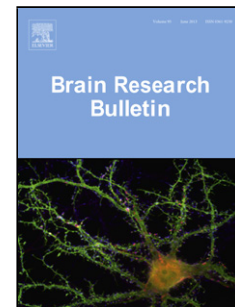


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# The OXTR Gene, Implicit Learning and Social Processing: Does Empathy Evolve from Perceptual Skills for Details?

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Highlights

- replicated association between the rs2268498 polymorphism and social processing
- empathy is related to implicit learning of details in social context
- oxytocin might improve social processing by altering perception and memory

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Keywords: oxytocin receptor gene; empathy; implicit learning; social processing; perception; affective neuroscience; rs2268498 polymorphism; memory

**Abstract**

Oxytocin is an important messenger in the brain that has been linked to a variety of social functions in pharmacological studies. Besides, functional genetic variations on the oxytocin receptor gene have been repeatedly associated with social processing and functioning. Despite this knowledge, there are very few studies investigating the mechanisms that may explain the link between oxytocin and social functions. In the endeavor to fill this gap in the literature, the current study searches for associations between the prominent rs2268498 polymorphism on the oxytocin receptor gene and participants' ability to perceive and store implicit social information, which is a fundamental function in social information processing. N = 121 healthy participants were experimentally tested with an implicit learning paradigm, answered questionnaires assessing empathy and autistic traits, and were genotyped for the rs2268498 polymorphism. T-allele carriers (TT and TC genotypes) exhibited significantly better implicit learning performance than carriers of the CC-genotype, and learning performance was positively associated with self-reported empathy and negatively with self-reported autistic traits. Results indicate that differences in implicit perception and storing of environmental details while watching social interactions could be an important mechanism to explain the association between differences in endogenous oxytocin activity and social functioning.. m

## Introduction

The neuropeptide oxytocin is an important messenger not only in the autonomic nervous system but also within the human brain. Due to its impact on the central nervous system it has been associated with a large variety of prosocial behaviors and processes in animals and humans. For example, it has been linked to bonding, nurturing behavior, altruism or emotion detection (e.g., Bosch, 2011; Campbell, 2008; Da Costa, Guevara-Guzman, Ohkura, Goode, & Kendrick, 1996; Galbally, Lewis, van Ijzendoorn, & Permezel, 2011; Heinrichs, von Dawans, & Domes, 2009; Ross & Young, 2009). An important strategy to investigate oxytocin in the context of human social behavior is the experimental manipulation of central nervous oxytocin activity by the administration of intranasal oxytocin. Results of these studies demonstrated a link between increased oxytocin activity and prosocial behaviors/empathy (e.g. enhanced abilities to correctly identify emotional facial expressions (Bartz et al., 2010) or increased levels of trust/ingroup altruism (e.g., De Dreu et al., 2010, Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005)). Furthermore, oxytocin application has been found useful in treatment of patients suffering from autism, depression, schizophrenia and other disorders (for an overview of effects of intranasal oxytocin in healthy controls and patients see Bakermans-Kranenburg & Van Ijzendoorn (2013) or MacDonald & MacDonald (2010)).

Next to the direct administration of oxytocin, the investigation of the molecular genetic basis of the oxytocin system is an important strategy to better understand individual differences in social functioning under (externally uninfluenced) physiological conditions (compare Melchers, Montag, Markett, & Reuter, 2013). Of special relevance is the gene coding for the oxytocin receptor (OXTR), which has been a focus of research in the social neurosciences over the last years (Meyer-Lindenberg, Domes, Kirsch, & Heinrichs, 2011; Montag & Reuter, 2014). An important functional polymorphism on this gene is the rs2268498 single nucleotide polymorphism (SNP), located in the putative promoter region of OXTR (3p25 of the short arm of chromosome 3). The rs2268498 has repeatedly been linked to social cognition in the literature. For example, it has been associated with trust (Reuter et al., 2009), moral ratings (Walter et al., 2012), emotion recognition abilities (Melchers et al., 2013), empathy and empathic accuracy (Christ, Carlo, & Stoltenberg, 2016; Laursen et al., 2014) or social perception

