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Vasopressin modulates neural responses during human reactive aggression

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The neuropeptide arginine vasopressin (AVP) is known to modulate aggressive behavior in mammals, but the neural mechanisms underlying this modulation are not clear yet. In the present study, we administered 20 IU AVP nasally in a randomized, placebo-controlled, double-blind manner to 36 healthy men using a between-subjects design. After drug administration, participants performed a competitive reaction time task (Taylor Aggression Paradigm, TAP) to elicit reactive aggressive behavior while functional magnetic resonance imaging was recorded. Under AVP treatment, we found increased activations in the right superior temporal sulcus in the decision phase during trials in which participants could get punished after losing the reaction time competition. At the behavioral level, no differences could be found between AVP treatment and placebo condition. The lack of AVP-related behavioral effects is discussed in terms of the general aggression model (GAM).

Keywords: Vasopressin; Aggression; Double blind; fMRI; General aggression model; Superior temporal cortex.

Reactive aggression is defined as a direct retaliating response to a perceived threat or provocation. According to Dodge and Coie, "perceptions of threat and experiences of anger push the reactively aggressive individual to retaliate" (Dodge & Coie, 1987 p. 1147). In contrast, proactive aggressive behavior is characterized as calculated and goal-directed acting with the intention to harm another person. The general aggression model (GAM) by Anderson and Bushman (2002) provides a theoretical framework for human aggressive behavior and posits that situational and personal variables influence aggressive behavior via the moderating impact of affect, cognition, and arousal. Situational variables include the provocation by another person, frustration, pain, and drugs, while personal variables comprise (among others) personality traits, sex, beliefs, and attitudes. According to the GAM, these feed into appraisal and decision processes that finally cause impulsive or thoughtful actions (Anderson & Bushman, 2002; Krämer, Jansma, Tempelmann, & Munte, 2007).

An established paradigm in social psychology is the Taylor aggression paradigm (TAP), which elicits reactive aggression in the laboratory by provoking the participant during a competitive reaction time task. During winning trials, participants are allowed to punish their opponent player, for example, with a loud noise or an electric shock of variable intensity, whereas during losing trials participants get punished by their opponent player. Since the aggressive interaction in the TAP is separated into a decision phase (selection of punishment level for the opponent player) and an outcome phase (punishment is applied or received), the paradigm is attractive for

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neuroscientific research as it allows to disentangle the neural underpinnings of different emotional and cognitive processes during reactive aggressive interaction. For example, Krämer et al. (2007) used functional magnetic resonance imaging (fMRI) and a version of the TAP in which healthy participants played in alternating trials against an unfair (high provocation) and a fair (low provocation) opponent in a competitive reaction time task with the punishment comprising aversive noise of different intensities as punishment. For the decision phase, provocation-dependent activations were seen in the bilateral anterior insula and the rostral part of the anterior cingulate cortex (ACC), brain regions that have been previously associated with negative emotions like anger or disgust (Damasio et al., 2000; Dougherty et al., 1999; Phillips et al., 1997). Aggressive behavior, as a direct response to provocations of the unfair opponent, was linked to enhanced neural activity within the dorsal striatum which, according to previous neuroimaging studies, is involved in reward processing (Balleine, Delgado, & Hikosaka, 2007; de Quervain et al., 2004; O'Doherty et al., 2004), but is also known to be active during effective punishment (de Quervain et al., 2004). Krämer et al. (2007) argued that this activation probably reflects the participants' anticipation to receive less provocations by their opponent player in the following trials. Besides the dorsal striatum, reactive aggressive behavior was further linked to increased activations in the dorsal part of the ACC, a brain site that has been associated with conflict monitoring and cognitive control in numerous previous studies (e.g., Botvinick, Nystrom, Fissell, Carter, & Cohen, 1999; Carter & Van Veen, 2007; Cohen, Botvinick, & Carter, 2000; Milham et al., 2001; Nelson, Reuter-Lorenz, Sylvester, Jonides, & Smith, 2003; Van Veen & Carter, 2002). For the outcome phase, Krämer et al. (2007) reported enhanced neural activity in the ventral striatum/nucleus accumbens associated for win compared to loss trials, which might reflect the rewarding properties of the avoidance of the opponents' punishment.

The question arises to what extent reactive aggression is modulated by neurotransmitter systems and/or neuropeptide hormones. With regard to the former, serotonin has been implicated by a wealth of studies in impulsive aggression (Bjork, Dougherty, Moeller, Cherek, & Swann, 1999, 2000; Cleare & Bond, 1995; Coccaro & Kavoussi, 1997; Manuck, Kaplan, & Lotrich, 2006; Moss, Yao, & Panzak, 1990; Pihl et al., 1995), even though a study using the TAP in conjunction with fMRI and an acute tryptophan depletion, a pharmacological manipulation known to reduce brain serotonin level, did not reveal any marked effects (Krämer, Riba, Richter, & Munte, 2011). One suggested pathway of serotonin to control aggressive behavior and the motivation to act aggressive is via an antagonistic impact on brain sites related to the regulation of the social neuropeptide arginine vasopressin (AVP, Ferris et al., 1997, 2008). Research on animal models have shown, that AVP itself is a key player in the control of aggression and other "male-typical behaviors" (Heinrichs & Domes, 2008) like pair-bond formation and stress responsiveness (Bos, Panksepp, Bluthe, & Honk, 2012; Caldwell & Albers, 2004; Ferris & Delville, 1994; Ferris et al., 1997; Goodson & Bass, 2001). For example, in animals like male Golden and Syrian hamsters, microinjections of AVP into the anterior hypothalamus and the lateral septum increased the number of aggressive interactions, while microinjections of AVP receptor 1a (AVPR1a) antagonists into the anterior hypothalamus inhibited aggressive behavior against intruders (Bos et al., 2012; Caldwell & Albers, 2004; Ferris & Delville, 1994; Ferris et al., 1997). In humans, there is actually little evidence for a direct link between AVP and reactive aggression. However, a first hint was given by Coccaro, Kavoussi, Hauger, Cooper, and Ferris (1998) reporting a positive correlation between cerebrospinal fluid AVP levels and life histories of general aggression, which was more pronounced for men than for women. Research by Thompson, Gupta, Miller, Mills, and Orr (2004) suggested that AVP acts on processes related to emotional social communication, which in turn could promote reactive aggressive behavior. In their initial study, they investigated facial electromyogram (EMG), while male participants watched facial expressions. Intranasally administered AVP led to an increase of EMG responses to neutral faces to a level comparable to that observed for angry faces in the placebo group. Thompson et al. (2004) argued that AVP alters the interpretation of social stimuli that are taken as if they were threatening. In a consecutive investigation, Thompson, George, Walton, Orr, and Benson (2006) described that, in men, AVP enhances agonistic facial motor patterns in response to faces of unfamiliar men and decreases the perception of the friendliness of those faces. In women, however, AVP stimulated affiliative facial motor patterns in response to faces of unfamiliar women and increased perceptions of those faces' friendliness. In a recent study, Uzefovsky, Shalev, Israel, Knafo, and Ebstein (2012) reported an inverse pattern of results. Their study revealed for men treated with AVP an impairment in the recognition of negative emotions while leaving the perception of positive emotions unaffected. According to the work by Guastella, Kenyon, Alvares, Carson, and Hickie (2010) and Guastella, Kenyon, Unkelbach,

Alvares, and Hickie (2011), the impact of AVP on the processing of social and interpersonal information is less specific. Instead, AVP seems to enhance the processing of social information generally, irrespective of the stimulus category's valence. Up to now, just a few studies using functional MRI have tried to elucidate the neural underpinnings of AVP's impact on the processing of social information. Zink, Stein, Kempf, Hakimi, and Meyer-Lindenberg (2010) and Zink et al. (2011) reported in men an impact of AVP administration on the brain's fear regulatory system (Zink et al., 2010) during an emotional-face matching task and also changes in the activity of the temporo-parietal junction (TPJ), a brain area known to be a key site in the theory of mind network, when processing socially relevant familiarity information (Meyer-Lindenberg, Domes, Kirsch, & Heinrichs, 2011). Additional evidence for AVP's modulatory influence on social behavior is given by Rilling et al. (2012). In their prisoner's dilemma paradigm, they reported for men treated with AVP, but not for men treated with oxytocin or placebo, increased cooperation in response to cooperative signs by the partner. In AVP-treated men who initiated such a cooperative interaction, the processing of the cooperative interaction's outcome resulted in increased activations in brain sites belonging to the vasopressin circuitry like the stria terminalis, the bed nucleus of the stria terminalis, and the lateral septum. In contrast to Rilling's behavioral results, Israel, Weisel, Ebstein, and Bornstein (2012) failed to find significant evidence for an impact of AVP on cooperative behavior. However, their nested social dilemma paradigm does not comprise any kind of reciprocity between acting persons, which might explain the missing impact of AVP on cooperative behavior. These findings imply that AVP influences processes linked to social communication.

Even though previous fMRI studies on the TAP have not revealed differential activations of the amygdala (Krämer et al., 2007, 2011; Lotze, Veit, Anders, & Birbaumer, 2007), this group of nuclei is involved undoubtedly in the appraisal of threat and the regulation of aggressive behavior (Dougherty et al., 1999; Nelson et al., 2003). Interestingly, the central amygdala harbors high quantities of Vasopressin V1 receptors (Huber, Veinante, & Stoop, 2005; Veinante & Freund-Mercier, 1997). The amygdala is connected to a widespread network of brain regions involved in the regulation of aggressive behavior (e.g., Passamonti et al., 2008, 2012) and these connections may allow AVP to exert a modulatory influence on aggressive behavior.

By using fMRI and the TAP, the current study tries to delineate the impact of AVP on the neural basis of the distinct stages of human reactive aggression. Following Wiswede et al. (2011), a modified version of the TAP was used in which participants played against just one opponent who selected relatively high punishments. As previous investigations were ambiguous with regard to the meaning of certain brain activations (e.g., a particular activation on win trials might have been due the possibility to punish the opponent or due to the fact that punishment by the opponent had been avoided), "passive" and "active" blocks were introduced. In "passive" blocks participants were punished by a loud aversive tone on loss trials but could not administer a punishment to the opponent player on win trials, whereas in "active blocks" the participant could punish the opponent player on win trials but did not get punished on loss trials.

