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No Association Between an Oxytocin Receptor Genetic Variant and Depressive Symptoms

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INTRODUCTION

- Depression has the greatest impact on daily functioning capability of all diseases and adversely effects individuals globally (Flint & Kendler, 2014).
- Human capital value of these losses has been about $40 billion dollars annually (Kessler, 2012).
- Analysis of the genetic and biological systems associated with depressive symptoms, such as the oxytocin system, could lead to identifying risk variants and possible treatment development.
- Genetic Variation in *OXTR* is associated with a variation in depressive symptoms including low self-esteem, pessimism, and low self-efficacy, etc. (Conner et al., 2018).
- The A allele of the SNP rs53576 is considered the risk allele as it's associated with decreased pro-social behavior and increased loneliness and suicide attempts (Parris et. Al., 2018)
- The exact mechanism has not been identified, but G/G homozygotes recorded to have higher oxytocin levels, associated with increased emotional responsiveness (Marsh et al., 2012; Tost et al., 2010)
- We hypothesize that: (1) individuals possessing the A allele of the rs53576 SNP of *OXTR* will have more depressive symptoms on average. (2) Females will have more depressive symptoms on average. (3) There is an interaction between genotype and biological sex, as A allele females will have more depressive symptoms on average.

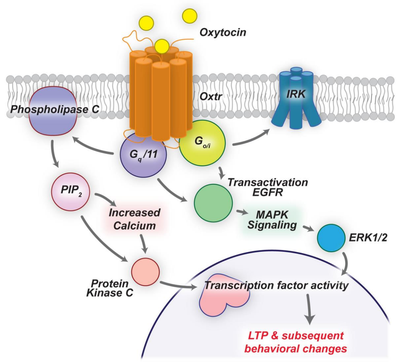

Figure 1: The reception of the oxytocin hormone or neurotransmitter by the oxytocin receptor, coded by the *OXTR.* This is what triggers signaling cascades that results in the physiological changes associated with oxytocin. The SNP 53576 is on the third intron of the *OXTR* gene. The possession of the A allele of this SNP is associated with decreased functional connectivity of certain brain regions, resulting in decreased prosocial behavior. (Stjepanovic et al., 2013).

METHODS

- Participants: Undergraduate Students (N=1,128) from the University of Nebraska-Lincoln (72% female; 76.1% White; with an age range = 19-61 years, *M* = 20.34) volunteered and received course credit for their participation.
- Measure: Each of the 21-items of the Beck Depression Inventory (BDI) asks participants to the select one statement most representative of their emotional state from four statements.
  - The first statement is scored as '0' and is least representative of depression, while the last statement is scored as a '3' and is most representative.
  - Scores range from 0-63, higher scores representing more severe depressive symptoms. One example question from the BDI representing severe depression would be "I can't make decisions at all anymore" (Beck et al., 1991).
- Procedure: The DNA was extracted from cheek cells using a Gentra Puregene Buccal Cell Kit (Qiagen, Valencia, CA). Then RT-PCR using TaqMan (Applied Biosystems, Foster City, CA) analysis was used to genotype the rs53576 SNP.
- Data Analysis: A 2x2 factorial ANOVA was used to test for the factors: Gender and SNP. "A" allele carries were grouped and compared to G/G homozygotes as is standardly performed with this SNP (Choi, Minote, & Watanuki, 2017; Gong et al, 2017). Race (White vs. non-white) and age were covariates within this study (Choi et al., 2019).

RESULTS

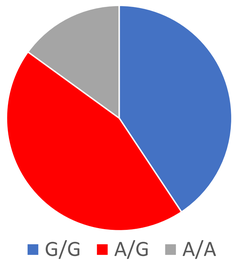

Fig. 2. The genotype distribution included 401 (40.7%) G/G, 437 (43.2%) A/G, and 148 (15.01%) A/A. The minor (A) allele frequency was .37. A allele carries were compared to G/G homozygotes for analysis. Our sample was in Hardy-Weinberg equilibrium ($\chi 2 = 2.765$, $p<0.05$).