(Melchers, Montag, Felten, & Reuter, 2015b). Overall, these studies suggest that the rs2268498 polymorphism is an important candidate to understand the genetic underpinnings of individual differences in social functioning. Furthermore, Reuter et al. (2016) were able to show a 50 % decrease in hippocampal mRNA expression (the tissue stemming from epilepsy patients) of TT carriers compared to C allele carriers of the rs2268498, a finding that was supported by means of cloning, i.e. in vitro reporter gene expression analysis after transfection of OXTR promoter plasmids into HEK-293 cells. This functionality of the rs2268498 polymorphism can explain the results described above, because it suggests putative differences in endogenous oxytocin activity depending on genotype. Besides, Chen et al. (2015) investigated whether pharmacological enhancement of oxytocin activity and genetic variation on the OXTR gene (including the rs2268498 in a haplotype) interact concerning their association to social cognition abilities (measured by an emotion recognition paradigm). The authors found that carriers of a T-Allele containing haplotype profited significantly stronger (concerning their emotion recognition abilities) from a dose of oxytocin than carriers of a C-Allele containing haplotype. This result suggests that the rs2268498 polymorphism might not only affect endogenous oxytocin activity itself, but also sensitivity to changes in oxytocin activity caused by external stimuli.

An important question, which yet has to be answered, concerns the psychological and neural mechanisms which bridge the gap between differences in endogenous oxytocin activity and individual differences in social behavior. At least for intranasal oxytocin application, Bartz, Zaki, Bolger, and Ochsner (2011) suggested three possible mechanisms: anxiety reduction, which should lead to less anxiety in social interaction, influences on perception, which should lead to more (social) information processing and storage, and affiliative motivation, which should enhance drive for interacting successfully with others. For all three mechanisms, regulation of the activity and connectivity of the amygdala has been discussed as an important neural mechanism to explain the influence of oxytocin on a neural level (compare Gamer, Zurowski, & Büchel, 2010; Kirsch et al., 2005; Labuschagne et al., 2010).

The aim of the current study is to test the idea that genetic variation of the rs2268498 oxytocin receptor polymorphism (putatively influencing oxytocin receptor density and thereby endogenous oxytocin activity) might be associated to perceptual processes as hypothesized by Bartz et al. (2011) and – in a second step – also to information storage. Previous research concerning perceptual processing, memory and other polymorphisms on the OXTR gene provided first evidence for a possible relationship between these variables (compare also Kumsta and Heinrichs (2013)). For example, Tops, Van Ijzendoorn, Riem, Boksem, and Bakermans-Kranenburg (2011) were able to show that carriers of the GG genotype on the OXTR rs53576 polymorphism had less problems in hearing and understanding people in noisy environments (e.g., at a crowded party) than carriers of the C+ genotypes. This implies that the GG-carriers “social perception system” is more sensitive to social stimuli. Skuse et al. (2013) demonstrated an association between the OXTR rs237887 polymorphism and face recognition memory in (healthy) parents and siblings of children with high-functioning autism. Here, carriers of the AA genotype exhibited impaired memory for faces compared to the other genotypes, which is an important disadvantage in social interactions. If a comparable association between social perception/memory and the rs2268498 polymorphism should be detectable, this would not only replicate the importance of this polymorphism for social abilities, but also give information on possible underlying processes.

To test our hypothesis, we constructed an implicit detail learning paradigm (IDL). Implicit learning is concerned with testing the recall of information which was learned with only limited awareness of the learning process and without intention to learn (e.g., Chun & Jiang, 1998). Research in psychology found that implicit learning helps to develop a tacit knowledge base which represents the structure of and regularities in a given environment (Kaufman et al., 2010; Reber, 1989). This knowledge can be helpful to solve problems and make decisions in novel situations not only in case of cognitive tasks (Reber, 1989) but also in social interaction and social decision making (e.g., Lieberman, 2000). For example, Heerey and Velani (2010) were able to show that implicit nonverbal cues can be used to predict another person’s behavior in social interaction. Therefore, individual differences in the ability to implicitly perceive and store information gained in social interaction might be one

97 explanation for differences in social processing abilities: People more capable of processing socially  
98 relevant information implicitly might simply have more information at hand allowing them to behave  
99 more adapted to the respective social situation.

