicates that women, compared to men, are more generous and more likely to cooperate (Croson & Gneezy, 2009). In terms of predator-prey contests, this suggests that compared to males observed in the current study, females may be less aggressive in both predator and prey roles.

Some scientists proposed that oxytocin increases social salience, such that what is positive and attractive becomes more positive and attractive under oxytocin while what is negative and aversive becomes more negative and aversive (Bartz et al., 2011; Shamay-Tsoory et al., 2009). Within predator-prey contests, the social-salience hypothesis implies increased fear and defense-related aggression among prey, which we did not find. With regard to predator greed, the social-salience hypotheses is less clear-cut. When we assume that greedy aggression is the default among predators, the social salience hypothesis predicts increased predator aggression under oxytocin, which we clearly did not observe. Because there is no evidence for this

assumption, however, the current context neither allows a test of the social-salience hypothesis, nor any conclusions about its validity. Future work aimed at discriminating between the social approach/avoidance hypothesis and the closely related social-salience hypothesis may proceed by identifying individual differences that dictate default tendencies in predators to aggress versus to appease, and among prey to aggress versus to withdraw. Such individual differences should have little effect under the currently supported social approach/avoidance framework, but should interact with oxytocin under the social-salience prediction.

Two findings regarding oxytocin were not anticipated, and may be specific to the predator-prey conflict examined here. First, we observed reduced activation in the amygdala for predators given oxytocin. Predation is, as argued, relatively instrumental and deliberated, but may not only recruit prefrontal activation related to impulse-control and cost-benefit analyses, but also sub-cortical circuitries involved in threat-detection and emotion-regulation (i.e., for predators the possibility of loss and injury are not at all excluded). Oxytocin in predators lowered decision latency, reduced activation in the superior frontal gyrus, and dampened activation in the amygdala. Combined this suggests that oxytocin lowers greedy appetite and therefore the risk of losing out; hence not only activation in the superior frontal gyrus but also in the amygdala was observed. Second, we observed reduced activation in the superior frontal gyrus for prey given oxytocin; possibly oxytocin reduces impulse-control in both predators and prey, with quite different consequences—reduced aggression in predators and maintained or even increased aggression in prey. We note, however, that we only obtained correlational evidence supporting the link between superior frontal gyrus and predator aggression.

The Predator-Prey Game enables a decomposition of competitive decision making, and aggression, in terms of its two core motives of greed and fear (Camerer, 2003; Coombs, 1973;

Ostrom, 1998). We uncovered that competition is relatively deliberate and calculated when greed-motivated, and relatively impulsive when fear-driven. In addition, we observed that human decision makers switched within a few trials from predator to prey and back, with massive consequences—aggression was up- or down-regulated instantly, associated neural circuitries were differentially activated, and neurohormonal modulation by oxytocin was flipped between present and absent. The human species operates as both predator and prey, and social contexts may dictate alternating roles; the ability to immerse oneself into either role swiftly and confidently sustains survival as well as prosperity (Salan et al., 2011). Our data suggest that humans evolved a capacity to compete impulsively as well as deliberately, and that greed rather than fear gives way to the evolutionary ancient oxytocinergic circuitry.

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Table 1

Means and Standard Deviations for Behavioral Responses in Predator-Prey Conflict broken down by Role and Treatment.

	Predator		Prey	
	Placebo	Oxytocin	Placebo	Oxytocin
Overall Investment	3.504 (2.218)	3.198 (2.360)	6.074 (1.397)	6.210 (0.959)
Force of Attack	4.208 (1.752)	3.924 (1.836)	6.275 (1.184)	6.449 (0.853)
Frequency of Attack	3.963 (1.407)	3.753 (1.552)	4.833 (0.704)	4.895 (0.304)
Decision Latency	4523.52 (1309.68)	4104.03 (1136.37)	4215.41 (1511.47)	4364.04 (1785.87)

*Note.* Entries are averages within 5-trial blocks; Standard deviations in brackets ( $N = 27$ ); Overall Investment ranges between 0 – 10; Force of attack ranges between 1 – 10; Frequency of attack ranges between 0 – 5; Decision Latency ranges between 0 – 6000ms.

