An Oxytocin Receptor Gene Variant Predicts Attachment Anxiety in Females and Autism-Spectrum Traits in Males

Frances S. Chen and Susan C. Johnson

Abstract

A molecular genetic approach was used to investigate the relationship between common variants of the oxytocin receptor (OXTR) gene and self-reported social functioning in healthy adults. Females with at least one copy of the A allele at OXTR rs2254298 reported greater attachment anxiety than females with two copies of the G allele. Males with at least one copy of the A allele at OXTR rs2254298 reported more autism-associated traits than males with two copies of the G allele. These results support the growing evidence that naturally occurring differences in the oxytocin system contribute to individual differences in social functioning in healthy adults. The authors discuss potential avenues by which sex may moderate the relationship between oxytocin and human social behavior.

Keywords
oxytocin, molecular genetics, attachment, broader autism phenotype, individual differences

The neuropeptide oxytocin plays a critical role in the formation and maintenance of social relationships. In nonhuman mammals, oxytocin has been implicated in a number of social behaviors, particularly in maternal behaviors, attachment, and pair bonding (for a review, see Lim & Young, 2006). In humans, administration of a single dose of intranasal oxytocin has numerous effects on social cognition and behavior (for a review, see Heinrichs, von Dawans, & Domes, 2009). For instance, oxytocin administration increases trusting behavior (Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005), enhances recognition of positive, socially relevant words (Unkelbach, Guastella, & Forgas, 2008), buffers against social stress (Heinrichs, Baumgartner, Kirschbaum, & Ehlert, 2003), and promotes secure interpretations of ambiguous events in insecurely attached adults (Buchheim et al., 2009).

In new mothers, plasma oxytocin levels in early pregnancy as well as during the postpartum period predict the frequency and intensity of a suite of maternal bonding behaviors including gaze, positive affect, affectionate touch, and attachment-related thoughts (Feldman, Weller, Zagoory-Sharon, & Levine, 2007). Research also suggests that abnormal functioning of the oxytocin system may be involved in the etiology of autism—a developmental disorder characterized by aversion to social interaction and difficulties in interpreting the emotions of others (American Psychiatric Association [APA], 1994). Low baseline plasma levels of oxytocin have been documented in individuals with autism (Modahl et al., 1998), and injection of oxytocin into the blood has been found to reduce certain physical and psychological symptoms of autism (Hollander et al., 2003; Hollander et al., 2007). Genetic methodologies have also linked variation in the oxytocin receptor (OXTR) gene to individual differences in social behavior. Oxytocin receptor gene knockout mice show a number of deficits in social behavior and social memory (Crawley et al., 2007; Takayanagi et al., 2005). In humans, single nucleotide polymorphisms (SNPs) of the human oxytocin receptor gene have been associated with risk for autism in several studies (Jacob et al., 2007; Lerer et al., 2008; Liu et al., 2010; Wu et al., 2005). Consistent with twin research showing that attachment patterns in healthy adults are heritable (Donnellan, Burt, Levendosky, & Klump, 2008), OXTR polymorphisms have also been linked to emotional support-seeking behavior in adults (Kim et al., 2010), as well as parental sensitivity (Bakermans-Kranenburg & van IJzendoorn, 2008), and the quality of infants’ attachment bonds with their caregivers (Chen, Barth, Johnson, & Gotlib, 2011). In patients with depression, OXTR polymorphisms have been linked to adult attachment style (Costa et al., 2009). On the neurological level, OXTR polymorphisms have been linked to individual differences in hypothalamic-limbic structure and function (Inoue et al., 2010; Tost et al., 2010).
Research on the genetic factors that influence patterns of human social behavior has important applications. Identifying genetic markers linked to risk for difficulties in adult social functioning may permit these difficulties to be addressed at an earlier stage, when the relevant behavioral and cognitive patterns are still in formation. It may also eventually facilitate the development of more effective, individually tailored treatments for individuals afflicted with autism, social anxiety, and attachment disorders. Thus, research on genetic factors influencing the function of the oxytocin system may have implications in a broad range of contexts.

Although significant progress has been made in specifying associations between OXTR gene variants and human social behavior, notable inconsistencies also exist in the literature. One large multisite study failed to find an association between autism and OXTR (Tansey et al., 2010), and another study found no association between OXTR polymorphisms and trusting behavior (Apicella et al., 2010). Additionally, ethnic differences have been found in the direction of association between particular alleles and traits (see Jacob et al., 2007; Thompson, Parker, Hallmayer, Waugh, & Gotlib, 2010; Wu et al., 2005). Across various studies investigating multiple SNPs simultaneously, discrepancies also appear in the exact SNP that is associated with social behavior.