In light of the evidence linking AVP to enhanced aggressive behavior (Bos et al., 2012; Caldwell & Albers, 2004; Coccaro et al., 1998; Ferris & Delville, 1994; Ferris et al., 1997; Thompson et al., 2004, 2006), it was predicted that AVP would lead to the selection of higher punishment levels during the decision phase compared to placebo. In addition, this effect should be more pronounced during trials of the "active" block, where participants can punish the opponent when winning the trial. On the neural level, AVP was expected to modulate activity in the anterior insula and the ACC during the decision phase, as these have been revealed in previous studies using the TAP. In addition, the predicted AVP-related increase in negative affect in response to the relatively high provoking opponent might also elicit an increased feeling of reward when being able to punish the opponent in "active" trials which should be associated with an increase in blood-oxygen-level-dependent (BOLD) signal in the ventral striatum during "active" trials for the comparison of win trials versus loss trials. As the amygdala was not modulated in previous studies using the TAP, we had no expectations with regard to this structure.

METHODS

Participants

Thirty-six healthy adult male volunteers (age = 19–32, mean = 25.8, SD = 3.4) were recruited from a volunteers' database at the Department of Neurology of the University of Magdeburg. The groups did not significantly differ in their age (the AVP group: mean = 26.5, SD = 4.3 and the placebo group:

mean = 25.0, SD = 4.0). Participants of both the groups were students of the University of Magdeburg to assure a uniform education level. Subjects were right handed and reported to be free of any psychiatric and neurological disorder, kidney disease, cardiovascular problems, asthma, and migraine. Two subjects were removed from further analysis because of extensive movement artifacts and three were excluded because during the debriefing it became apparent that they had not been completely deceived by the experimental set-up. Thus, data analyses are based on 31 participants (16 treated with AVP) using a between-subjects design. All subjects gave written informed consent and were paid for participation. The study had been approved by the ethical committee of the University of Magdeburg and conducted in accordance with the Declaration of Helsinki.

Drug administration

Participants randomly received either an intranasal dose of 20 IU of AVP or a placebo in a double-blind manner. As in Born et al. (2002), nasal sprays were self-administered by the participants under the supervision of the experimenter. Each subject self-administered four sprays, two per nostril. The original 1-ml synthetic vasopressin solution (Goldshield Pharmaceutical Ltd., Croydon, UK) contained 0.5% chlorobutanol, while the only active substance was argipressin. In order to get 20 IU AVP per four sprays, the solution was filled up with 0.9% saline solution. In the placebo condition, four sprays of 0.9% saline solution were administered. Ten minutes before entering the scanner, AVP was self-administered by the subjects under the supervision of the experimenter. After 5 minutes of premeasures (T1 and IR-EPI image) and a further task lasting 20 minutes, participants started with the TAP 35 minutes after AVP administration. The entire duration of the experimental procedure was 24 minutes (12 minutes per run). Subsequently to the TAP a diffusion tensor imaging protocol (14 minutes) was performed. Finally, 120 minutes after AVP administration, subjects filled out the Buss and Perry Aggression Questionnaire (AQ) and the interpersonal reactivity index (IRI). The questionnaires were presented at the end of the session in order to avoid any hint to the main target of this paradigm's intention to induce aggression. There was no report of altered water retention or any other side effects when subjects were debriefed at the end of the experiment. Scanning sessions took place between 8 am and 6 pm.

Experimental procedure

Participants were told that they would play a reaction time task against another male player who unbeknownst to them was a confederate of the experimenter. They were informed that they have won a trial, whenever they responded faster than the opponent, but lost a trial, when the opponent responded faster. In the TAP's experimental procedure, it was predefined that, in two-third of the trials, the participant loses the competitive reaction time task. Prior to the experiment, the participant and the confederate were introduced to each other. The confederate was introduced as the other "player" the participant had to play against and was a male, 26-year-old student. The confederate was not acquainted with anybody of the participants. Before the participant entered the scanner, he had to complete eight test trials outside the scanner. After being convinced that the participant understood the task, the confederate was brought to another room and the participant was told that they would be interconnected via a network computer during the game. At the end of the experimental procedure, participants were debriefed by explaining the experimental set-up and the investigation aims.

Aggression paradigm

A modified version of the TAP was used in two runs. Each run consisted of six "passive" blocks and six "active" blocks. Each "passive" and "active" block comprised four trials and blocks were presented alternately. In "passive" blocks, the participant was punished when he lost the reaction time competition, while in "active" blocks the participant could administer a punishment to the opponent player in the case that he won during the reaction time task. The punishment was a loud polystyrene scratching noise presented at four different levels. The adjustment of the volume was accomplished prior to the experiment such that participants judged level 4 as unpleasant but not painful. Each trial started with a fixation phase which was followed by a decision phase during which the participant received an indication whether the actual trial was a "passive" or an "active" one by presenting either the German word for threat (in passive trials) or punish (in active trials; see Figure 1 illustrating the experimental procedure). In both, "active" and "passive" blocks, participants had to select the magnitude of the punishment (four different levels) during the decision phase. The selection of the punishment level was done by a button press on a keyboard with key 1 reflecting the lowest and key 4 reflecting the highest punishment level. The decision phase was followed by a "!", which

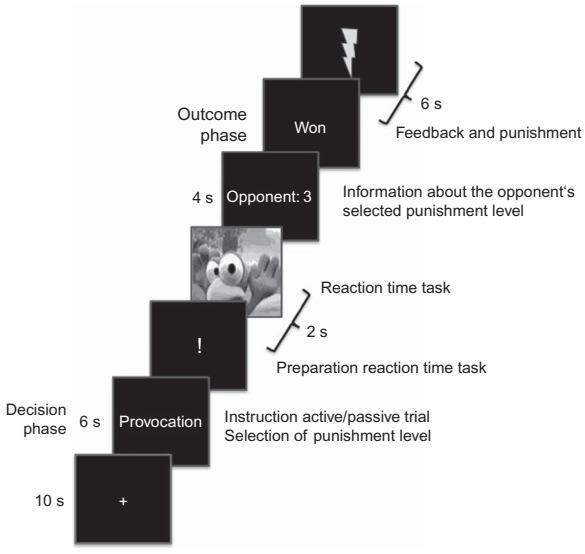

Figure 1. Trials of the experiment comprised a decision phase, the reaction time task, and an outcome phase. During the decision phase, participants made the selection of punishment level for the opponent (strength 1–4). This was then followed by the reaction time task where participants had to react as fast as possible when a chicken appeared on the screen. Directly after the reaction time task, they received feedback about the punishment level chosen by their "opponent player". In the upcoming outcome phase, participants were informed about whether they have won or lost the trial and either could punish the "opponent player" or received the punishment by the "opponent player". In "active" trials, participants could punish the opponent in case of winning the trial, whereas the participant received no punishment when losing the trial. On the contrary, in "passive" trials, participants could get punished when losing the reaction time task, but the "opponent player" received no punishment when losing the reaction time task.

cued the participant for the upcoming reaction time task. For the reaction time task, a visual cue (a bird from a computer game) was presented on the screen and participants were instructed to press a button as fast as possible when the visual cue appeared on the screen. The duration of the visual cues appearance was similar for all trials, irrespective of the participant's reaction time (see Figure 1). Directly after the reaction time task, participants were presented with the opponents' selection of the punishment level. Feedback of the opponents' punishment level selection was given in every single trial, no matter if it was an "active" or a "passive" one. They were also informed that feedback regarding their selection of punishment magnitude was given to the opponent as well, serving as a threat for the opponent. Subsequently, the information whether they had won or lost the trial was given by presenting the German words for "won" or "lost". At the end of the trial, the punishment was administered depending on the actual block.

Questionnaires

Following the scanning session, participants completed the Buss and Perry AQ (Buss & Perry, 1992) and the German version of the IRI (Paulus, 2009). The AQ comprises 29 items scored from 1 ("extremely uncharacteristic of me") to 5 ("extremely characteristic of me") and assessed the four aggression dimensions physical aggression, verbal aggression, anger, and hostility. The IRI includes four 7-item subscales: *Perspective taking* is the ability to capture the psychological perspective of another person and is thought to involve several cognitive, but not affective, empathic processes. The *fantasy* scale reflects the tendency to put oneself into the role and behavior of characters from novels or movies. The third subscale—*empathic concern*—measures the sympathy and care for others, whereas the *personal distress* scale taps into feelings of inner restlessness and uneasiness when confronted with extreme situations such as an emergency. For the AQ, a total score was calculated by summing up the scores of the four aggression dimensions. To test for differences between the groups, one multivariate analysis of variance (MANOVA) per questionnaire was calculated comprising the between-factor group (AVP, placebo) and the within-subjects factor scale (AQ: physical aggression, verbal aggression, anger, and hostility; IRI: perspective taking, fantasy scale, empathic concern, and personal distress).

fMRI data acquisition

A 3-T Siemens Magnetom Trio syngo MR 2004A Scanner was used to record functional (Gradient-Echo-EPI-sequence; TR = 2000 ms; TE = 30 ms; FOV = 224 mm; flip angle = 80°; matrix = 64 × 64; slice thickness = 3.5 mm; interslice gap = 0 mm) and structural images (T1-weighted MPRage: 256 × 256 matrix; FOV = 256 mm; 192 1-mm sagittal slices). Three hundred and eighty-eight volumes were recorded in each of the two runs. Each volume comprised 32 transversal slices (3.5 × 3.5 × 3.5 mm) recorded parallel to the anterior and posterior commissure (AC–PC).

fMRI analyses

FMRI data were analyzed using Statistical Parametric Mapping toolbox (SPM8, Wellcome Department of Imaging Neuroscience, University College London, London, UK). Preprocessing implemented slice time correction, motion correction, coregistration, spatial normalization, and spatial smoothing (Gaussian

Kernel, full width at half maximum (FWHM) 8 mm). A filter width of 128 s was used for temporal high pass filtering. Preprocessed data were entered into a random effects analysis. For the decision phase, the regressors "active" and "passive" blocks were defined (6s). For the outcome phase, the regressors "win" and "loss" were defined for active and passive blocks separately (6s). Regressors of noninterest regarding the target (2s) as well as the information about the opponents selected punishment level (4s) were included in the general linear model (GLM). In addition, movement parameters (x, y, z, pitch, roll, and yaw) from movement correction were included in the statistical analysis to minimize signal-correlated movement effects. In order to control for serial correlations, the standard SPM autoregressive model was applied. The resulting regressors were convolved with the standard hemodynamic response function. Aggression-related effects during the decision phase were delineated by means of contrast maps calculated for each subject by comparing "active" trials versus "passive" trials. This contrast was entered into a one-sample t-test for both groups separately. In order to test the influence of AVP treatment, two-sample t-test's (AVP vs. placebo and vice versa) were conducted with the contrast images "active" trials vs. "passive" trials from the first-level analysis. This analysis essentially tests for an interaction of group and condition. In order to further investigate this interaction, the resulting active brain sites—the right superior temporal sulcus (STS), the ACC, and the fusiform gyrus—were used as a basis for post hoc functional region of interest (ROI) analyses. This was done by creating a 10-mm sphere centered at the peak voxel of the between-group comparison placebo versus AVP. In order to reveal this interaction's direction, percent signal changes were extracted using rfxplot (Glascher, 2009) and finally entered into a 2 × 2 repeated-measures ANOVA implementing the following factors: drug (AVP and placebo) and block (active and passive).

