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Infancy onset maltreatment and the development of suicide ideation: an investigation of moderation by oxytocin-related gene polymorphisms

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Abstract

Background: Suicide ideation and behavior remains a significant public policy concern. The interpersonal-psychological theory of suicide posits that thwarted belongingness potentiates risk for suicide. Early disruptions in caregiving have documented effects on lifespan social and interpersonal development, and therefore warrants further investigation in suicide research. This novel study investigates risk for suicide ideation conferred by infant-onset child maltreatment and oxytocin genotypes (OXTR and CD38) and tests interactive effects of genetics and early maltreatment experiences.

Methods: Participants (*N*=251) were from a longitudinal follow-up study of emerging adults who participated in a research summer camp program as children (wave 1). Childhood maltreatment was coded from child protective service records and buccal cells were obtained from children and genotyped. At wave 2, self-reported suicide ideation and internalizing symptomatology were obtained.

Results: Maltreatment onset in infancy was significantly related to lifetime suicide ideation. The CD38 gene variation moderated this association such that early onset maltreatment was related to suicide ideation among C-carriers only. The OXTR gene did not relate to lifetime suicide ideation, nor did it moderate early onset maltreatment risk.

Limitations: This study was conducted with a relatively small sample, necessitating the combination of genotypes into binary groups. Replication is necessary.

Conclusions: Child maltreatment experienced early in development confers significant risk for lifetime suicide ideation. Furthermore, greater risk for suicide ideation was present for those with specific oxytocin genotypes. These findings further emphasize the importance of preventive interventions aimed at decreasing the incidence of maltreatment and increasing support for high risk families.

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Contributors

All authors have contributed to and approved of the final manuscript. EDH and JMW conceptualized the study. EDH conducted the analyses and interpretation of the data. DC and FAR designed the original study as principal investigators, collected the data, and provided feedback on the conceptual framework of the current study and text of the manuscript.

Keywords

child maltreatment; suicide ideation; oxytocin; polymorphism; OXTR; CD38

Introduction

Suicide is the leading cause of death among youth worldwide (WHO, 2017) and the second leading cause of death among youth in the United States (Hedegaard et al., 2018). Estimates of lifetime suicide ideation among youth range from 5.6–24.0% (Nock et al., 2008). Because individuals who experience suicide ideation are at heightened risk for later suicide attempts (Cha et al., 2018), identifying young people at greatest risk for suicide ideation is essential for addressing this alarming public health concern.

Individuals who have experienced child maltreatment, including physical and sexual abuse, emotional abuse, and neglect, are at well-documented risk for suicide ideation and behavior (Jianbo Liu et al., 2017; Zatti et al., 2017). A recent meta-analysis found a two- to three-fold increased risk for suicide ideation and attempts among individuals who experienced sexual, physical, or emotional abuse as children, compared to those who did not experience childhood maltreatment (Angelakis et al., 2019).

The interpersonal-psychological theory of suicide (IPTS; Joiner et al., 2009; Van Orden et al., 2010) provides an important theoretical framework for understanding why individuals who experienced child maltreatment may be at heightened risk for suicide ideation and behavior. IPTS asserts that suicide ideation develops as a result of two primary cognitive processes: 1) a sense of perceived burdensomeness to loved ones; and 2) a belief that one does not belong, or a perception that one is disconnected from others. These cognitive processes may result in death by suicide when coupled with an acquired capability to enact lethal self-injury. Joiner posits that individuals who have been habituated to pain, injury, or fear, may develop the capability of completing suicide.

Based on this theory, individuals who experienced maltreatment as children are especially vulnerable. Maltreated children often experience significant disruptions in secure attachment with caregivers (e.g., Cicchetti and Toth, 2016) and the lack of secure attachment is a developmentally salient experience of social disconnection with negative consequences throughout the life course (Sroufe, 2005). Maltreated children may also experience repeated physical injury and/or witness domestic violence, increasing their exposure to violent behavior which could enhance their capability for suicide. Thus, individuals with a history of maltreatment are at risk for suicide ideation and behavior, and the IPTS provides an important framework for understanding this risk.