Some of these apparently inconsistent results may in fact be reconciled through greater attention to the role of sex differences, which have not been taken into account in many existing molecular genetic studies investigating the oxytocin receptor. Sex-specific associations between genotype and phenotype are relatively common and can arise, for instance, as a result of the different hormonal milieu of the cellular environment in men and women (Weiss, Pan, Abney, & Ober, 2006). In the case of oxytocin, estrogen is known to modulate the effects of oxytocin on social behavior (McCarthy, 1995).

The presence of oxytocin has also been linked to different neurological and behavioral consequences in men and women. While oxytocin administration decreases amygdala reactivity to emotional faces in men (Domes et al., 2007), it increases amygdala reactivity to emotional faces in women (Domes et al., 2010). Levels of plasma oxytocin rise in both mothers and fathers after the birth of a child but are correlated with different parenting behaviors (affectionate behavior in mothers vs. stimulating play in fathers; Gordon, Zagoory-Sharon, Leckman, & Feldman, 2010).

In several social disorders in which oxytocin is thought to play a role, prevalence varies significantly by sex. Autism, for instance, is diagnosed approximately four times more often in males than in females (see Volkmar, Szatmari, & Sparrow, 1993), while social anxiety is diagnosed more often in females than in males (see Chapman, Mannuzza, & Fyer, 1995). Higher attachment anxiety in young adult females than in males has also been reported in some studies (see Del Giudice, 2009). Furthermore, different cultural norms regarding seeking social support in times of distress have been found to moderate the role of OXTR polymorphisms on the social support-seeking behavior of Koreans and Americans (Kim et al., 2010). By extension, prevalent gender norms influencing how males and females interpret their own social behavior are also likely to moderate the role of OXTR polymorphisms on self-reported social functioning. Taken together, these results highlight biologically and environmentally influenced sex differences as potential mediators of the relationship between oxytocin receptor gene variants and human social behavior.

In the current study, we investigated two SNPs of the OXTR gene, rs2254298 and rs53576, that have been previously linked to risk for autism and various attachment-related behaviors. We hypothesized that polymorphisms at these locations would show sex-specific linkage patterns to specific measures of social functioning in healthy adults. First, given the previously established connection between oxytocin and attachment-related behaviors in both humans and nonhuman mammals, we predicted a relationship between OXTR gene polymorphisms and adult attachment as measured by the Experiences in Close Relationships (ECR) Scale (Brennan, Clark, & Shaver, 1998). Given the previously cited sex differences in prevalence of social anxiety and high attachment anxiety, we predicted that the relationship would be particularly pronounced in females. The relationship between OXTR rs2254298 and adult attachment in particular has not yet been tested using the ECR. On the other hand, two previous studies (Gillath et al., 2008, Rodrigues, Sasaki, Garcia, John, & Keltner, 2009) failed to identify a relationship between OXTR rs53576 and adult attachment as measured by the ECR, and one previous study (Costa et al., 2009) failed to identify a relationship between OXTR polymorphisms and attachment in healthy adults using a different attachment questionnaire (the ASQ: Feeney, Noller, & Hanrahan, 1994). Notably, however, neither Gillath et al. (2008) nor Costa et al. (2009) specifically report the inclusion of participant sex in analyses.

Second, given the numerous documented links between oxytocin and clinically diagnosed autism, we predicted that OXTR polymorphisms would be linked to the broader autism phenotype (BAP) in the general population, particularly in males. The BAP includes milder manifestations of the social and communicative difficulties and preferences for restricted or repetitive activities that characterize individuals with autism; these characteristics are particularly common in males (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). Research on twins has also previously suggested a significant heritable component to the BAP (Hoekstra, Bartels, Verweij, & Boomsma, 2007). However, the BAP has so far not been linked to any specific genes.

Method
One hundred seventy-eight individuals (70 male, 108 female) participated for payment or partial course credit. The sample was ethnically diverse (42% Caucasian, 28% Asian, 8% African American, 5% Hispanic/Latino, and 18% other, mixed, or not reported).