For the outcome phase, win trials were contrasted against loss trials for each subject and entered into one-sample t-tests. Based on the hypothesis that it might be more rewarding for the AVP group relative to the placebo group to punish the opponent during active trials, a ventral striatum ROI was defined as a 5-mm sphere centered at the peak voxel of the win trials versus loss trial contrast. This latter step was done separately for both the groups. Extracted percent signal changes were subjected to a 2 × 2 ANOVA with the factors block (active and passive) and outcome (win and loss) for both the groups separately. Between-group comparisons were conducted by entering the win trials versus loss trials contrast into a two-sample t-test.

Behavioral data

The average punishment level was calculated for each participant and "active" and "passive" trials separately. Data were subjected to a 2 × 2 ANOVA comprising the factors drug (AVP and placebo) and block condition (active blocks and passive blocks). In addition, the total number of high punishment level selections (levels 3 and 4) was calculated for each participant and for "active" and "passive" blocks separately and again entered to an ANOVA. Furthermore, the decision times for the participants' decision for high (levels 3 and 4) and low (levels 1 and 2) punishment levels were calculated for both the blocks separately. A 2 × 2 × 2 ANOVA with the factors drug (AVP and placebo), punishment level (low and high) and block condition (active and passive) was conducted. Finally, the reaction times during the reaction time task (rtt) were calculated for both the blocks and entered into a 2 × 2 ANOVA with the factors drug (AVP and placebo) and block condition (active and passive).

RESULTS

Questionnaires

The mean AQ scores of the AVP/placebo groups were (standard deviation in brackets) physical aggression scale, 27.5 (7.3)/27.1 (6.1); verbal aggression scale, 12.8 (4.0)/11.0 (3.8); anger subscale, 23.5 (4.8)/25.2 (3.7); and hostility, 26.8 (5.7)/27.3 (7.7). The statistical test revealed neither significant differences between the groups ($F < 0.001$, $p > .99$, $df = 1.35$) nor a significant group × scale interaction ($F = 1.63$, $p = .2$, $df = 3.33$). Only the main effect scale reached significance ($F = 142.9$, $p < .001$, $df = 3.33$); however, for the current study's implication, this effect is of no interest. Mean IRI scores were perspective taking, 16.85 (4.02)/18.93 (3.37); fantasy, 15.0 (3.33)/16.47 (4.41); empathic concern, 17.5 (1.86)/18.13 (3.91); and personal distress, 9.25 (3.32)/10.27 (2.28). The pattern of statistical results was similar to the analysis of the AQ, showing a nonsignificant group ($F = 1.33$; $p = .25$; $df = 1.29$) and group × scale test ($F = 0.19$; $p > .9$; $df = 3.27$), but a significant scale effect ($F = 37.07$, $p < .001$; $df = 3.27$).

TAP task: behavior

The average punishment level, the average of the total number of high punishment level selections, the decision times of punishment level selection and the

TABLE 1
Average punishment level, average of the total number of high punishment level selections, mean reaction times of punishment level selection, and mean reaction times from the reaction time task are illustrated for both groups

	AVP		*Placebo*	
	Active blocks	*Passive blocks*	*Active blocks*	*Passive blocks*
Average of punishment level selection	2.54 (*SD* = 0.3)	2.38 (*SD* = 0.5)	2.58 (*SD* = 0.3)	2.54 (*SD* = 0.48)
Average of the total number of high punishment selection	11.2 *times* (*SD* = 6.9)	10.2 *times* (*SD* = 6.6)	10.7 *times* (*SD* = 4.5)	10.9 *times* (*SD* = 4.8)
Mean reaction times (s) for high punishment selection	1.01 (*SD* = 0.4)	1.11 (*SD* = 0.4)	1.13 (*SD* = 0.5)	1.11 (*SD* = 0.48)
Low punishment selection	1.0 (*SD* = 0.33)	1.05 (*SD* = 0.24)	1.14 (*SD* = 0.38)	1.02 (*SD* = 0.3)
Mean reaction times (s) of reaction time task	1.2 (*SD* = 0.7)	1.18 (*SD* = 0.56)	1.6 (*SD* = 1.7)	1.38 (*SD* = 0.84)

reaction times to the bird stimulus did not differ between the groups (Table 1).

fMRI data

In the whole brain analysis, the contrast "active" versus "passive" showed activity in the hippocampus during the decision phase in both the groups, which extended to the amygdala in the AVP group only (Figure 2). Activation was also observed in the fusiform gyrus in both the groups (see Table 2). Whereas the placebo group showed enhanced activity for active trials in the medial frontal gyrus, the temporal cortex (STS, superior temporal gyrus, middle temporal gyrus, inferior temporal gyrus, Figure 2, left column), and the ACC, these activations were not present in the AVP group (see Table 2). "Passive" trials, on the other hand, showed more pronounced activity in the lingual gyrus in both the groups. Additionally, the AVP group showed activations in the parahippocampal gyrus, the precuneus, the precentral gyrus, and the superior parietal gyrus (see Table 3). Thus, whereas in the AVP group the contrast "passive"

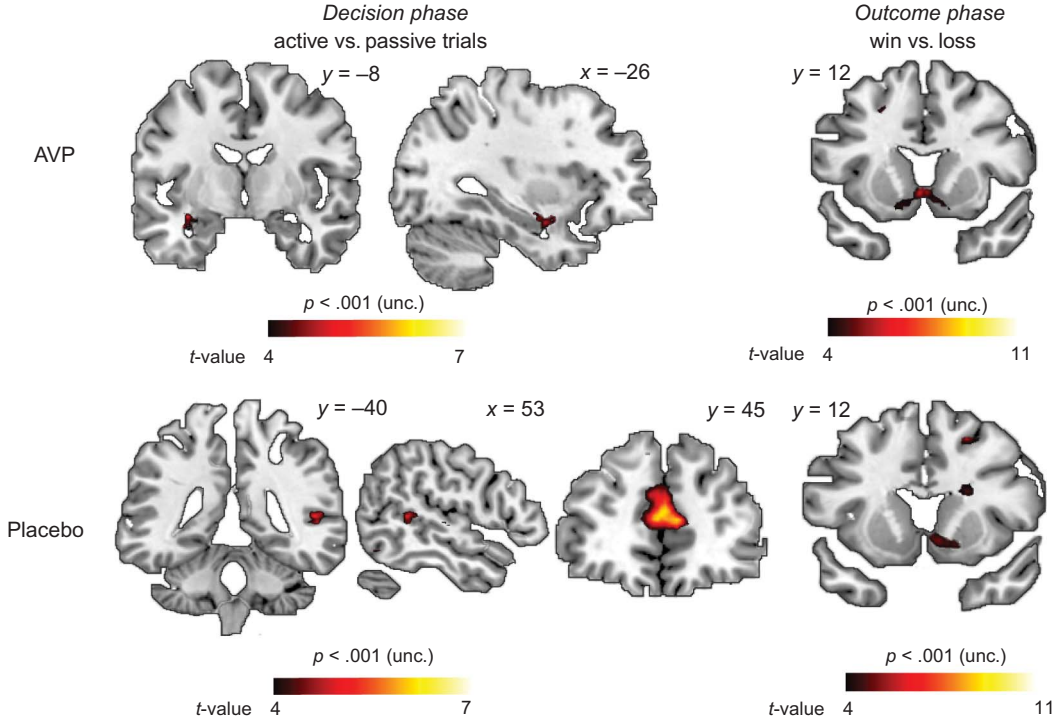

Figure 2. Neural activations are illustrated for the AVP group and the placebo group for the contrast active trials versus passive trials from the decision phase and win trials versus loss trials from the outcome phase.