### Figure Legend

Fig 1. Outline of Decision Trial, Regions of Interest (Superior Frontal Gyrus shown above; Right Amygdala shown below), and their regressions on investment decisions. Fixation was jittered at 6000-9000ms, and decision making (and trial feedback) was maximized at 6000ms. Scatterplot shows predator (prey) investments associate negatively (positively) with Superior Frontal Gyrus (Right Amygdala).

Fig 2. Frequency with which investment options were chosen, compared to game-theoretic predictions. **(A)** Predators aggress more frequently than predicted, and overinvest; **(B)** Prey aggress more frequently than predicted, and overinvest substantially.

Fig 3 Aggression in predator and prey as a function of treatment. **(A)** Force of aggression in predators and prey under oxytocin versus placebo (range 1-10, displayed  $\pm$ SE); **(B)** Compared to placebo, oxytocin reduces aggression frequency of predator but not of prey (range 0-5, displayed  $\pm$ SE); **(C)** Compared to placebo, oxytocin reduces time in milliseconds taken to decide in predators but not in prey (range 0—6000; displayed  $\pm$ SE). Contrasts marked with \* are significant at  $p < 0.05$  (directional t-tests, with  $N = 27$ ).

Fig 4 Activation in amygdala and superior frontal gyrus as a function of treatment and role. **(A)** Oxytocin dampens right amygdala in predators but not in prey (normalized activity; displayed  $\pm$ SE); **(B)** Oxytocin reduces activation in superior frontal gyrus (SFG) in predators more than in prey (normalized activity; displayed  $\pm$ SE). Contrasts marked with \* (\*\*) are significant at  $p < 0.05$  ( $p < 0.025$ ) (directional t-tests, with  $N = 27$ ).