Participants completed the ECR scale (Brennan et al., 1998) as well as the Autism-Spectrum Quotient (Baron-Cohen et al., 2002).
Table 1. Relationship Between OXTR rs2254298 Polymorphism, Attachment, and Broader Autism Phenotype in Males and Females

<table>
<thead>
<tr>
<th></th>
<th>GG Male</th>
<th>AG/AA Male</th>
<th>GG Female</th>
<th>AG/AA Female</th>
<th>Group Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>45</td>
<td>18</td>
<td>58</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>ECR attachment avoidance</td>
<td>3.0 (±1.1)</td>
<td>3.4 (±1.2)</td>
<td>3.2 (±1.2)</td>
<td>3.0 (±1.1)</td>
<td>F(1,163) = 0.5, ns</td>
</tr>
<tr>
<td>ECR attachment anxiety</td>
<td>3.8 (±1.2)</td>
<td>3.8 (±1.3)</td>
<td>3.8 (±1.0)</td>
<td>4.3 (±1.0)</td>
<td>F(1,163) = 5.0*</td>
</tr>
<tr>
<td>Autism Spectrum Quotient</td>
<td>16.0 (±5.1)</td>
<td>20.1 (±7.5)</td>
<td>16.7 (±5.6)</td>
<td>15.3 (±4.9)</td>
<td>F(1,163) = 11.6*</td>
</tr>
<tr>
<td>Social subscales</td>
<td>4.4 (±3.3)</td>
<td>6.2 (±4.4)</td>
<td>5.1 (±3.7)</td>
<td>4.6 (±3.2)</td>
<td></td>
</tr>
<tr>
<td>Nonsocial subscales</td>
<td>9.8 (±2.8)</td>
<td>10.8 (±2.6)</td>
<td>9.8 (±3.3)</td>
<td>9.9 (±2.7)</td>
<td>F(1,163) = 0.9, ns</td>
</tr>
</tbody>
</table>

Individual cells depict means ± one standard deviation. Group comparisons depict interactions between polymorphism and sex.
* p < .05.
† p < .06.

Table 2. Relationship Between OXTR rs2254298 Polymorphism, Attachment Anxiety, and Broader Autism Phenotype in Ethnic Subgroups (Caucasians, Asians, and Other/Mixed)

<table>
<thead>
<tr>
<th></th>
<th>GG Male</th>
<th>AG/AA Male</th>
<th>GG Female</th>
<th>AG/AA Female</th>
<th>Group Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>24</td>
<td>8</td>
<td>29</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>ECR anxiety</td>
<td>3.6 (±1.1)</td>
<td>3.4 (±1.4)</td>
<td>4.0 (±1.1)</td>
<td>4.5 (±1.0)</td>
<td>F(1,69) = 3.4, p = .07</td>
</tr>
<tr>
<td>AQ</td>
<td>15.3 (±4.9)</td>
<td>18.3 (±6.5)</td>
<td>15.8 (±6.3)</td>
<td>13.2 (±4.8)</td>
<td>F(1,69) = 5.2, p = .03</td>
</tr>
<tr>
<td>Asian</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>11</td>
<td>7</td>
<td>9</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>ECR anxiety</td>
<td>3.7 (±0.9)</td>
<td>4.0 (±1.5)</td>
<td>4.1 (±0.9)</td>
<td>4.1 (±0.9)</td>
<td>F(1,45) = 0.1, p = .79</td>
</tr>
<tr>
<td>AQ</td>
<td>15.5 (±4.4)</td>
<td>20.9 (±7.8)</td>
<td>14.9 (±3.1)</td>
<td>15.9 (±4.6)</td>
<td>F(1,45) = 1.9, p = .18</td>
</tr>
<tr>
<td>Other/Mixed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>15</td>
<td>5</td>
<td>22</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>ECR anxiety</td>
<td>4.1 (±1.6)</td>
<td>3.6 (±1.3)</td>
<td>3.5 (±0.9)</td>
<td>4.4 (±1.0)</td>
<td>F(1,49) = 3.9, p = .06</td>
</tr>
<tr>
<td>AQ</td>
<td>16.6 (±6.1)</td>
<td>19.8 (±9.4)</td>
<td>18.0 (±5.6)</td>
<td>16.7 (±4.9)</td>
<td>F(1,49) = 2.2, p = .15</td>
</tr>
</tbody>
</table>

Individual cells depict means ± one standard deviation. Group comparisons depict interactions between polymorphism and sex.