TABLE 2
Brain regions indicating increased activity in active trials compared with passive trials

		Active > Passive trials					
Hem	*Brain region*	*BA*	*x*	*y*	*z*	*T*	*Size*
AVP p < *.001 (uncorrected)*							
L	Fusiform gyrus	20	−36	−10	−24	5.12	98
L	Hippocampus and partly the amygdala		−26	−8	−12	3.91	
R	Middle occipital gyrus	18	34	−96	−2	5.12	88
L	Lingual gyrus	18	−26	−94	−12	4.36	19
Placebo p < *.001 (uncorrected)*							
L	Anterior cingulate gyrus	32	−2	50	12	6.40	1297
R	Anterior cingulate gyrus	32	8	44	12	6.29	
L	Anterior cingulate gyrus	24	−6	38	10	5.50	
L	Middle occipital gyrus	39	−42	−70	22	5.85	61
R	Medial frontal gyrus	9	6	54	40	5.54	172
L	Medial frontal gyrus	9	−6	44	44	4.41	
L	Medial frontal gyrus	9	−2	52	42	4.31	
R	Superior temporal sulcus	21	50	−42	6	5.37	334
R	Superior temporal gyrus	48	48	−22	4	4.60	
R	Superior temporal gyrus	41	48	−30	10	4.56	
L	Superior temporal gyrus	41	−42	−30	10	5.36	379
L	Middle temporal gyrus	20	−38	−24	−4	5.27	
R	Middle occipital gyrus	18	38	−88	4	5.31	232
R	Inferior occipital gyrus	19	34	−84	−2	4.50	
R	Inferior occipital gyrus	18	24	−100	0	4.42	
L	Medial frontal gyrus	11	−6	52	−14	5.26	86
R	Medial frontal gyrus	11	2	50	−16	4.20	
R	Middle temporal pole	20	42	14	−40	4.87	38
L	Cerebellum		−20	−86	−30	4.75	49
L	Cerebellum		−20	−84	−38	3.94	
R	Hippocampus	20	32	−8	−24	4.11	28
R	Inferior temporal gyrus	37	52	−60	−14	4.43	15
L	Inferior temporal gyrus	20	−46	−16	−30	4.41	23
L	Fusiform gyrus	20	−34	−14	−24	4.17	
L	Cerebellum		−6	−54	−18	4.37	36
R	Middle temporal gyrus	21	58	−34	−4	4.24	11
L	Cerebellum		−4	−84	−22	4.24	11
L	Inferior frontal gyrus		−54	26	−2	4.21	13
L	Inferior occipital gyrus	18	−28	−94	−8	4.05	13

Notes: Hem = hemisphere, BA = Brodmann area, *xyz* = MNI coordinates, *T* = *t*-values, size = cluster size.

versus "active" trials comprised more activated brain sites, the placebo group showed more activated brain regions in the "active" versus "passive" trials contrast.

With regard to the between-group comparison and the contrast "active" trials versus "passive" trials, no brain region showed higher activity for AVP compared with placebo at the specified significance level ($p < .001$ (uncorrected)). However, the reverse contrast (placebo > AVP) revealed increased activity in the right STS, the middle occipital gyrus, the anterior cingulate gyrus, and the fusiform gyrus (Table 4, Figure 3). The subsequent functional ROI analyses for the STS and the ACC revealed a main effect of block (STS: $F(1, 29) = 7.93$, $p = .008$, ACC: $F(1, 29) = 23.98$, $p < .001$) and a drug × block interaction (STS: $F(1, 29) = 13.52$, $p < .001$; ACC: $F(1/29) = 20.22$, $p < .001$). In both functional ROIs, the interaction is driven by an increase of the BOLD signal for the condition "passive" trial in the AVP group that reached a level comparable to that for the condition "active" trial in both the groups (Figure 4). The analysis of the FFG ROI revealed a significant drug × block interaction ($F(1/29) = 9.77$, $p < .004$), whereas the main effects failed to reach significance.

In the outcome phase, the contrast win > loss trials showed activity in the ventral striatum in both the groups, which was present in both hemispheres in the AVP group and confined to the right hemisphere in the placebo group (Figure 2, right column). Additional activity was seen in several frontal areas (medial frontal, middle frontal, and superior frontal

TABLE 3
Neural correlates showing enhanced activity for the passive trials versus active trials contrast

		Passive trials > Active trials					
Hem	*Brain region*	*BA*	*x*	*y*	*z*	*T*	*Size*
AVP p < *.001 (unc.)*							
R	Lingual gyrus	17	8	−92	2	8.87	1787
L	Superior occipital gyrus	17	−14	−94	10	8.15	
R	Lingual gyrus	17	8	−90	4	7.02	
R	Superior occipital gyrus	19	24	−86	44	5.37	59
R	Superior occipital gyrus		10	−86	46	4.54	
R	Parahippocampal gyrus	20	34	−28	−16	5.03	14
L	Precentral gyrus	6	−44	2	54	4.71	10
R	Sulcus calcarinus	17	8	−70	8	4.46	11
R	Lingual gyrus	17	0	−72	8	3.95	
L	Precuneus	7	−8	−78	52	4.19	14
R	Superior parietal gyrus		22	−80	54	4.16	28
Placebo p < *.001 (unc.)*							
L	Lingual gyrus	18	−14	−92	−4	5.56	116

Notes: Hem = hemisphere, BA = Brodmann Area, *xyz* = MNI coordinates, *T* = *t*-values, size = cluster size.

TABLE 4
Brain regions for the between-group comparison placebo versus AVP and the contrast active trials versus passive trials are illustrated

		Placebo > AVP (Active trials > Passive trials)					
Hem	*Brain region*	*BA*	*x*	*y*	*z*	*T*	*Size*
p < *.001 (unc.)*							
R	Superior temporal sulcus	42	48	−40	10	4.62	63
R	Middle occipital gyrus	19	36	−74	6	4.49	35
L	Anterior cingulate gyrus	24	−4	38	12	4.44	113
R	Anterior cingulate gyrus	24	4	38	10	4.22	
R	Anterior cingulate gyrus	32	4	44	16	3.59	
R	Fusiform gyrus	37	40	−48	−20	4.44	115

Notes: Hem = hemisphere, BA = Brodmann area, *xyz* = MNI coordinates, *T* = *t*-values, size = cluster size.

gyrus) and in the fusiform and the lingual gyrus in both the groups. For the AVP group, additional increased activity was seen in the anterior cingulate gyrus and the supramarginal gyrus (SMG), whereas the placebo group showed activations in the precuneus, cuneus, hippocampus, precentral gyrus, inferior temporal gyrus, and thalamus (Table 5).

In order to test the predicted differences in the ventral striatum, a functional ROI analysis centered at the peak voxel of the ventral striatum revealed a main effect of outcome in both the groups (the AVP group: $F(1, 29) = 36.4$, $p < .001$; the placebo group: $F(1, 29) = 15.5$, $p = .002$). In both the groups, there was neither a main effect of block nor a significant interaction. Loss trials were associated with enhanced activity in the superior temporal pole and inferior parietal lobule in the AVP group (see Table 6), whereas in the placebo group no brain region was activated at chosen statistical threshold and after decreasing the threshold to $p < .005$ (uncorrected).

With regard to the between-group comparison of win trials versus loss trials, for the comparison AVP > placebo no brain region survived the significance level ($p < .001$ (uncorrected)) while for the placebo > AVP contrast the left SMG showed increased activity (see Table 7). As can be seen from the subsequent ROI analysis (Figure 5), this effect is driven by an activation decrease under AVP treatment, while under placebo win outcome is associated with an activation increase. The statistical test of the extracted percent signal changes revealed a significant drug × outcome interaction ($F(1, 29) = 18.57$, $p < .001$), but no significant main effect (drug $F(1, 29) = 1.32$, $p = .25$; outcome $F(1, 29) = 3.98$, $p = .055$).

DISCUSSION

The present fMRI study asked whether AVP, a neuropeptide that has previously been shown to modulate aggressive behavior in animals and humans, would influence behavior and neural responses in a laboratory task designed to study reactive aggression.

The present study used a between-groups design, as the nature of the TAP paradigm precludes repeated testing. It is therefore important to note that neither for AQ nor for the IRI significant differences between groups were found. However, we have to state, as it is already described in the "Methods" section, that the questionnaire data were collected at the end of our investigation. We did so in order to ensure that participants were not primed regarding the aim of the present investigation. Since the used questionnaires captured situation independent traits and a sufficient long lag was used between drug administration and collecting the questionnaire data, it is justified to assume that the questionnaire data were unaffected either by the TAP or by the drug administration. Thus, any group differences in aggressive behavior and/or neural responses

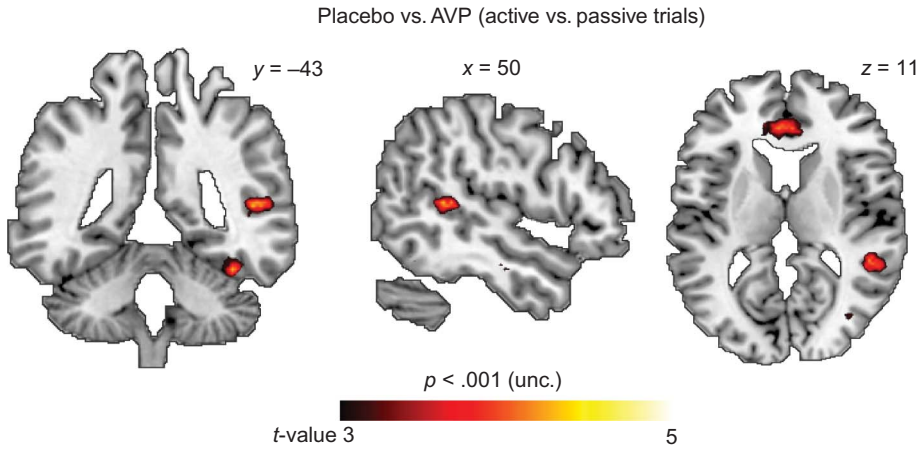

Figure 3. Between-group comparison (placebo vs. AVP) for the contrast active trials versus passive trials.

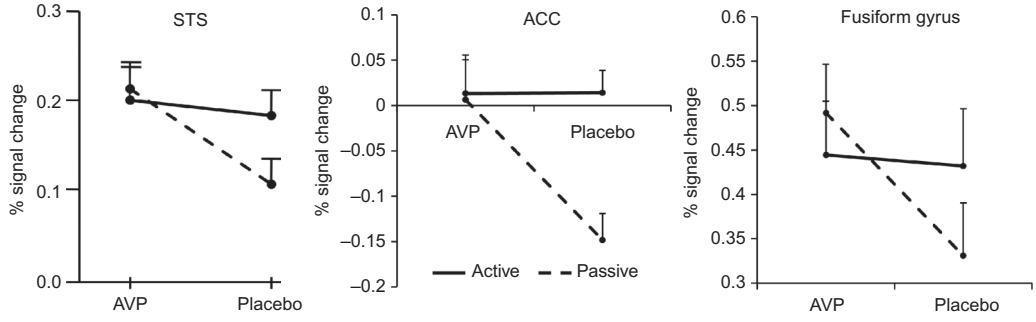

Figure 4. The interaction in the right STS, the anterior cingulate cortex, and the fusiform gyrus is based upon an AVP-promoted increase in BOLD signal during the selection of punishment level in passive blocks.

in the TAP can be related to an effect of AVP rather than trait differences in aggressive behavior between both the groups.