Fig 1

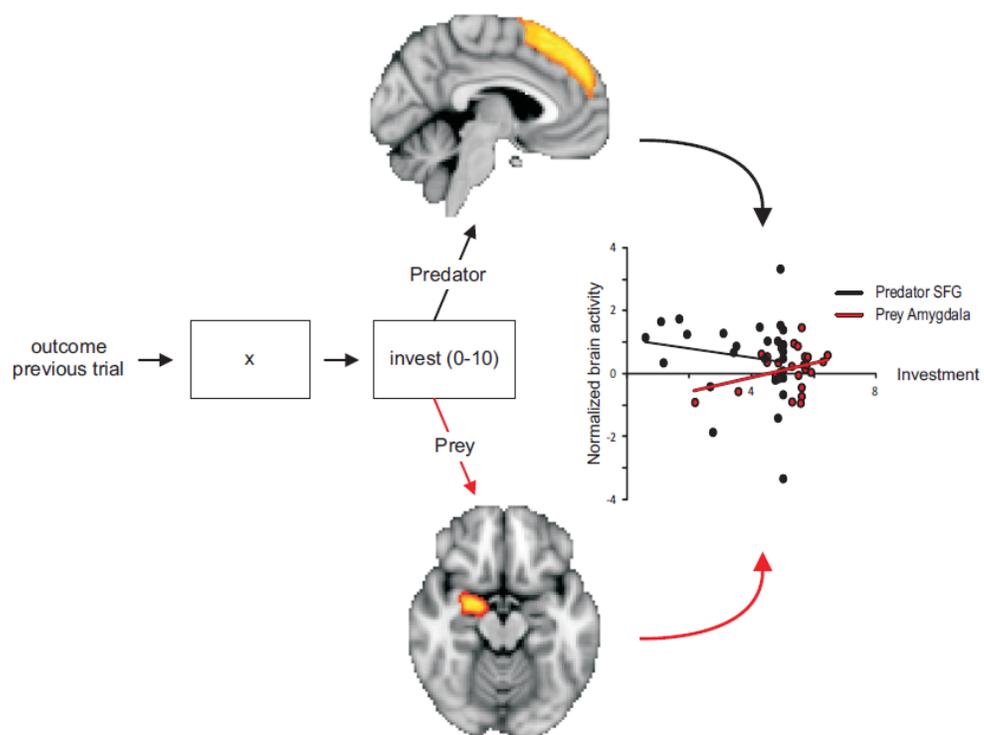


Fig 2

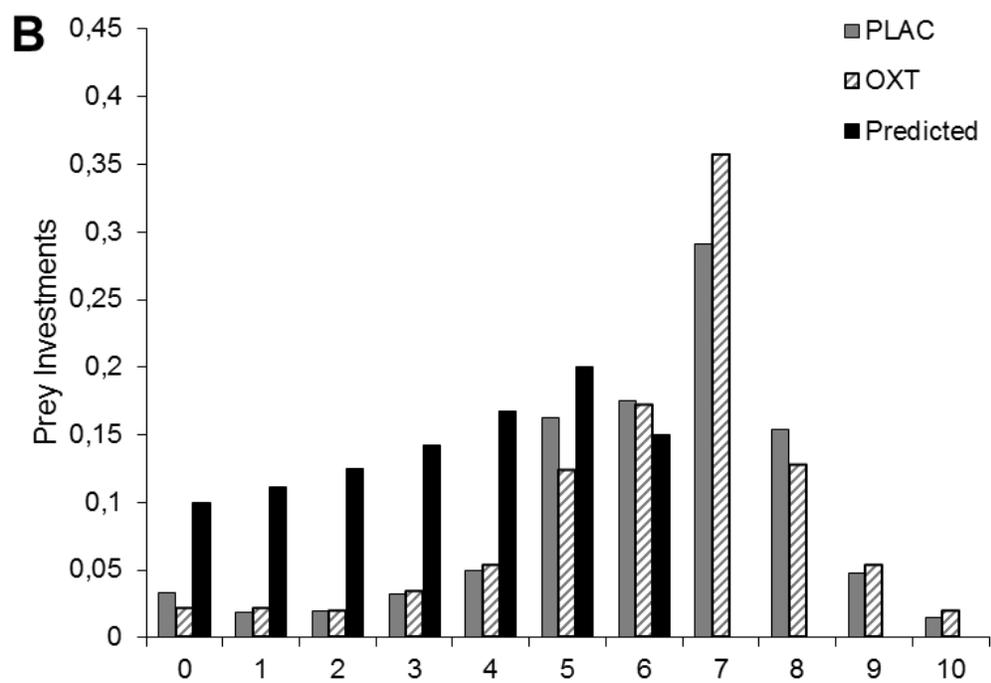
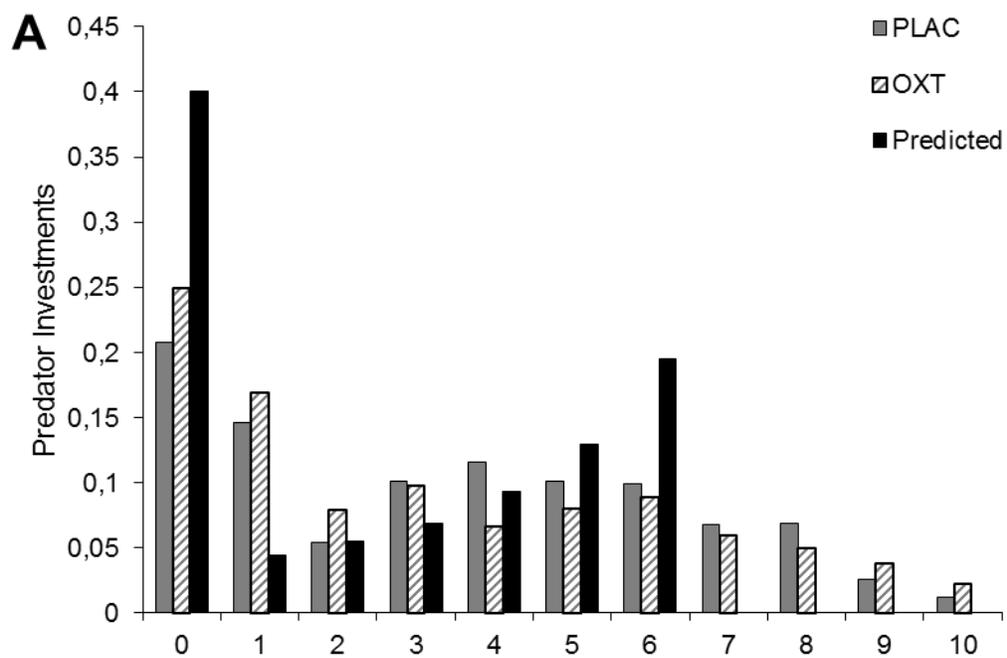