100 In our implicit learning paradigm, participants watched short video clips of people in social  
101 interactions. After video presentation, participants were asked for details from the respective scene,  
102 and accuracy scores were calculated for each subject. Next, all participants answered self-report  
103 questionnaires asking for empathy and autistic traits. These questionnaires were applied because we  
104 wanted to investigate whether participants' performance concerning the IDLP is positively related to  
105 self-perceived empathic abilities, which would once again hint that perception and memory  
106 functioning could be relevant to explain the relationship between genetic makeup and social abilities.  
107 In case of autism spectrum disorders, many studies have provided evidence for social attention  
108 impairments, for example related to social orienting, joint attention, or attention to distress (e.g.,  
109 Charman et al., 1997; Dawson et al., 2004). Furthermore, differences between children with autism  
110 and children of control groups have been reported in the field of non-social attention (e.g., Landry &  
111 Bryson, 2004; Plaisted, Swettenham, & Rees, 1999). Simultaneously, it has been shown that  
112 participants with autism spectrum disorder deploy enhanced attention to details (Baron-Cohen,  
113 Ashwin, Ashwin, Tavassoli, & Chakrabarti, 2009; Smith & Milne, 2009), which is an important  
114 prerequisite for strong systemizing abilities, defined as the ability to recognize repeating patterns in  
115 stimuli and associated rules in a system (Baron-Cohen et al., 2009). This strong attention to the  
116 functioning of systems which can be applied to a variety of systems (e.g. numerical, abstract,  
117 mechanical) may explain talents in areas like visuospatial transformation or rote memory (Baron-  
118 Cohen et al., 2009; Howlin, Goode, Hutton, & Rutter, 2009). At the same time, it has been argued that  
119 this attention to detail can be a disadvantage in social interaction, because it may shift attention from  
120 social to nonsocial characteristics of a stimulus (e.g., Valla, Maendel, Ganzel, Barsky, & Belmonte,  
121 2013). Differences in attention between participants with autism spectrum disorder and healthy  
122 controls might also be reflected in the relation between healthy participants' inclination to autism and  
123 our IDLP: The higher the autism score, the lower the ability to perceive and remember social details  
124 might be. For details regarding the data collection and measures, see the methods section.



Considering the previously reported results, we expect to find an association between the rs2268498 polymorphism and participants' abilities in the IDLP. Previous studies concerning the rs2268498 with only one exception (Laursen et al., 2014) reported advantages in social processing for carriers of the TT-genotype compared to carriers of the CC-genotype and the heterogeneous genotype somewhere in between (Chen et al., 2015; Christ et al., 2016; Melchers et al., 2013; Melchers et al., 2015b; Reuter et al., 2009; Walter et al., 2012). Therefore, we hypothesize an allele load effect with respect to the T-allele, i.e. best IDLP performance in carriers of the TT-genotype, worst IDLP performance in carriers of the CC-genotype and intermediate IDLP performance in carriers of the heterozygous CT-genotype. Since we distinguish between social and nonsocial questions (compare methods), this effect should primarily be visible within the "social" IDLP score. With respect to the questionnaires, we expect the same associations, with highest empathy (lowest autistic traits) in TT-genotype and lowest empathy (highest autistic traits) in CC-genotype. Applying the same argument, we expect positive correlations between empathy ratings and implicit detail learning and negative correlations between ratings for autistic traits and behavioral performance.

## Material and Methods

### Participants

N = 121 healthy Caucasians (n = 98 women, n = 23 men) participated in the present study. Because all of our participants (age M = 22.55; SD = 5.15) were psychology students at the University of Bonn, the gender distribution in our sample is rather skewed with more female than male participants. All participants were screened for a history of psychiatric or neurological illnesses by means of questionnaires prior to testing. None of the participants had to be excluded as the result of the screening. Written informed consent to participate was obtained prior to the experiment. The study was approved by the local ethics committee at the University Clinics of Bonn.

## Genotyping

DNA was extracted from buccal cells, which were collected by a combination of buccal swabs and mouthwashes (for details compare Schonlau et al., 2010). The purification of genomic DNA was conducted automated by means of the MagNA Pure®LC system using a commercial extraction kit (MagNA Pure LC DNA isolation kit; Roche Diagnostics, Mannheim, Germany). Genotyping of the OXTR rs2268498 polymorphism was implemented via real time PCR using fluorescence melting curve detection analysis by means of the Light Cycler System 1.5 (Roche Diagnostics, Mannheim, Germany). The primers and hybridization/ simple probes (TIB MOLBIOL, Berlin, Germany) were as follows:

Forward primer: 5'-ACCGGTCAGGGGCTCATA-3';

Reverse primer: 5'-TGTGCAATCTGAGGGTCAA-3';

Anchor hybridization probe: 5'-LCRed640-CTGGATGAAGGCAGATTTTCCCTATGA-phosphate-3';

Sensor hybridization probe [C]: 5'-AAAACACC\_GCCTCACCCACG-fluorescein-3'.