Like in some other studies (Brunnlieb, Münte, Tempelmann, & Heldmann, 2013; Pietrowsky, Struben, Molle, Fehm, & Born 1996; Zink et al., 2010, 2011), we found AVP-related changes in brain activation patterns, but against our own hypothesis no AVP-related behavioral effects. Based on animal studies, showing that microinjections of AVP in the lateral septum or in the anterior hypothalamus led to increased aggression in male rodents (Bos et al., 2012; Caldwell & Albers, 2004; Ferris & Delville, 1994; Ferris et al., 1997), and derived from investigations in humans, reporting an AVP-mediated bias in the perception and processing of social and emotional information, it had been expected that AVP would lead to higher punishment levels, whereas the selection of higher punishment levels was hypothesized to be more pronounced in "active" trials than in "passive" trials. In contrast to studies reporting an impact of AVP treatment on observable behavior (Guastella et al., 2010, 2011; Rilling et al., 2012; Thompson et al., 2004, 2006; Uzefovsky et al., 2012), but in line with the above-cited investigations (Pietrowsky et al. 1996; Zink et al., 2010, 2011) and a study by Israel et al. (2012), which also did not find an impact of AVP on social behavior, the expected behavioral effects did not show up. As AVP effects on behavior may be relatively small, one reason for these inconsistent findings might be the small group sizes in the present study and the studies by Zink et al. (2010, 2011). The study by Israel et al. (2012) investigated 96 male participants, however, rendering the sample size explanation for the lack of behavioral effects insufficient. Therefore, there is a clear need for future research to identify additional factors moderating the impact of AVP on human social behavior.

Both, the reported brain activation patterns and the fact that after intranasal application of desglycinamide-arginine-vasopressin detectable levels of this analog to AVP can be found in the CSF as early as 5 minutes (Born et al., 2002; Riekkinen et al., 1987) suggest that the nasally applied AVP indeed reached the brain within the current protocol. The question arises whether the dosage used in the present

TABLE 5
Neural correlates for the comparison of win trials versus loss trials

		Win trials > Loss trials					
Hem	*Brain region*	*BA*	*x*	*y*	*z*	*T*	*Size*
AVP p < *.001 (unc.)*							
R	Medial frontal gyrus	6	12	−16	54	7.73	86
R	Medial frontal gyrus		8	−26	58	4.75	
L	Middle frontal gyrus		−32	24	30	5.00	134
L	Middle frontal gyrus		−34	20	42	4.86	
L	Ventral striatum		−2	12	−4	6.18	1061
L	Anterior cingulate gyrus		−8	34	4	6.10	
R	Supramarginal gyrus		40	−44	34	5.72	13
R	Medial frontal gyrus	9	16	26	36	5.47	181
R	Middle frontal gyrus	9	32	22	38	5.43	
L	Middle occipital gyrus		−24	−80	6	5.06	207
L	Lingual gyrus		−24	−82	−10	5.04	
L	Fusiform gyrus	19	−26	−78	−18	4.47	
L	Superior frontal gyrus		−20	52	14	4.86	60
L	Middle frontal gyrus		−34	56	12	4.35	
R	Middle frontal gyrus		34	36	22	4.44	17
R	Superior frontal gyrus		16	46	42	4.33	21
R	Superior frontal gyrus		22	60	14	4.25	11
Placebo p < *.001 (unc.)*							
L	Cuneus	18	−14	−88	16	10.31	10938
L	Cuneus	19	−4	−96	20	9.12	
L	Lingual gyrus	17	−10	−90	0	8.97	
L	Cerebellum		−8	−60	−46	6.87	226
L	Cerebellum		−14	−46	−50	6.41	
L	Cerebellum		−22	−58	−44	5.00	
R	Hippocampus		36	−24	−10	6.64	362
R	Fusiform gyrus	19	36	−46	−10	6.15	
R	Ventral striatum		18	22	−8	6.34	1345
R	Superior frontal gyrus		22	12	52	6.18	42
R	Superior frontal gyrus	10	12	64	24	5.84	430
R	Superior frontal gyrus		22	28	48	5.71	
R	Middle frontal gyrus		28	34	48	5.24	
R	Precentral gyrus		32	−18	54	5.41	71
R	Middle frontal gyrus		26	−12	54	4.07	
L	Inferior temporal gyrus		−52	−4	−36	5.11	45
L	Inferior temporal gyrus	20	−44	−6	−34	4.27	
L	Middle frontal gyrus		−16	46	−10	4.73	21
L	Thalamus		−14	−30	10	4.70	40
−L	Thalamus		−22	−32	2	4.22	
R	Thalamus		4	−14	10	4.67	71
R	Precuneus		10	−60	56	4.57	24
R	Precuneus	7	14	−52	54	4.31	
L	Superior frontal gyrus		−10	56	2	4.30	32
L	Medial frontal gyrus	10	−6	60	14	4.27	34
R	Thalamus		10	−32	4	4.13	14

Notes: Hem = hemisphere, BA = Brodmann area, *xyz* = MNI coordinates, *T* = *t*-values, size = cluster size.

TABLE 6
Results of the contrast loss trials > win trials

		Loss trials > Win trials					
Hem	*Brain region*	*BA*	*x*	*y*	*z*	*T*	*Size*
AVP p < *.001 (unc.)*							
L	Superior temporal pole		−40	2	−20	5.04	92
L	Superior temporal pole		−38	−2	−10	4.74	
L	Inferior parietal lobule	40	−54	−34	22	4.68	126
L	Inferior parietal lobule	40	−62	−32	30	3.81	

Notes: Hem = hemisphere, BA = Brodmann area, *xyz* = MNI coordinates, *T* = *t*-values, size = cluster size.

TABLE 7
Results for the between-group comparison placebo > AVP and the contrast win trials > loss trials are illustrated

		Win trials vs. Loss trials Placebo vs. AVP					
Hem	*Brain region*	*BA*	*x*	*y*	*z*	*T*	*Size*
p < *.001 (uncorrected)*							
L	Supramarginal gyrus	48	−56	−34	28	3.7	15

Notes: Hem = hemisphere, BA = Brodmann area, *xyz* = MNI coordinates, *T* = *t*-values, size = cluster size.

investigation was sufficient to induce effects on brain activations might have been too low to induce a behavioral effect. In several previous investigations, 20 IU AVP did induce a behavioral effect, although this was not the case in others. Also, in Zink et al. (2010, 2011), even 40 IU AVP did not cause a behavioral effect. Thus, there is no consistent relationship between dosage of AVP administration and behavioral effect. A similar phenomenon is already known regarding the influence of exogenous oxytocin on social cognition and prosocial behavior. Inconsistencies in effects resulted in the assumption that prosocial behavior is not directly affected by exogenous oxytocin, but rather is the result of oxytocin's interaction with situational/contextual variables and situationally independent, individual stable personality traits (Bartz, Zaki, Bolger, & Ochsner, 2011; Guastella & MacLeod, 2012).

Numerous variables are supposed to impact aggressive behavior in humans with each of these interacting factors contributing just a small fraction of the variance in order to prevent erratic aggressive responses and to stabilize behavior. This implies that the pharmacological impact of AVP can be present without behavioral effect, if other factors are able to even the neuropeptide's impact on overt aggressive behavior out. As Guastella and MacLeod (2012) already noted with respect to the varying impact of exogenous

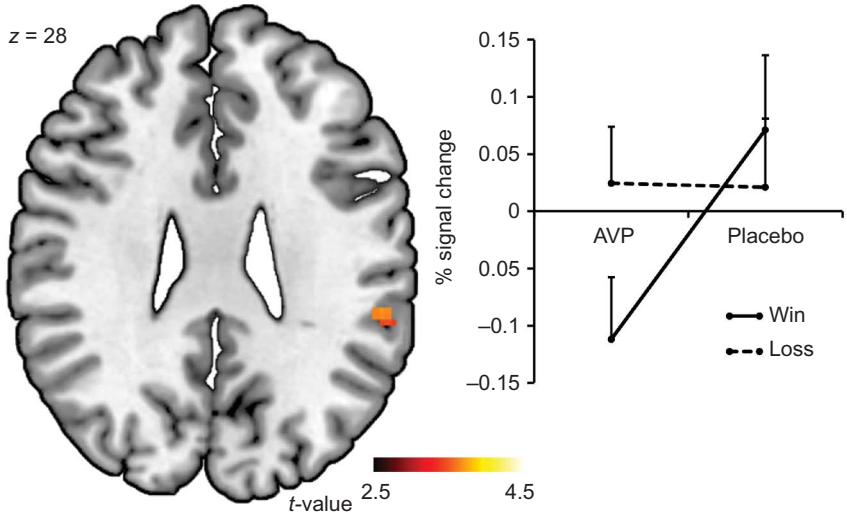

Figure 5. Between-group comparison (placebo vs. AVP) for the contrast win trials versus loss trials.

oxytocin on prosocial behavior, the impact of a neuropeptide is underestimated in case its influence on behavior is highly variable between subjects, but the neuropeptide's effect is pooled across subjects. This is usually the case in all between-subjects designs like in the present one. Thus, future research has to focus on the meaning of interindividual differences for the relationship between AVP treatment and aggressive behavior in humans.