2001), and then provided a saliva sample for genetic analyses. We selected two SNPs of the oxytocin receptor gene for analysis based on their known association with autism (Jacob et al., 2007; Wu et al., 2005): OXTR rs2254298 and OXTR rs53576. Both are located in the third intron of the oxytocin receptor gene on human chromosome 3 (Inoue et al., 1994) and are likely non-coding markers of unidentified functional variations in the OXTR gene.

Questionnaires
The ECR scale is designed to measure attachment-related anxiety and close relationships. Participants are asked to think about their close relationships, without focusing on a specific partner, and rate the extent to which each item accurately describes their feelings in close relationships. Half of the items address attachment anxiety and the other half address attachment avoidance (Brennan et al., 1998). As recommended by the authors (Fraley, 2005), the continuous dimensions of anxiety and avoidance—rather than categorical attachment classifications—were used for individual difference analyses. The mean and standard deviation of the ECR Avoidance and Anxiety subscale scores in our sample (Avoidance M = 3.05, SD = 1.15, Anxiety M = 3.93, SD = 1.12) were comparable with those obtained (Avoidance M = 2.93, SD = 1.18, Anxiety M = 3.64, SD = 1.33) in a large online survey of 22,000 individuals (Fraley, 2005).

The Autism Spectrum Quotient (AQ) assesses features of the broad phenotype of autism in healthy adults, including subscales for social skill, attention switching, attention to detail, communication, and imagination. The mean and standard deviation of the Autism-Spectrum Quotient scores in our student sample (M = 16.31, SD = 5.65) were comparable with those reported in the original student sample tested (M = 17.6, SD = 6.4; Baron-Cohen et al., 2001).

AQ scores were moderately correlated to both ECR Attachment Avoidance (r = .31, p < .01) and ECR Attachment Anxiety (r = .23, p < .01) scores, suggesting some overlap in the constructs measured by these scales. To test the relationship between oxytocin receptor gene polymorphisms and the independent aspects of each respective construct, we therefore included the non-targeted questionnaire as a covariate in each analysis.

Genotyping
Saliva samples were collected using the Oragene Kit (DNA Genotek, Ottawa, Ontario, Canada), which allow for the collection, preservation, transportation, and purification of DNA. Genotyping was carried out by KBiosciences using their internal KASP chemistry, a form of fluorescence-based competitive allele-specific PCR using FRET quencher cassette oligonucleotides. Amplification of rs2254298 was performed with the
primers 5’-TGAAAGCAGAGGTGTGTGGACAGG-3’ and the 5’-AACGCCACCCCCAGTTCTTC3’ under standard conditions. Amplification of rs53576 was performed with the primers GCCCACCATGCTCCTCACATC and GCTGGACTCAGGAAGATAAGGGAC. Further details of the assay design are available directly from KBiosciences (http://www.kbioscience.co.uk).

At the rs2254298 locus, 110 individuals were homozygous for the G allele and 61 individuals were heterozygous with one A and one G allele. Only seven individuals were homozygous for the A allele. Therefore, after confirming that the mean questionnaire scores of the seven AA carriers did not differ from the scores of the AG carriers, these two groups were combined to create one single group with at least one A allele. At the rs53576 locus, 58 individuals were homozygous for the G allele, 90 were heterozygous with one A and one G allele, and 28 individuals were homozygous for the A allele (genotypes were not obtained for two samples).

The inclusion of various ethnic groups in a single association study adds the complexity of possible population stratification due to genetic drift. Thus, we conducted both overall analyses on the whole sample—first confirming that there were no significant main effects of ethnicity (Caucasian, Asian, and Other/Mixed) or interactions between ethnicity and genotype on the questionnaire measures—and then conducted analyses separately for three subgroups divided by ethnicity (Caucasian, Asian, and Other/Mixed). Importantly, the distributions of polymorphisms in our Caucasian and Asian samples were comparable to those reported in previous studies (Jacob et al., 2007; Wu et al., 2005) as well as the human genome database (www.hapmap.org). In our Caucasian subsample, the distribution at rs2254298 was 71% GG, 26% AG, and 3% AA; at rs53576, the distribution was 46% GG, 50% AG, and 4% AA. In our Asian subsample, the distribution at rs2254298 was 40% GG, 50% AG, and 10% AA; at rs53576, the distribution was 16% GG, 47% AG, and 37% AA.