## Questionnaires

To measure participants' empathic abilities, we administered the *Interpersonal Reactivity Index* (IRI; Davis, 1983) and the *Empathy Quotient* (EQ; Baron-Cohen & Wheelwright, 2004). Furthermore, we administered the *Autism-Spectrum Quotient* (AQ; Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) to assess participants' inclination to autistic traits. The IRI is a multidimensional measure which is able to distinguish between cognitive and affective components of empathy. Furthermore, it measures participants' fantasy and distress experienced in difficult social interactions. The EQ has been developed in context of autism research as a one-dimensional measure including all empathy components. The AQ was constructed to measure autistic traits in adults with normal intelligence. For more details on the questionnaires and their psychometric properties, please see Melchers, Montag, Markett, and Reuter (2015c).

## **Implicit learning paradigm**

We constructed a computerized implicit learning paradigm with the E-Prime 2.0 software (Psychology Software Tools, 2012). Five short clips from German TV-formats with diverse topics (breakfast, business meeting, shopping, family celebration, talking to the neighbors on the street) were selected for presentation. The main aim was on the one hand to select films which included a lot of details that might be implicitly recognized by the participants and, on the other hand, to select films depicting social interactions. For each clip, 10 questions asking for details of the scene (e.g., “what is depicted on the picture in the background of the scene”) and the protagonists (e.g., “what is the name of the secretary”) were created. Half of these questions were in open format, the other half was in multiple choice format (one out of four options to choose from). Percentage of correct responses was calculated as the dependent variable. We calculated three scores: One for all questions, one for the non-social detail questions and one for the social protagonist questions. Participants were invited to the computer laboratory and tested in individual booths. To prevent that participants guessed the aim of the study prior to testing, they were told that they were taking part in a follow up study concerning vicarious embarrassment (Melchers et al., 2015a). The five video clips of the paradigm were presented in randomized order (at the subject level). After the presentation of all clips, subjects answered the 50 questions, which were also presented in randomized order (at the subject level). In both cases there was no effect of order of presentation on subjects’ performance.

## **Statistical Methods**

Distribution of genotypes was tested for Hardy-Weinberg-Equilibrium (Hardy, 1908). We checked whether age and gender were associated with genotype, because the sample size would allow for random age or gender differences between genotypes, which could confound results concerning the IDLP.

Questionnaire measures were inspected for reliability (Cronbach's alpha). Furthermore, influences of age and gender were tested for all dependent measures and in case of significance controlled for.

For the IDLP, we calculated item difficulties to ensure that the task included items of variable difficulty.

Possible associations between the rs2268498 polymorphism and the IDLP were analyzed by use of an ANOVA with the genotype groups of the OXTR rs2268498 (TT vs. CT vs. CC group) as between-subject factor. Finally, post hoc analyses (Scheffé's test of bivariate mean difference) were applied to compare the performance of individual genotypes. The p-values of these tests were adjusted for alpha error accumulation using Bonferroni correction. We report adjusted p-values.

## Results

### Genetic distribution

The genotype frequencies in our sample (TT: n = 33; CT: n = 56; CC: n = 32) were in Hardy-Weinberg-Equilibrium ( $\chi^2_{(1)} = 0.668$ ,  $p = 0.414$ ). We did not find age differences between genotypes of rs2268498 ( $F_{(2, 118)} = 0.737$ ,  $p = 0.481$ ) and gender was distributed equally between genotypes ( $\chi^2_{(1)} = 0.031$ ,  $p = 0.985$ ). Descriptive data for age and gender are shown in table 1.

[table 1 about here]

### IDLP performance and questionnaire data

Means, standard deviations and (in case of the questionnaires) Cronbach's alphas of participants' questionnaire and behavioral data are presented in table 2.

[table 2 about here]