The establishment of a secure attachment with a caregiver is a critical milestone of the early years of life. Because maltreatment may thwart this process, maltreatment occurring in very early childhood may pose a unique risk for negative outcomes (Doyle and Cicchetti, 2017). Although not widely studied, there is some evidence that individuals who experience maltreatment very early in development may be especially vulnerable to suicidal thoughts and behaviors, presumably due to lack of a perceived secure base (i.e., thwarted

belongingness). Indeed, Dunn and colleagues (2013) found that individuals with early childhood onset sexual abuse evidenced a 146% increase in the odds of suicide ideation compared to those with adolescence-onset abuse (Dunn et al., 2013). Moreover, Khan and colleagues (2015) showed that for men, parental verbal abuse at age 5 predicted suicide ideation in young adulthood, whereas for women, sexual abuse at age 18 predicted suicide ideation. However, Gomez and colleagues (2017) did not find that the association between maltreatment and adolescent suicidal behaviors varied by timing of maltreatment onset. Further research is necessary to understand whether the developmental timing of maltreatment is associated with increased risk for suicidal ideation and behavior.

In addition to the potential relevance of maltreatment timing on suicide ideation, genetic variation may also function to identify those at greatest risk. Given prior theoretical and empirical work, an examination of gene polymorphisms implicated in social processes represents a theoretically salient potential moderator of child maltreatment risk for suicide ideation. Oxytocin is a neuropeptide produced in the hypothalamus with associations with affiliative behaviors, attachment, social cognitive processes, and the stress response system (Bartz and Hollander, 2006; Ebstein et al., 2012; Feldman et al., 2016; Meyer-Lindenberg et al., 2011) thus making it theoretically relevant to the examination of child maltreatment and suicide risk.

The oxytocin receptor gene (OXTR) is located on chromosome 3p25. A single nucleotide polymorphism (SNP) of the OXTR gene, rs53576, involving a guanine (G) to adenine (A) substitution has been the focus of much OXTR research to date. Prior findings suggest that the G allele is associated with higher levels of sociality (Li et al., 2015) and increased sensitivity to the social environment (Kumsta and Heinrichs, 2013). McQuaid and colleagues (2016) advanced the OXTR social sensitivity hypothesis which asserts that individuals who display seemingly beneficial prosocial traits may be more vulnerable to negative social environments.

Consistent with this social sensitivity hypothesis is research showing that individuals who are homozygous for the G allele of OXTR rs53576 exhibit more prosocial behaviors (Li et al., 2015) including trust (Krueger et al., 2012) empathy (Gong et al., 2017; Smith et al., 2014), and maternal sensitivity (Bakermans-Kranenburg and van Ijzendoorn, 2008). However, carriers of the G allele appear to also be more vulnerable to negative childhood experiences, including child maltreatment (see Cataldo et al., 2018 for a review). For instance, G-carriers with a history of child maltreatment are at increased risk for adult emotion dysregulation and disorganized attachment (Bradley et al., 2011), lower levels of perceived social support (Hostinar et al., 2014), and internalizing and depressive symptoms (Hostinar et al., 2014; McQuaid et al., 2013), compared to A-carriers. Structural magnetic resonance imaging results show that among G/G homozygotes (vs A-allele carriers), higher levels of child maltreatment are associated with less gray matter volume. Importantly, gray matter volume of the ventral striatum has been linked with prosocial characteristics (Dannlowski et al., 2016). Interestingly, and consistent with the social sensitivity/plasticity hypothesis, G-carriers demonstrate higher levels of adult positive affect and resilient coping in the context of a positive childhood family environment (Bradley et al., 2013).

Research has begun to examine links between OXTR, the social environment, and suicide ideation and behavior, with inconsistent findings. For instance, among a sample of adult patients with major depressive disorder or bipolar disorder, self-reported history of sexual or physical abuse and OXTR interacted to predict suicide attempt history (Parris et al., 2018). Moreover, McQuaid and colleagues (2016) did not find evidence that OXTR moderated the association between self-reported traumatic life events and suicide ideation among college students. However, Lebowitz et al. (2019) showed that negative peer social interaction was associated with suicide ideation more strongly among anxious youth with high salivary oxytocin levels compared to anxious youth with low salivary oxytocin levels; thus lending preliminary support for the social sensitivity hypothesis with regards to suicide risk.

The CD38 gene also plays a critical role in social affiliative processes by regulating oxytocin secretion (Bartz and McInnes, 2007; Feldman et al., 2016; Higashida et al., 2012). The most commonly studied CD38 SNP in relation to social processes is rs3796863, involving a cytosine (C) to adenine (A) substitution in intron 7 of CD38 on chromosome 4p15 (Brunetti and Malavasi, 2012). Prior research indicates that C-carriers demonstrate suboptimal parental care (Feldman et al., 2013, 2012) and A-carriers evidence more prosocial behavior (Jinting Liu et al., 2017). Regarding suicide ideation and behavior, results are mixed. Among Caucasian individuals with bipolar disorder, C-carriers are more likely to make a suicide attempt than A/A homozygotes (Parris et al., 2018). Furthermore, Parris and colleagues did not find evidence that child abuse history moderated the association between CD38 genotype and suicide attempts. Alternatively, a study of Caucasian college students found that traumatic life experiences was predictive of suicide ideation more strongly for A/A homozygotes (McQuaid et al., 2016). Taken together it is evident that OXTR and CD38 polymorphisms are related to social and affiliative processes. However, there is equivocal evidence that traumatic life experiences or maltreatment may interact with oxytocin-related genes to affect suicide ideation and behavior.