Both SNPs were in Hardy-Weinberg equilibrium in all three ethnic subsamples (all p > .05). To test for association between the two SNPs, we used Haploview 4.2 (http://www.broad.mit.edu/mpg/haploview) to calculate $r^2$, a measure of linkage disequilibrium. In our overall sample as well as within the three ethnic subsamples, negligible linkage disequilibrium was observed (all $r^2 < .08$).

**Results**

**OXTR and Attachment**

In a univariate analysis of variance (ANOVA) of attachment anxiety, OXTR rs2254298 polymorphism and sex were entered as fixed factors, and AQ score was entered as a covariate. There was a significant main effect of sex on ECR anxiety score, with females scoring higher than males (Male $M = 3.72$, $SD = 1.23$; Female $M = 4.06$, $SD = 1.01$, $F(1, 173) = 7.14$, $p < .05$, partial $\eta^2 = .04$). Higher levels of attachment anxiety in young adult females have been documented in prior literature (see Del Giudice, 2009).

There was no significant main effect of OXTR polymorphism on attachment anxiety, consistent with the results of Costa et al. (2009). However, there was a significant interaction between polymorphism and sex on attachment anxiety, controlling for AQ score, $F(1, 173) = 5.30$, $p < .05$, partial $\eta^2 = .03$. Further inspection of the result (summarized in Table 1) revealed that the effect of polymorphism on attachment anxiety was primarily driven by females. Females with at least one copy of the A allele reported higher attachment anxiety (controlling for AQ score) than females with two copies of the G allele (AA/AG $N = 48$, $M = 4.32$, $SD = 0.95$; GG $N = 60$, $M = 3.84$, $SD = 1.02$). This represents the first evidence of a significant relationship between oxytocin receptor gene polymorphisms and attachment anxiety in females.

We found no significant relationship between rs2254298 and attachment avoidance. Replicating the results of Gillath et al. (2008) and Rodrigues et al. (2009), we also found no relationship between polymorphism at locus rs53576 and either attachment anxiety or attachment avoidance. Even when the AA and AG groups were combined, as has been done in some previous studies (Bakermans-Kranenburg & van IJzendoorn, 2008; Rodrigues et al., 2009), rs53576 polymorphism did not predict adult attachment.

We also analyzed the interaction between rs2254298 polymorphism and sex on attachment anxiety separately for three subgroups divided by ethnicity (Caucasian, Asian, and Mixed/Other). As summarized in Table 2, patterns similar to that observed in the overall sample emerge in the Caucasian and Other/Mixed subgroups (with partial $\eta^2 = .05$ and .07, respectively), though not in the Asian subgroup. Given the relatively small sample sizes used these analyses, further research with larger single-ethnicity samples will be necessary to confirm the robustness of these effects within different ethnic groups.

**OXTR and the BAP**

In a univariate ANOVA of the BAP, OXTR rs2254298 polymorphism and sex were entered as fixed factors, and ECR anxiety score was entered as a covariate. There was a
significant main effect of sex on AQ score (Male $M = 16.83$, $SD = 6.05$; Female $M = 15.97$, $SD = 5.38$, $F(1, 173) = 6.44$, $p < .05$, partial $\eta^2 = .04$). This conforms to previous findings that that males score higher on the AQ than females (Baron-Cohen et al., 2001).

There was no significant main effect of $OXTR$ polymorphism on AQ score. However, there was a significant interaction between polymorphism and sex on AQ score, controlling for attachment anxiety, $F(1, 173) = 10.35$, $p < .01$, partial $\eta^2 = .06$. Further inspection of the result (summarized in Table 1) revealed that the effect of polymorphism on AQ score was primarily driven by males. Males with at least one copy of the A allele reported higher AQ scores (controlling for attachment anxiety) than males with two copies of the G allele (AA/AG $N = 20$, $M = 19.55$, $SD = 7.41$; GG $N = 50$, $M = 15.74$, $SD = 5.10$). This represents the first evidence of a significant relationship between oxytocin receptor gene polymorphisms and the BAP in males.

To follow up on this result, we separately examined social and nonsocial aspects of the BAP; predicting that the sex-specific effects of rs2254298 would be more strongly linked to social aspects of the BAP. We conducted separate ANOVAs with either the sum of the two most socially relevant subscales of the Autism Spectrum Quotient (social skill and communication), or the two most nonsocial subscales (attention switching and attention to details), as dependent variables. Polymorphism and sex were entered as fixed factors. As summarized in Table 1, the interaction between polymorphism and sex was indeed stronger on social scales than on the nonsocial scales. This pattern suggests that the sex-specific relationship between rs2254298 polymorphisms and the BAP may be particularly pronounced for social aspects of the phenotype.