The main finding on the neural level was that AVP modulated the activity in the right STS during the decision phase of "passive" trials during which participants could get punished by the opponent after losing the reaction time competition. In the present investigation, AVP enhanced the BOLD signal in the right STS during the decision phase of "passive" trials to a level comparable to that observed for "active" trials in both the groups. Previous work has linked the STS region to humans' ability to infer intentions and goal-directed behavior of other's referred to as mentalizing processes (Calder et al., 2002; Castelli, Happe, Frith, & Frith, 2000; Gallagher et al., 2000; Gobbini, Koralek, Bryan, Montgomery, & Haxby, 2007; Heberlein, Adolphs, Tranel, & Damasio, 2004; Narumoto, Okada, Sadato, Fukui, & Yonekura, 2001; Vogeley et al., 2001; Vollm et al., 2006). Accordingly, this suggests an AVP effect on neural processes supporting mentalizing/appraisal processes. The difference between "active" and "passive" trials is that only in "active" trials the punishment level selection had an instantaneous impact on the opponent. However, the opponent was also informed about the selected punishment level in "passive" trials, which indicated the player's intentions and could influence the opponent's behavior as well. The STS activation during "passive" trials can be interpreted as an indication that under AVP these indirect consequences of punishment level selection were taken more into account. This explanation is supported by the increased activation for passive trials under AVP treatment in the ventral-rostral ACC and the fusiform gyrus, brain sites known to process social cognitions. The ventral-rostral ACC is involved in the integration of action monitoring and emotions (Bush, Luu, & Posner, 2000; Etkin, Egner, & Kalisch, 2011), but is also active during cooperation (Chaminade, Marchant, Kilner, & Frith, 2012), mentalizing processes (Amodio & Frith, 2006; Camchong et al., 2011; Gilbert, Gonen-Yaacovi, Benoit, Volle, & Burgess, 2010; Sommer et al., 2007), and theory of mind-related tasks (Abu-Akel & Shamay-Tsoory, 2011; Apps, Balsters, & Ramnani, 2012; Weiland, Hewig, Hecht, Mussel, & Miltner, 2012). The fusiform gyrus is involved in theory of mind tasks as well, but also in the appraisal of aggression-provoking situations (Krämer et al., 2007).

The interpretation of an increased involvement of mentalizing processes under AVP is corroborated by group differences in activation patterns for the comparison "passive" trials versus "active" trials. Whereas in the placebo group, only the lingual gyrus was found activated at the chosen statistical threshold, activations in the AVP group were found in a number of brain regions including the precuneus, a brain region previously associated with mentalizing processes as well (Döhnel et al., 2012; Krämer, Mohammadi, Donamayor, Samii, & Munte, 2010; Spreng, Mar, & Kim, 2009). Although the results of the present investigation are in line with previous studies reporting

that AVP moderates the processing of social-emotional information, the nature of AVP's impact on these processes is less clear. On the one hand, AVP treatment in men seems to promote the processing of emotional (Guastella et al., 2010), sexual (Guastella & MacLeod 2012), and social information (Rilling et al., 2012), which results in increased activations of related brain sites (Rilling et al., 2012; Zink et al., 2010). On the other hand, studies by Thompson et al. (2004, 2006) have shown that AVP treatment resulted selectively in an aggressive/threatening interpretation of neutral, emotionally ambiguous information, while having no effect on the processing of positive or negative affective information. This effect seems to be similar to the reported activation pattern for "passive" trials in the present investigation. It is still an open question whether this effect is caused by an AVP-mediated increase of the salience of social/emotional information or by a more general affective relevant connotation of previous neutral stimuli under AVP treatment. At least at the neural level, there is some evidence speaking against a global activation effect under AVP, since Zink et al. (2011) reported a decrease of the temporal parietal junction's activation under AVP when social-affective stimuli are processed.

Interestingly, an activation of the hippocampus extending to the amygdala was found for "active" trials (decision phase) in the AVP group. For the placebo group, a cluster in the hippocampus was identified as well, but did not extend to the amygdala. While this is a first hint at a direct influence of AVP on the amygdala, it needs to be interpreted with caution as it was only present when the activation patterns of the two groups were considered separately but not on statistical comparison of the two groups. Similar to Krämer et al. (2007), the comparison of win trials versus loss trials (outcome phase) yielded increased activity in the ventral striatum, a key structure of reward processing. One of the hypotheses of the present study was that, under AVP, it might be more rewarding to punish the opponent, which should be reflected in a higher BOLD signal in the ventral striatum for win trials in "active" blocks. This hypothesis was not borne out, however, as a functional ROI analysis for the ventral striatum did not show any interaction between the factors outcome and block in both the groups. Thus, AVP did not lead to an increase in reward-related activity in the ventral striatum when receiving the information to be allowed to punish a relatively highly provoking opponent. Instead, we found a differential effect in the outcome phase in the SMG. Several studies related the SMG not only to the processing of intentions (Osaka, Ikeda, & Osaka, 2012) and the perception of social cooperation (Leube et al., 2012) but also to the processing of perspective taking (self vs. others, Morey et al., 2012). Indicated by the decreased activations for the win trials under AVP treatment, AVP seems to level such postdecisional processes. Together with the findings from the decision phase, one may conclude that AVP rather influences appraisal and mentalizing processes in emotional social exchange, but does not have a direct impact on processes related to the aggressive act per se.

Although the present investigation focuses on the impact of AVP on aggressive behavior, it is quite clear that AVP as well as oxytocin modulate socially relevant behavior in a more general sense. In contrast to AVP, only two social situations have been described in the literature in which oxytocin is associated with aggressive behavior: maternal aggression (Lee, Macbeth, Pagani, & Young, 2009) and defensive aggression against competing outgroups in the context of parochial altruism (De Dreu et al., 2010). Apart from that, oxytocin is closely related to bonding and prosocial behavior (McCall & Singer, 2012; Meyer-Lindenberg et al., 2011; Zink & Meyer-Lindenberg, 2012). It increases the ability to detect emotional and social signs in facial expressions, acts as an anxiolytic and, as a secondary effect, promotes trust in other persons (Baumgartner, Heinrichs, Vonlanthen, Fischbacher, & Fehr, 2008). While functional imaging studies suggest that the amygdala is a key brain site for oxytocin effects, only indirect support is available for the hypothesis that AVP acts via the amygdala as well. The dampening effect of oxytocin on the amygdala is very often accompanied by decreased activations in the orbito- and medial prefrontal brain sites (Kirsch et al., 2005; Sripada et al., 2012). Just a few studies have reported increased activations in mentalizing-related brain sites, when processing social stimuli under oxytocin treatment (Riem et al., 2011, 2012). However, the oxytocin treatment related effects in the superior temporal cortex were found in women (Domes et al., 2010), while the present investigation and the study by Zink et al. (2011) found the AVP-treatment-related effect in men. To summarize, there is some evidence that exogeneous oxytocin and AVP seem to act on overlapping brain circuitries. Future research has to disentangle the mechanisms of action and the potential differences between sexes.

As a final cautionary note, we would like to point to two limiting aspects of the reported results. As can be seen from other studies, the differential impact of AVP on BOLD responses related to cognitive functions seems to be relatively small. Accordingly, previous investigations have focused their analyses on a priori defined ROIs, i.e., Brodmann area (BA) 25/32 and the amygdala (Zink et al., 2010) or the amygdala alone

(Rilling et al., 2012), and restricted corrections for multiple testing to these ROIs. In contrast, our results are based on a whole brain analysis. Since the reported *t*-values for between-group comparisons are at least as high as in the Zink et al. (2010) or Rilling et al. (2012) study (our study, see Table 4: $t = 4.62$; Zink et al. (2010), see Table 1: Vasopressin > Placebo, $t = 4.5$; Rilling et al. (2012), see Supplementary Table 3, AVP > PL, $t = 3.1$), but the criteria for a statistical test to survive a correction for multiple comparisons are more restrictive for a whole brain than for an ROI analysis, our statistical tests do not survive corrections for multiple comparisons. Due to the fact that the outcome of our statistical tests is similar to the effects of the cited studies, we regard these results as reliable. However, it is obvious that future research on AVP has to incorporate larger samples. Second, the present study only involved healthy men since in women an AVP treatment could interact with the hormonal cycle. Previous studies by Thompson et al. (2004, 2006) have revealed sex differences in AVP effects in humans. Moreover, it is known that vasopressin interacts with estrogen and oxytocin (Akaishi & Sakuma, 1985; Gabor, Phan, Clipperton-Allen, Kavaliers, & Choleris, 2012; Sarkar, Frautschy, & Mitsugi, 1992). Thus, further studies that also involve female participants at specific points of the hormonal cycle are needed to investigate, whether one can generalize the AVP effect seen in the current study also to women.

Supplementary material

Supplementary (Table 3) is available via the 'Supplementary' tab on the article's online page (http://dx.doi.org/10.1080/17470919.2013.763654).

REFERENCES

Abu-Akel, A., & Shamay-Tsoory, S. (2011). Neuroanatomical and neurochemical bases of theory of mind. *Neuropsychologia*, *49*, 2971–2984.

Akaishi, T., & Sakuma, Y. (1985). Estrogen excites oxytocinergic, but not vasopressinergic cells in the paraventricular nucleus of female rat hypothalamus. *Brain Research*, *335*, 302–305.

Amodio, D. M., & Frith, C. D. (2006). Meeting of minds: The medial frontal cortex and social cognition. *Nature Reviews. Neuroscience*, *7*, 268–277.

Anderson, C. A., & Bushman, B. J. (2002). Human aggression. *Annual Review Psychology*, *53*, 27–51.

Apps, M. A., Balsters, J. H., & Ramnani, N. (2012). The anterior cingulate cortex: Monitoring the outcomes of others' decisions. *Society for Neuroscience*, *7*, 424–435.

Balleine, B. W., Delgado, M. R., & Hikosaka, O. (2007). The role of the dorsal striatum in reward and decision-making. *Journal of neuroscience*, *27*, 8161–8165.

Bartz, J. A., Zaki, J., Bolger, N., & Ochsner, K. N. (2011). Social effects of oxytocin in humans: Context and person matter. *Trends in Cognitive Sciences*, *15*, 301–309.

Baumgartner, T., Heinrichs, M., Vonlanthen, A., Fischbacher, U., & Fehr, E. (2008). Oxytocin shapes the neural circuitry of trust and trust adaptation in humans. *Neuron*, *58*, 639–650.

Bjork, J. M., Dougherty, D. M., Moeller, F. G., Cherek, D. R., & Swann, A. C. (1999). The effects of tryptophan depletion and loading on laboratory aggression in men: Time course and a food-restricted control. *Psychopharmacology (Berlin)*, *142*, 24–30.