Overall accuracy for detail learning was  $M = 0.63$  ( $SD = 0.11$ ), which means that a mean of 63 % of the items were answered correctly. Keeping in mind that half of the questions offered a guessing

probability of 25 %, while the other half was open, this mean value represents a good performance. Partition of the social (65 %) versus the nonsocial (61 %) questions delivered nearly the same results. The span of item difficulty was 0.04 to 0.96 with a normal distribution of item difficulties in between. Female and male participants' performance did not differ significantly (all questions:  $F_{(1, 118)} = 2.145$ ,  $p = 0.146$ ; social questions:  $F_{(1, 118)} = 0.642$ ,  $p = 0.426$ ; nonsocial questions:  $F_{(1, 118)} = 3.456$ ,  $p = 0.065$ ), and performance was not related to age (all questions:  $r = -0.050$ ,  $p = 0.584$ ; social questions:  $r = -0.092$ ,  $p = 0.315$ ; nonsocial questions:  $r = -0.003$ ,  $p = 0.974$ ). Descriptive statistics of the questionnaire data are in line with findings in comparable samples (compare Melchers et al., 2015c). Age was not associated with questionnaire responses, but female participants exhibited higher EQ scores ( $F_{(1, 118)} = 6.834$ ,  $p = 0.010$ ,  $\eta^2 = 0.054$ ) and higher scores in IRI affective empathy ( $F_{(1, 118)} = 3.909$ ,  $p = 0.05$ ,  $\eta^2 = 0.032$ ). Details on the association between the IDLP and the questionnaire measures are presented in table 3.

[table 3 about here]

The IDLP exhibits a medium size positive correlation with the EQ and smaller size positive correlations with the empathy subscales of the IRI (affective and cognitive empathy). At the same time, the IDLP performance is also negatively associated with participants' AQ-scores. Once again, splitting the IDLP into social and nonsocial questions delivers the same results.

### **Association of the rs2268498 with detail perception performance and questionnaire measures**

Results of the ANOVA revealed significant differences concerning accuracy in the IDLP between genotypes of the rs2268498 polymorphism ( $F_{(2, 118)} = 10.066$ ,  $p < 0.001$ ,  $\eta^2 = 0.146$ ). Carriers of the TT-genotype showed the highest level of accuracy ( $M = 0.685$ ,  $SD = 0.090$ ) followed by carriers of the TC- ( $M = 0.634$ ,  $SD = 0.112$ ) and the CC- genotype ( $M = 0.576$ ,  $SD = 0.076$ ) (figure 1).

[figure 1 about here]

Post hoc analyses revealed no significant difference between heterozygous and homozygous carriers of the T-allele (TT vs. TC; mean difference MD = 0.051,  $p = 0.055$ ), while carriers of the CC-

genotype performed significantly worse than both TC-carriers (MD = 0.058,  $p = 0.022$ ) and TT-carriers (MD = 0.109,  $p < 0.001$ ).

The separate analysis of social and nonsocial questions delivers comparable results: Once again there are the same significant differences depending on genotype in favor of the T-allele (social questions:  $F_{(2, 118)} = 7.301$ ,  $p = 0.001$ ,  $\eta^2 = 0.110$ ; nonsocial questions:  $F_{(2, 118)} = 8.444$ ,  $p < 0.001$ ,  $\eta^2 = 0.125$ ). Besides, in case of the social questions there is the same split up between carriers and noncarriers of the T-allele (TT vs. TC: MD = 0.042,  $p = 0.0235$ ; TT vs. CC: MD = 0.101,  $p = 0.001$ ; TC vs. CC: MD = 0.059,  $p = 0.042$ ). In case of the nonsocial questions, post hoc analyses show differences between the carriers and noncarriers of the C allele, while homozygous and heterozygous carriers of the C-allele do not differ significantly (TT vs. TC: MD = 0.061,  $p = 0.043$ ; TT vs. CC: MD = 0.114,  $p < 0.001$ ; TC vs. CC: MD = 0.053,  $p = 0.105$ ).

Concerning the questionnaire data, we observed no significant association to the rs2268498 polymorphism.

## Discussion

The present study investigates the association between the rs2268498 polymorphism on the OXTR gene and implicit detail learning abilities as measured by an IDLP. Furthermore, the study tests for an association of the polymorphism and the IDLP with self-report measures for empathy and autistic traits. Based on evidence from previous studies demonstrating the importance of oxytocin for social processes, and because of studies outlining the relevance of the functional rs2268498 polymorphism in this context, we hypothesized significant differences in the quality of detail perception and self-reported empathy depending on genotype. Besides, we expected positive correlations between empathy ratings and implicit detail learning performance and negative correlations between ratings for autistic traits and implicit detail learning performance.