The current study sought to clarify associations between developmental timing of child maltreatment, oxytocin-related gene polymorphisms, and youth suicide risk. Specifically, we tested whether the developmental timing of child maltreatment was predictive of suicide ideation among a sample of high-risk African American emerging adults. Moreover, we tested whether oxytocin-related genetic polymorphisms that may enhance or mitigate child maltreatment risk for suicide ideation. We assessed the presence of lifetime suicide ideation, and controlled for lifetime depression so that we could determine whether effects found would hold over and above depression, a robust predictor of suicide ideation. To our knowledge, this is the first study to utilize Department of Human Services (DHS) record data to code maltreatment timing for the prospective investigation of the effect of early maltreatment on emerging adult suicide risk, as well as the first to incorporate oxytocin-related gene variation within this longitudinal study.

Method

Participants.

Participants (N=251) were from a longitudinal follow-up study of emerging adults who participated in a research summer camp program as children. The original study (wave 1)

included 680 low-income maltreated (n=360) and nonmaltreated (n=320) children aged 10 to 12 (*M*=11.28, *SD*= .97). The original sample was racially and ethnically diverse (71.6% African-American, 11.8% Caucasian, 12.6% Hispanic, 4.0% biracial/other race) and evenly distributed by gender (50.1% male). The majority of children were from single parent families (68.7%) with a history of receiving public assistance (96.1%).

Participants for this study included 251 of the original participants. Of the original participants assessed in childhood, 420 completed the wave 2 emerging adult assessment. Of these, only the African-American participants with maltreatment timing information were included in this current study (*N*=251). This was done because genetic variation can differ across ancestral groups, making interpretation of gene by environment interactions more difficult. At wave 2, emerging adults were on average 20.18 years old (SD=1.38), 46.6% male, 56.2% with a history of childhood maltreatment.

When comparing the sample of 251 African-Americans included in the present study to 236 assessed only at wave 1, there were no differences in child maltreatment status, family income, maternal marital status at wave 1, child gender, and age at wave 1. Moreover, there were no differences in OXTR and CD38 polymorphisms.

Approval for the conduct of this research was obtained from the University of Rochester Institutional Review Board. Informed consent was obtained from parents for their child's participation in the summer camp program and for examination of any Department of Human Services (DHS) records pertaining to the family. Children in the maltreated group were recruited by a DHS liaison who examined Child Protective Services reports to identify children who had been maltreated and/or were part of a family with a history of maltreatment. Children living in foster care often experience early and extreme maltreatment. They were not recruited for the current investigation to reduce heterogeneity among the maltreated sample. The DHS liaison contacted eligible families and explained the study. Parents who were interested in having their child participate provided signed permission for their contact information to be shared with project staff. These families were representative of those receiving services through DHS. Comprehensive reviews of all DHS records for each family were conducted. Maltreatment information was coded by trained research staff and a clinical psychologist, using the Barnett, Manly, and Cicchetti (1993) nosological system for classifying child maltreatment. Coding is based on all available information and did not rely on DHS determinations.

Because maltreating families primarily have low socioeconomic status (National Incidence Study – NIS-4; Sedlak et al., 2010), nonmaltreating families were recruited from those receiving Temporary Assistance to Needy Families (TANF) in order to ensure socioeconomic comparability between maltreated and nonmaltreated groups. A DHS liaison contacted eligible nonmaltreating families and described the project. Parents who were interested in participating signed a release allowing their contact information to be given to project staff for recruitment. The families were recruited as nonmaltreated families after comprehensive DHS record searches confirmed the absence of any documented child maltreatment. Families who received preventative DHS services due to concerns over risk for maltreatment were not included within the nonmaltreated comparison group. Mothers of

children recruited for both the maltreatment and nonmaltreatment groups were interviewed by trained research assistants using the *Maternal Child Maltreatment Interview* (Cicchetti, Toth, & Manly, 2003). This was used to further verify a lack of DHS involvement among the children recruited for the nonmaltreatment group. For the nonmaltreatment group, records were reviewed in the year following camp participation to assure that all information had been assessed.