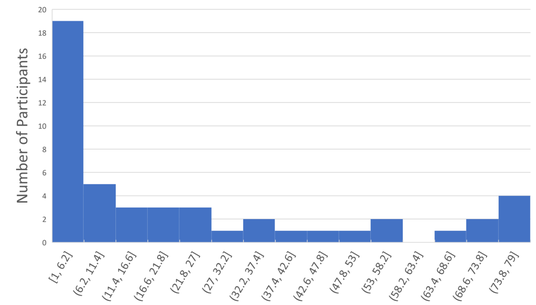

Fig. 3. Frequency distribution of BDI scores. There is a positive skew to the distribution (*M*=9.65, *SD*=8.74, skew=1.60, kurtosis=3.46).

Table 1. Between-subjects effects of OXTR/rs53576 genotype and biological sex on BDI score

Source	df	Mean Square	F	p
Age	1	2.265	.033	.856
Race	1	212.635	3.084	.079
rs53576	2	54.153	.785	.376
Sex	1	925.285	13.419	<.01
rs53576 * Sex	2	1.478	.021	.884

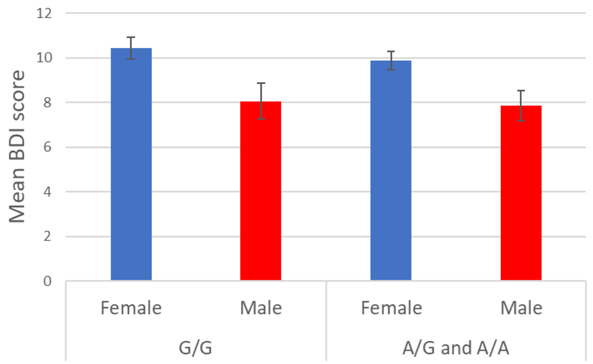

Fig. 4. rs53576 genotype by sex in BDI scores. Bars indicate standard error. There was no significant main effect of genotype, p =.376, or interaction between sex and genotype, p =.884.

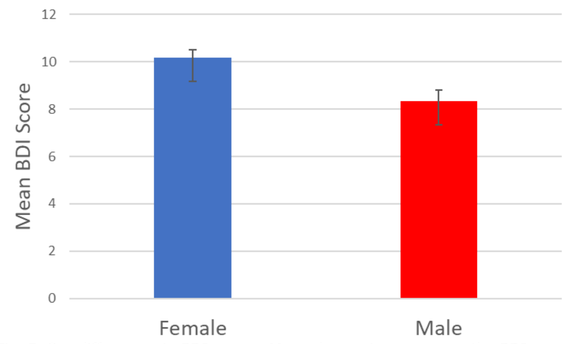

Fig. 5. Sex differences in BDI scores. Mean depression scores on the BDI are indicated for each sex. Bars indicate standard error. There was a significant effect of sex, p<.01.

DISCUSSION

- Consistent with previous findings, females had higher average depressive symptom scores (Albert, 2015; Picco et al., 2017).
- No significant difference in depressive symptoms scores found between A allele carries and G/G homozygotes.
- Contrary to the results of this study, A allele carries have been found to demonstrate, on average, higher depressive symptoms as calculated through the BDI (Thompson et al., 2014).
- Although there is some evidence for an association between rs53576 genotypes and depressive symptoms, this association isn't present in our non-clinical population, some previous findings may have been false positives (Hong et al., 2012).
- Most previous studies that found significant results used structured interviews, physician diagnosis of various forms of depression, and observation during stress-inducing activities along with questionnaires, while the present study relied solely on self-reporting (Conner et al., 2018; McQuaid et al., 2016).
- Studies that found significant results relied on clinical populations and smaller sample sizes than this study, the generalizability of results could be questioned and may be why results were not repeated within this study (Conner et al., 2018; McQuaid et al., 2016).
- Strengths of this study: sample size; validity and reliability of BDI scale
- Limitations: self-reported surveys and homogenous sample population, specifically age and ethnicity- may not generalize well to general population
- Research may benefit from analyzing the genetic variants of the rs53576 SNP in the context of other SNPs associated with decreased levels of oxytocin, including rs2254298 and *CD38* rs3796863.
- As depression adversely affects individuals around the world, it is essential to continue research into a better understanding of their biological and genetic underpinnings to form effective treatments.

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