We were able to show that carriers of at least one T-allele exhibit superior performance in implicit detail learning compared to the homozygous carriers of the C-allele while performance did not

differ significantly between homozygous and heterozygous carriers of the T-allele. A split up between the social and the nonsocial questions of the IDPL delivered comparable results in favor of the T-allele. Although we did not find an entire allele load effect, this fits nicely with previous findings demonstrating enhanced social abilities in carriers of the TT-genotype/T-allele carriers in areas like trust (Reuter et al., 2009), moral ratings (Walter et al., 2012) or facial emotion recognition (Melchers et al., 2013) compared to carriers of the CC-genotype, because once again the T-allele carriers exhibit characteristics that are advantageous for social processing/interaction. Though, one would expect to find this effect only in case of the social questions (compare below). Concerning the questionnaires measuring empathic abilities and autistic traits, we did not find a significant association to the rs2268498 polymorphism. Possibly, this may be explained by the much broader phenotype which is measured by the questionnaires in comparison to the IDLP. Besides, questionnaires in general (and especially in case of a social desirable feature like empathy) are susceptible for socially desirable response behavior, while behavioral paradigms are not. Finally, studies measuring empathy (as a trait) by use of questionnaires need more power (which means bigger samples) to detect genetic associations. In this context it is also interesting to note that most associations found between the rs2268498 polymorphism and social processes (compare introduction) originate from behavioral measurement. Most interestingly, we found a significant medium size positive correlation between the IDLP performance and the EQ as well as smaller size significant correlations between the IRI subscales measuring affective and cognitive components of empathy. At the same time, we observed negative correlations between the AQ and implicit detail learning. Again, the results for social and nonsocial questions of the IDPL are comparable. Participants with better IDLP performance tend to describe themselves as more empathic and less prone to autistic traits. This might indicate that pronounced abilities to perceive and store information from social interaction may be helpful to act empathically. Concerning the inclination to autism the negative correlation might be explained by less “social attention” of participants with higher AQ scores. Although in this case one would expect differences between the social and the nonsocial IDLP scores.

Taken together, our findings indicate that differences in the ability to implicitly perceive and store detailed information when observing others might be a candidate mechanism to explain the influence of individual differences in oxytocin system activity on social processing. In our study, the participants who previously depicted the most pronounced social processing (T-carriers) exhibited the best behavioral performance. Therefore, we hypothesize that this better performance of the T-carriers might indeed be partially explained by better social information processing and storing capacity. With more information at hand which can be used to adapt cognitions and behaviors to the respective social demands, it should be more easy (for the T-carriers compared to the CC-carriers) to think and act empathically. This proposed mechanism could also explain other associations found concerning the rs2268498: More available information could, for example, be very helpful to better understand the reasons for others' moral decisions (Walter et al., 2012) or help to detect emotions in faces (Melchers et al., 2013). A connection between empathic abilities and social perception has also been supposed by the results of Hooker, Verosky, Germine, Knight, and D'Esposito (2010). In their study, the authors observed relations between cognitive empathy and activity of the mentalizing network and between affective empathy and activity of the precentral gyrus during social signal perception, supporting the assumption that social perception processes interact with individual prosocial skills.

In interpreting our results, we must keep in mind that our study can only be a first step to better understand how individual differences in perception and memory represent an important mechanism to link the rs2268498 and oxytocin activity to social processing abilities. For example, performance in our IDLP contains aspects of perception as well as aspects of memory likewise. Therefore, we cannot be sure whether carriers of the T-allele showed better performance because they perceived more information, or because they memorized a greater proportion of the same amount of information perceived, or a mix of both. Follow-up studies should therefore try to distinguish between perception and memory processes, for example by use of an imaging genetics approach (compare for example Murray, Bussey, & Saksida, 2007). Existent research concerning the influence of oxytocin on memory functions is inconsistent. While older studies reported a negative influence of oxytocin on memory (e.g., Engelmann, Wotjak, Neumann, Ludwig, & Landgraf, 1996; Heinrichs, Meinlschmidt, Wippich,