Fig 3

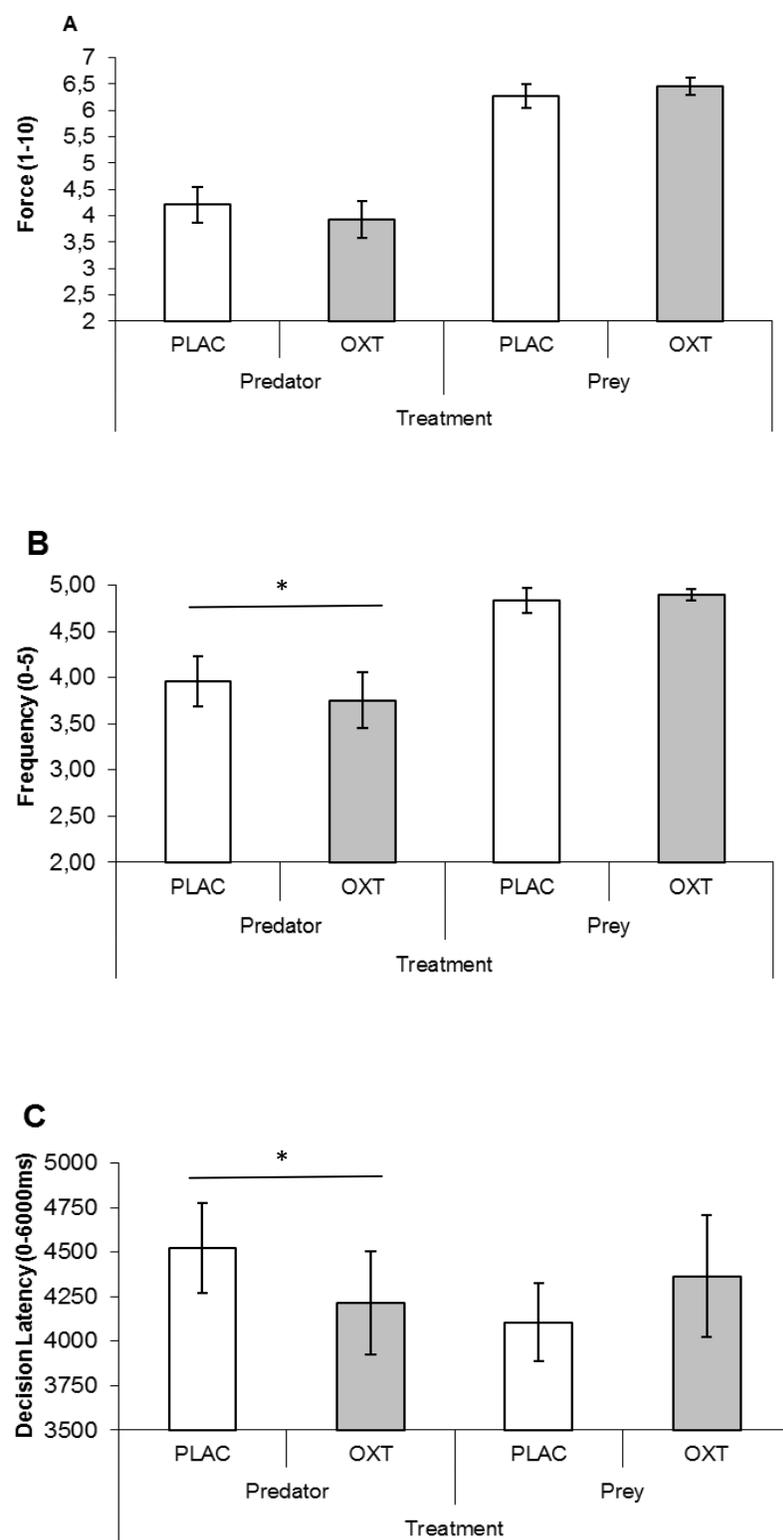


Fig 4