We found no relationship between polymorphism at locus rs53576 and AQ score, neither when the AA and AG groups were considered separately nor when they were combined.

We also analyzed the interaction between rs2254298 polymorphism and sex on BAP separately for three subgroups divided by ethnicity (Caucasian, Asian, and Mixed/Other). As summarized in Table 2, similar patterns emerge in all three subgroups (with partial $\eta^2 = .07$, .04, and .04, respectively). Given the relatively small sample sizes used these analyses, further research with larger single-ethnicity samples will be necessary to confirm the robustness of these effects within different ethnic groups.

**Discussion**

We documented sex-specific relationships between polymorphisms of the $OXTR$ gene and two measures of social functioning in a sample of healthy adults. The A allele at locus rs2254298 was associated with higher attachment anxiety in females, and with more autism-spectrum traits in males. These patterns of association were similar across three different subgroups divided by ethnicity (Caucasian, Asian, and Other/Mixed). These associations not only support the growing evidence that adult attachment patterns are influenced by the functioning of the oxytocin system but also document for the first time a link between a specific set of genetic variants and the BAP. As noted by Piven (2001), identifying specific genes linked to specific components (e.g., social vs. nonsocial) of the BAP is one way to isolate relevant elements of the complex genetic interactions that likely contribute to more severe manifestations of autism. These results therefore have implications for the broad project of identifying genetic factors contributing to individual differences in complex social behaviors and also may have implications for clinical research.

Future research should continue to investigate the moderating role of sex in the relationship between $OXTR$ polymorphisms and social behavior. It is possible that sex differences at the biological or neurological level (for instance, involving estrogen or patterns of amygdala activation) contribute to a stronger link between oxytocin and attachment anxiety in females, or to a stronger link between oxytocin and autism-spectrum characteristics in males. Additionally, males and females are likely subject to different social norms regarding acceptable forms of interpreting and reporting their difficulties in social relationships, which may well contribute to sex-specific manifestations of oxytocin effects. These possibilities highlight the need for further research to specify the antecedents and consequences of sex differences in human oxytocin effects.

The existing research highlights several of the challenges of association studies linking SNPs and complex human behavior. First, functional mechanisms are not currently known for the intronic (non-coding) SNPs investigated in this study. However, the previously documented associations between these polymorphisms and autism, anxiety, and amygdala structure and function suggest that these SNPs are non-coding markers of unidentified functional variations in the $OXTR$ gene. Alternatively, these variants may interact with enhancers or repressors acting on the $OXTR$ promoter and thereby influence gene expression. Furthermore, the degree of independence in the contribution of variations at rs2254298 and rs53576 to different human social behaviors remains an open question. In the current study, we did not find a relationship between these particular measures of social functioning and variation at $OXTR$ rs53576, which has previously been linked to autism. On the other hand, our pattern of results is consistent with previous studies that have also found no relationship between rs53576 and adult attachment. An important project for future research will be to integrate the findings with various SNPs through haplotype analyses on larger samples.

It is also important to stress that the effect sizes found in these studies are comparable to those found in other candidate gene studies, in that they explain only between 3% and 7% of the variance in the effects reported. Outcomes as complex as self-reported attachment anxiety and autism-associated traits are undoubtedly influenced by numerous genetic and environmental factors. The issues that have already arisen in this line of investigation reinforce the need for continued research on diverse samples and various social behaviors; the associations between $OXTR$ gene variants and human social behaviors are certain to prove more complex than has been currently...
described. For the time being, however, these results should motivate the continued inclusion of rs2254298 and sex-specific analyses in future research examining links between OXTR gene variants and human social behavior.

The ease or difficulty with which individuals build and maintain social relationships is a critical predictor of psychological and physical health. Variants of the oxytocin receptor gene appear to be one of the factors contributing to individual differences in this domain. We expect that future research in this area will continue to refine our understanding of the biological bases of human social behavior.

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Notes

1. The interaction between polymorphism and sex on attachment anxiety is also significant \((p < .01)\) when AQ score is not entered as a covariate.

2. The interaction between polymorphism and sex on AQ score is marginal \((p = .13)\) when attachment anxiety is not entered as a covariate, suggesting that the effect is stronger on aspects of the broader autism phenotype that are independent of attachment anxiety.

References


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