Ehlert, & Hellhammer, 2004), newer research draws a more differentiated picture including beneficial effects of oxytocin (e.g., Feifel, MacDonald, Cobb, & Minassian, 2012; Savaskan, Ehrhardt, Schulz, Walter, & Schächinger, 2008). Therefore, more research is warranted to clarify the relationship between memory functions and activity of the endogenous oxytocin system. A second question concerns the type of information tested for in the IDPL: In our sample, we did not find the expected differences in results when comparing the social and the nonsocial questions. However, it is difficult to make a sharp distinction between both categories. Our approach was to differentiate depending on whether the question asked for information concerning the protagonists versus information concerning the scene. A limitation here might be that we presented only social situations to our participants. It could well be that the kind of situation presented (social interaction vs. no social interaction) is more important for the implicit learning process than the information asked for. Besides, studies investigating learning processes in infants have shown important differences between social and nonsocial learning (Meltzoff, Kuhl, Movellan, & Sejnowski, 2009). Finally, the correlation between our participants' social and nonsocial learning scores is rather high ( $r = 0.656$ ,  $p < 0.001$ ) indicating an overlap. Therefore, future studies should investigate other methods of distinction between social and nonsocial learning to see if these create more distinctive results concerning the association to the OXTR. Other aspects which should be considered in future research are the meaning of the presented information for the respective subject or the type of social interaction observed. A final limitation of our study is the unequal gender distribution with much more female than male participants, which possibly shifted the observed task performance compared to a gender-balanced sample (compare Melchers et al., 2013). On the other hand, we did not find differences in IDLP performance depending on gender, which reduces the relevance of the sex ratio in our sample.

Our results may have implications for practitioners. If differences in social processing can in parts be explained by perceptual and memory effects which themselves are associated with a specific genetic makeup, it should be possible to train persons which are prone to social deficits (in parts due to their genetic makeup; e.g., by training them to focus their attention) to improve their social abilities. Of course such training presupposes a more differentiated knowledge concerning the genetic and

349 environmental effects (and their interactions) on social processing/social abilities. Corresponding  
350 training procedures already exist, for example in the context of autism therapy (e.g., Ryan &  
351 Charragáin, 2010).

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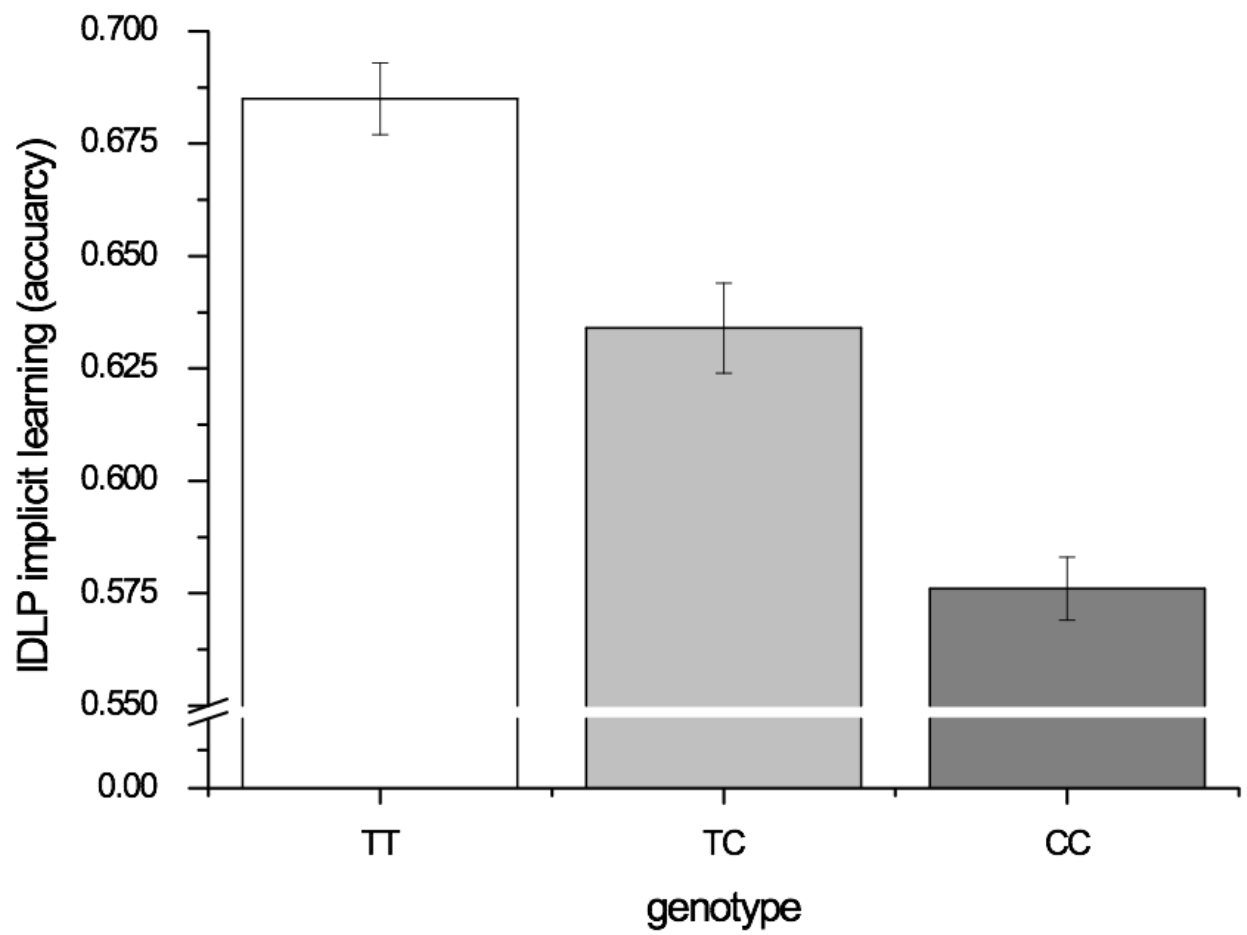