Bjork, J. M., Dougherty, D. M., Moeller, F. G., & Swann, A. C. (2000). Differential behavioral effects of plasma tryptophan depletion and loading in aggressive and nonaggressive men. *Neuropsychopharmacology*, *22*, 357–369.

Born, J., Lange, T., Kern, W., Mcgregor, G. P., Bickel, U., & Fehm, H. L. (2002). Sniffing neuropeptides: A transnasal approach to the human brain. *Nature Neuroscience*, *5*, 514–516.

Bos, P. A., Panksepp, J., Bluthe, R. M., & Honk, J. V. (2012). Acute effects of steroid hormones and neuropeptides on human social-emotional behavior: A review of single administration studies. *Frontiers in Neuroendocrinology*, *33*, 17–35.

Botvinick, M., Nystrom, L. E., Fissell, K., Carter, C. S., & Cohen, J. D. (1999). Conflict monitoring versus selection-for-action in anterior cingulate cortex. *Nature*, *402*, 179–181.

Brunnlieb, C., Münte, T. F., Tempelmann, C., & Heldmann, M. (2013). Vasopressin modulates neural responses related to emotional stimuli in the right amygdala. *Brain Research*. Retrieved from http://dx.doi.org/10.1016/j.brainres.2013.01.009

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences*, *4*, 215–222.

Buss, A. H., & Perry, M. (1992). The aggression questionnaire. *Journal of Personality and Social Psychology*, *63*, 452–459.

Calder, A. J., Lawrence, A. D., Keane, J., Scott, S. K., Owen, A. M., Christoffels, I., & Young, A. W. (2002). Reading the mind from eye gaze. *Neuropsychologia*, *40*, 1129–1138.

Caldwell, H. K., & Albers, H. E. (2004). Effect of photoperiod on vasopressin-induced aggression in Syrian hamsters. *Hormones and Behavior*, *46*, 444–449.

Camchong, J., MacDonald, A. W., 3rd, Nelson, B., Bell, C., Mueller, B. A., Specker, S., & Lim K. O. (2011). Frontal hyperconnectivity related to discounting and reversal learning in cocaine subjects. *Biological Psychiatry*, *69*, 1117–1123.

Carter, C. S., & Van Veen, V. (2007). Anterior cingulate cortex and conflict detection: An update of theory and data. *Cognitive, Affective, & Behavioral Neuroscience*, *7*, 367–379.

Castelli, F., Happe, F., Frith, U., & Frith, C. (2000). Movement and mind: A functional imaging study of perception and interpretation of complex intentional movement patterns. *NeuroImage*, *12*, 314–325.

Chaminade, T., Marchant, J. L., Kilner, J., & Frith, C. D. (2012). An fMRI study of joint action in

varying levels of cooperation correlates with activity in sensorimotor control, but not mentalization, networks. *Frontiers in Human Neuroscience*, *6*, 179. doi:10.3389/fnhum.2012.00179

Cleare, A. J., & Bond, A. J. (1995). The effect of tryptophan depletion and enhancement on subjective and behavioural aggression in normal male subjects. *Psychopharmacology (Berlin)*, *118*, 72–81.

Coccaro, E. F., & Kavoussi, R. J. (1997). Fluoxetine and impulsive aggressive behavior in personality-disordered subjects. *Archives of General Psychiatry*, *54*, 1081–1088.

Coccaro, E. F., Kavoussi, R. J., Hauger, R. L., Cooper, T. B., & Ferris, C. F. (1998). Cerebrospinal fluid vasopressin levels: Correlates with aggression and serotonin function in personality-disordered subjects. *Archives of General Psychiatry*, *55*, 708–714.

Cohen, J. D., Botvinick, M., & Carter, C. S. (2000). Anterior cingulate and prefrontal cortex: Who's in control? *Nature Neuroscience*, *3*, 421–423.

Damasio, A. R., Grabowski, T. J., Bechara, A., Damasio, H., Ponto, L. L., Parvizi, J., & Hichwa, R. D. (2000). Subcortical and cortical brain activity during the feeling of self-generated emotions. *Nature Neuroscience*, *3*, 1049–1056.

De Dreu, C. K., Greer, L. L., Handgraaf, M. J., Shalvi, S., Van Kleef, G. A., Baas, M., . . . Feith, S. W. W. (2010). The neuropeptide oxytocin regulates parochial altruism in intergroup conflict among humans. *Science*, *328*, 1408–1411.

De Quervain, D. J., Fischbacher, U., Treyer, V., Schellhammer, M., Schnyder, U., Buck, A., & Fehr, E. (2004). The neural basis of altruistic punishment. *Science*, *305*, 1254–1258.

Dodge, K. A., & Coie, J. D. (1987). Social-information-processing factors in reactive and proactive aggression in children's peer groups. *Journal of Personality and Social Psychology*, *53*, 1146–1158.

Döhnel, K., Schuwerk, T., Meinhardt, J., Sodian, B., Hajak, G., & Sommer, M. (2012). Functional activity of the right temporo-parietal junction and of the medial prefrontal cortex associated with true and false belief reasoning. *NeuroImage*, *60*, 1652–1661.

Domes, G., Lischke, A., Berger, C., Grossmann, A., Hauenstein, K., Heinrichs, M., & Herpertz, S.C. (2010). Effects of intranasal oxytocin on emotional face processing in women. *Psychoneuroendocrinology*, *35*, 83–93.

Dougherty, D. D., Shin, L. M., Alpert, N. M., Pitman, R. K., Orr, S. P., Lasko, M., . . . Rauch, S. L. (1999). Anger in healthy men: A PET study using script-driven imagery. *Biological Psychiatry*, *46*, 466–472.

Etkin, A., Egner, T., & Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences*, *15*(2), 85–93.

Ferris, C. F., & Delville, Y. (1994). Vasopressin and serotonin interactions in the control of agonistic behavior. *Psychoneuroendocrinology*, *19*, 593–601.

Ferris, C. F., Melloni, R. H. Jr, Koppel, G., Perry, K. W., Fuller, R. W., & Delville, Y. (1997). Vasopressin/serotonin interactions in the anterior hypothalamus control aggressive behavior in golden hamsters. *Journal of Neuroscience*, *17*, 4331–4340.

Ferris, C. F., Stolberg, T., Kulkarni, P., Murugavel, M., Blanchard, R., Blanchard, D. C., & Simon, N. G. (2008). Imaging the neural circuitry and chemical control of aggressive motivation [Research Support, N.I.H., Extramural]. *BMC Neuroscience*, *9*, 111. doi:10.1186/1471-2202-9-111

Gabor, C. S., Phan, A., Clipperton-Allen, A. E., Kavaliers, M., & Choleris, E. (2012). Interplay of oxytocin, vasopressin, and sex hormones in the regulation of social recognition. *Behavioral Neuroscience*, *126*, 97–109.

Gallagher, H. L., Happe, F., Brunswick, N., Fletcher, P. C., Frith, U., & Frith, C. D. (2000). Reading the mind in cartoons and stories: An fMRI study of 'theory of mind' in verbal and nonverbal tasks. *Neuropsychologia*, *38*, 11–21.

Gilbert, S. J., Gonen-Yaacovi, G., Benoit, R. G., Volle, E., & Burgess, P. W. (2010). Distinct functional connectivity associated with lateral versus medial rostral prefrontal cortex: A meta-analysis. *NeuroImage*, *53*, 1359–1367.

Glascher, J. (2009). Visualization of group inference data in functional neuroimaging. *Neuroinformatics*, *7*, 73–82.

Gobbini, M. I., Koralek, A. C., Bryan, R. E., Montgomery, K. J., & Haxby, J. V. (2007). Two takes on the social brain: A comparison of theory of mind tasks. *Journal of Cognitive Neuroscience*, *19*, 1803–1814.

Goodson, J. L., & Bass, A. H. (2001). Social behavior functions and related anatomical characteristics of vasotocin/vasopressin systems in vertebrates. *Brain Research. Brain Research Reviews*, *35*, 246–265.

Guastella, A. J., Kenyon, A. R., Alvares, G. A., Carson, D. S., & Hickie, I. B. (2010). Intranasal arginine vasopressin enhances the encoding of happy and angry faces in humans. *Biological Psychiatry*, *67*, 1220–1222.

Guastella, A. J., Kenyon, A. R., Unkelbach, C., Alvares, G. A., & Hickie, I. B. (2011). Arginine vasopressin selectively enhances recognition of sexual cues in male humans. *Psychoneuroendocrinology*, *36*, 294–297.

Guastella, A. J., & MacLeod, C. (2012). A critical review of the influence of oxytocin nasal spray on social cognition in humans: Evidence and future directions. *Hormones and Behavior*, *61*, 410–418. doi:10.1016/j.yhbeh.2012.01.002

Heberlein, A. S., Adolphs, R., Tranel, D., & Damasio, H. (2004). Cortical regions for judgments of emotions and personality traits from point-light walkers. *Journal of Cognitive Neuroscience*, *16*, 1143–1158.

Heinrichs, M., & Domes, G. (2008). Neuropeptides and social behaviour: Effects of oxytocin and vasopressin in humans. *Progress in Brain Research*, *170*, 337–350.

Huber, D., Veinante, P., & Stoop, R. (2005). Vasopressin and oxytocin excite distinct neuronal populations in the central amygdala. *Science*, *308*, 245–248.

Israel, S., Weisel, O., Ebstein, R. P., & Bornstein, G. (2012). Oxytocin, but not vasopressin, increases both parochial and universal altruism. *Psychoneuroendocrinology*, *37*, 1341–1344.

Kirsch, P., Esslinger, C., Chen, Q., Mier, D., Lis, S., Siddhanti, S., . . . Meyer-Lindenberg, A. (2005). Oxytocin modulates neural circuitry for social cognition and fear in humans. *Journal of Neuroscience*, *25*, 11489–11493.

Krämer, U. M., Jansma, H., Tempelmann, C., & Munte, T. F. (2007). Tit-for-tat: The neural basis of reactive aggression. *NeuroImage*, *38*, 203–211.

Krämer, U. M., Mohammadi, B., Donamayor, N., Samii, A., & Munte, T. F. (2010). Emotional and cognitive aspects of empathy and their relation to social cognition – An fMRI study. *Brain Research*, *1311*, 110–120.

Krämer, U. M., Riba, J., Richter, S., & Munte, T. F. (2011). An fMRI study on the role of serotonin in reactive aggression. *PLoS One*, *6*, e27668.

Lee, H. J., Macbeth, A. H., Pagani, J. H., & Young, W. S., 3rd (2009). Oxytocin: The great facilitator of life. *Progress in Neurobiology*, *88*, 127–151.

Leube, D., Straube, B., Green, A., Blumel, I., Prinz, S., Schlotterbeck, P., & Kircher, T. (2012). A possible brain network for representation of cooperative behavior and its implications for the psychopathology of schizophrenia. *Neuropsychobiology*, *66*, 24–32.

Lotze, M., Veit, R., Anders, S., & Birbaumer, N. (2007). Evidence for a different role of the ventral and dorsal medial prefrontal cortex for social reactive aggression: An interactive fMRI study. *NeuroImage*, *34*, 470–478.

Manuck, S., Kaplan, J., & Lotrich, F. (2006). Brain serotonin and aggressive disposition in humans and nonhuman primates. In R. Nelson (Ed.), *Biology of aggression*. New York, NY: Oxford University Press.

McCall, C., & Singer, T. (2012). The animal and human neuroendocrinology of social cognition, motivation and behavior. *Natural Neuroscience*, *15*, 681–688.

Meyer-Lindenberg, A., Domes, G., Kirsch, P., & Heinrichs, M. (2011). Oxytocin and vasopressin in the human brain: Social neuropeptides for translational medicine. *Nature Reviews Neuroscience*, *12*, 524–538.

Milham, M. P., Banich, M. T., Webb, A., Barad, V., Cohen, N. J., Wszalek, T., & Krämer, A. F. (2001). The relative involvement of anterior cingulate and prefrontal cortex in attentional control depends on nature of conflict. *Cognitive Brain Research*, *12*, 467–473.

Morey, R. A., McCarthy, G., Selgrade, E. S., Seth, S., Nasser, J. D., & LaBar, K. S. (2012). Neural systems for guilt from actions affecting self versus others. *NeuroImage*, *60*, 683–692.

Moss, H. B., Yao, J. K., & Panzak, G. L. (1990). Serotonergic responsivity and behavioral dimensions in antisocial personality disorder with substance abuse. *Biological Psychiatry*, *28*, 325–338.

Narumoto, J., Okada, T., Sadato, N., Fukui, K., & Yonekura, Y. (2001). Attention to emotion modulates fMRI activity in human right superior temporal sulcus. *Cognitive Brain Research*, *12*, 225–231.

Nelson, J. K., Reuter-Lorenz, P. A., Sylvester, C. Y., Jonides, J., & Smith, E. E. (2003). Dissociable neural mechanisms underlying response-based and familiarity-based conflict in working memory. *Proceedings of the National Academy of Sciences of the USA*, *100*, 11171–11175.

O'Doherty, J., Dayan, P., Schultz, J., Deichmann, R., Friston, K., & Dolan, R. J. (2004). Dissociable roles of ventral and dorsal striatum in instrumental conditioning. *Science*, *304*, 452–454.

Osaka, N., Ikeda, T., & Osaka, M. (2012). Effect of intentional bias on agency attribution of animated motion: An event-related FMRI study. *PLoS One*, *7*, e49053.

Passamonti, L., Crockett, M. J., Apergis-Schoute, A. M., Clark, L., Rowe, J. B., Calder, A. J., & Robbins, T. W. (2012). Effects of acute tryptophan depletion on prefrontal-amygdala connectivity while viewing facial signals of aggression. *Biological Psychiatry*, *71*, 36–43.

Passamonti, L., Rowe, J. B., Ewbank, M., Hampshire, A., Keane, J., & Calder, A. J. (2008). Connectivity from the ventral anterior cingulate to the amygdala is modulated by appetitive motivation in response to facial signals of aggression. *NeuroImage*, *43*, 562–570.

Paulus, C. (2009). *Der Saarbruecker Persoenlichkeitsfragebogen SPF (IRI) zur Messung von Empathie: Psychometrische Evaluation der deutschen Version des Interpersonal Reactivity Index*. Retrieved from http://www.uni-saarland.de/fak5/ezw/personal/paulus/empathy/SPF_Artikel.pdf

Phillips, M. L., Young, A. W., Senior, C., Brammer, M., Andrew, C., Calder, A. J., . . . David, A. S. (1997). A specific neural substrate for perceiving facial expressions of disgust. *Nature*, *389*, 495–498.

Pietrowsky, R., Struben, C., Molle, M., Fehm, H. L., & Born, J. (1996). Brain potential changes after intranasal vs. intravenous administration of vasopressin: Evidence for a direct nose-brain pathway for peptide effects in humans. *Biological Psychiatry*, *39*, 332–340.

Pihl, R. O., Young, S. N., Harden, P., Plotnick, S., Chamberlain, B., & Ervin, F. R. (1995). Acute effect of altered tryptophan levels and alcohol on aggression in normal human males. *Psychopharmacology (Berlin)*, *119*, 353–360.

Riekkinen, P., Legros, J. J., Sennef, C., Jolkkonen, J., Smitz, S., & Soininen, H. (1987). Penetration of DGAVP (Org 5667) across the blood-brain barrier in human subjects. *Peptides*, *8*, 261–265.

Riem, M. M., Bakermans-Kranenburg, M. J., Pieper, S., Tops, M., Boksem, M. A., Vermeiren, R. R., . . . Rombouts, S. A. (2011). Oxytocin modulates amygdala, insula, and inferior frontal gyrus responses to infant crying: A randomized controlled trial. *Biological Psychiatry*, *70*, 291–297.

Riem, M. M., van, I. M. H., Tops, M., Boksem, M. A., Rombouts, S. A., & Bakermans-Kranenburg, M. J. (2012). No laughing matter: Intranasal oxytocin administration changes functional brain connectivity during exposure to infant laughter. *Neuropsychopharmacology*, *37*, 1257–1266.

Rilling, J. K., DeMarco, A. C., Hackett, P. D., Thompson, R., Ditzen, B., Patel, R., & Pagnoni, G. (2012). Effects of intranasal oxytocin and vasopressin on cooperative behavior and associated brain activity in men. *Psychoneuroendocrinology*, *37*, 447–461.

Sarkar, D. K., Frautschy, S. A., & Mitsugi, N. (1992). Pituitary portal plasma levels of oxytocin during the estrous cycle, lactation, and hyperprolactinemia. *Annals of the New York Academy of Sciences*, *652*, 397–410.

Sommer, M., Dohnel, K., Sodian, B., Meinhardt, J., Thoermer, C., & Hajak, G. (2007). Neural correlates of true and false belief reasoning. *NeuroImage*, *35*, 1378–1384.

Spreng, R. N., Mar, R. A., & Kim, A. S. (2009). The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: A quantitative meta-analysis. *Journal of Cognitive Neuroscience*, *21*, 489–510.

Sripada, C. S., Phan, K. L., Labuschagne, I., Welsh, R., Nathan, P. J., & Wood, A. G. (2012). Oxytocin enhances resting-state connectivity between amygdala and medial frontal cortex. *International Journal of Neuropsychopharmacol*, 1–6. doi:10.1017/S1461145712000533

Thompson, R., Gupta, S., Miller, K., Mills, S., & Orr, S. (2004). The effects of vasopressin on human

facial responses related to social communication. *Psychoneuroendocrinology*, *29*, 35–48.

Thompson, R. R., George, K., Walton, J. C., Orr, S. P., & Benson, J. (2006). Sex-specific influences of vasopressin on human social communication. *Proceedings of the National Academy of Sciences USA*, *103*, 7889–7894.

Uzefovsky, F., Shalev, I., Israel, S., Knafo, A., & Ebstein, R. P. (2012). Vasopressin selectively impairs emotion recognition in men. *Psychoneuroendocrinology*, *37*, 576–580.

Van Veen, V., & Carter, C. S. (2002). The timing of action-monitoring processes in the anterior cingulate cortex. *Journal of Cognitive Neuroscience*, *14*, 593–602.

Veinante, P., & Freund-Mercier, M. J. (1997). Distribution of oxytocin- and vasopressin-binding sites in the rat extended amygdala: A histoautoradiographic study. *Journal of Comparative Neurology*, *383*, 305–325.

Vogeley, K., Bussfeld, P., Newen, A., Herrmann, S., Happe, F., Falkai, P., . . . Zilles, K. (2001). Mind reading: Neural mechanisms of theory of mind and self-perspective. *NeuroImage*, *14*, 170–181.

Vollm, B. A., Taylor, A. N., Richardson, P., Corcoran, R., Stirling, J., Mckie, S., & Elliott, R. (2006). Neuronal correlates of theory of mind and empathy: A functional magnetic resonance imaging study in a nonverbal task. *NeuroImage*, *29*, 90–98.

Weiland, S., Hewig, J., Hecht, H., Mussel, P., & Miltner, W. H. (2012). Neural correlates of fair behavior in interpersonal bargaining. *Society for Neuroscience*, *7*, 537–551.

Wiswede, D., Taubner, S., Munte, T. F., Roth, G., Struber, D., Wahl, K., & Krämer, U. M. (2011). Neurophysiological correlates of laboratory-induced aggression in young men with and without a history of violence. *PLoS One*, *6*, e22599.

Zink, C. F., Kempf, L., Hakimi, S., Rainey, C. A., Stein, J. L., & Meyer-Lindenberg, A. (2011). Vasopressin modulates social recognition-related activity in the left temporoparietal junction in humans. *Translational Psychiatry*, *1*, e3.

Zink, C. F., & Meyer-Lindenberg, A. (2012). Human neuroimaging of oxytocin and vasopressin in social cognition. *Hormones and Behavior*, *61*, 400–409.

Zink, C. F., Stein, J. L., Kempf, L., Hakimi, S., & Meyer-Lindenberg, A. (2010). Vasopressin modulates medial prefrontal cortex-amygdala circuitry during emotion processing in humans. *Journal of Neuroscience*, *30*, 7017–7022.