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## Figure Legends

Figure 1: Implicit learning performance depending on genotype of the rs2268498 polymorphism

Figr-1



Note: The figure displays means in implicit detail learning performance (accuracy) depending on genotype. On each bar, standard errors of mean for the respective genotype group are depicted.

Table 1: Distribution of gender and age by genotype.

Variable	TT-genotype	TC-genotype	CC-genotype	statistical comparison
gender (female / male)	27 / 6	45 / 11	26 / 6	$\chi^2_{(1)} = 0.031$ , $p = 0.985$
age (mean / SD)	23.48 / 5.95	22.20 / 5.41	22.22 / 3.61	$F_{(2, 118)} = 0.737$ , $p = 0.481$

Table 2: Means, standard deviations and (in case of questionnaires) Cronbach's alpha of participants' detail learning and questionnaire data.

Measure	M	SD	Cronbach's alpha
implicit detail learning (IDLP) all questions	0.63	0.11	-
implicit detail learning (IDLP) social questions	0.65	0.11	-
implicit detail learning (IDLP) nonsocial questions	0.61	0.12	-
Empathy Quotient (EQ)	45.00	10.73	0.886
Autism-Spectrum Quotient (AQ)	16.80	7.29	0.806
IRI fantasy	17.91	4.42	0.786
IRI perspective taking (cognitive empathy)	18.50	3.69	0.789
IRI empathic concern (affective empathy)	19.42	3.63	0.808
IRI personal distress	13.49	3.96	0.787

Table 3: Correlation between the IDLP performance and questionnaire measures.

	IDLP	IDPL social questions	IDPL nonsocial questions	EQ	AQ
EQ	$r = 0.436,$ $p < 0.001$	$r = 0.390,$ $p < 0.001$	$r = 0.407,$ $p < 0.001$	X	$r = -0.453,$ $p < 0.001$
AQ	$r = -0.218,$ $p = 0.016$	$r = -0.212,$ $p = 0.020$	$r = -0.183,$ $p = 0.045$	$r = -0.453,$ $p < 0.001$	X
IRI Fantasy	$r = 0.212,$ $p = 0.020$	$r = 0.152,$ $p = 0.097$	$r = 0.229,$ $p = 0.012$	$r = 0.195,$ $p = 0.033$	$r = -0.002,$ $p = 0.982$
IRI Perspective Taking (cognitive empathy)	$r = 0.347,$ $p < 0.001$	$r = 0.340,$ $p < 0.001$	$r = 0.228,$ $p = 0.001$	$r = 0.433,$ $p < 0.001$	$r = -0.248,$ $p = 0.006$
IRI Empathic concern (affective empathy)	$r = 0.184,$ $p = 0.045$	$r = 0.173,$ $p = 0.059$	$r = 0.168,$ $p = 0.067$	$r = 0.559,$ $p < 0.001$	$r = -0.353,$ $p < 0.001$
IRI Personal distress	$r = -0.082,$ $p = 0.370$	$r = -0.127,$ $p = 0.168$	$r = -0.026,$ $p = 0.777$	$r = -0.124,$ $p = 0.177$	$r = 0.242,$ $p = 0.008$

Note: IDLP=Implicit Detail Learning Paradigm (Accuracy), EQ=Empathy Quotient, AQ=Autism Spectrum Quotient, IRI=Interpersonal Reactivity Index.

Because we found gender differences for the EQ and dimensions of the IRI, correlations were also calculated separately for female and male participants and compared by means of z-statistics. These analyses did not reveal any significant gender differences.

For reasons of clarity, correlations between the IRI subscales have been omitted as they are not in focus of this research paper.