A range of strategies were used to relocate and recruit participants at wave 2. Records of last known addresses, extensive public internet searches (e.g., LexisNexis), contact information from medical records and neighborhood canvasing were part of a comprehensive recruitment design. Additionally, the DHS liaison was again utilized to locate participants through access to DHS records.

Procedures

Emerging adult participants were individually interviewed in private interview rooms by trained research assistants who were unaware of the participant's maltreatment group status and the research hypotheses. The participants completed a variety of assessments including self-report measures and a diagnostic clinical interview.

Measures.

Childhood maltreatment.—Maltreatment information was coded using the Maltreatment Classification System (Barnett et al., 1993) which is a well-validated and widely used systematic method for coding DHS records and classifiying child maltreatment (Cicchetti, 2004). Coding is based on all available information and does not rely on DHS determinations. The MCS codes all incidents that have been documented in DHS records and, based on operational criteria, designates the developmental periods in which maltreatment occurred, as well as other relevant maltreatment parameters, such as maltreatment subtype (i.e., physical abuse, emotional maltreatment, neglect).

Children were classified into 3 groups based on the developmental timing of their maltreatment experiences. Nonmaltreated (NM) children were coded '0' (43.8%). Children who experienced infancy onset (IO) maltreated were coded '1' (13.9%) and children who experienced later onset (LO) maltreatment (maltreatment onset after infancy) were coded '2' (42.2%).

The two maltreatment groups (infancy onset and later onset) were compared on subtype of maltreatment experienced prior to age 12. Maltreatment groups did not differ significantly on the experiences of neglect (IO: 85.7%, LO: 81.1%), physical abuse (IO: 22.3%, LO: 33.0%), and sexual abuse (IO: 5.7%; LO: 6.6%). Infancy onset maltreated individuals were significantly more likely to experience emotional maltreatment (71.4%) compared to later onset maltreated individuals (46.2%; χ^2 (1)=6.70, p=.01). This suggests that individuals with infancy onset maltreatment not only experienced maltreatment earlier in life than their maltreated counterparts, but also were more likely to experience emotional maltreatment throughout childhood.

Suicide ideation (SI).—SI was measured using two items from the depression section of the Diagnostic Interview Schedule-IV (DIS-IV; Robins et al., 1995) measuring lifetime suicide ideation and thoughts of death. The endorsement of either item resulted in a score of '1,' indicating SI. Prior research supports the utility of assessing suicide ideation via items from a scale primarily designed to measure depressive symptoms (Desseilles et al., 2012). Among the current sample, 10.8% reported SI.

Depressive Symptoms.—Lifetime depressive symptoms were assessed using an item from the DIS-IV (Robins et al., 1995) asking "In your lifetime, have you ever had at least two weeks when nearly early day you felt sad, depressed, or empty most of the time?" The endorsement of this item resulted in a score of '1,' with 29.1% of the sample endorsing lifetime depressive symptoms.

DNA collection, extraction, and genotyping.—Using an established protocol, trained research assistants obtained DNA samples from children by collecting buccal cells with the Epicentre Catch-All Collection Swabs. Using the conventional method, DNA was extracted with the Epicentre BuccalAmp DNA Extraction Kit, in order to prepare DNA for PCR amplification. Genotyping was conducted following previously published protocols. DNA was whole-genome amplified using the Repli-g kit (Qiagen, Chatsworth, CA, Catalog No. 150043) per the kit instructions to ensure the availability of data over the long term for this valuable sample. Amplified samples were then diluted to a working concentration.

In addition, human DNA samples from cell lines were purchased from Coriell Cell Repositories for all representative genotypes and genotypes confirmed by sequencing using DTCS chemistry on an ABI 3130×1. These and a no template control were run alongside study samples representing 9% of the total data output. Any samples that were not able to be genotyped to a 95% or greater confidence level were repeated under the same conditions. Genotype distributions were in Hardy-Weinberg equilibrium (HWE; all $p>.05$).

OXTR: The SNP rs53576 is found in an intron of the OXTR gene at Chr.3: 8762685 on GRCh38 (NC_000003.12:g.8762685A>G). Genotyping was completed using TaqMan SNP assay C___15981334_10 (Thermo Fisher Scientific, Cat. No. 4351379) with TaqMan Genotyping Master Mix (Thermo Fisher Scientific, Catalog No. 4371357). Amplification was carried out on an ABI 9700 thermal cycler followed by endpoint fluorescence detection using a Tecan M200 with genotype determination using JMP 10.0 (SAS, Inc.). If individual genotypes were not determined after 3 attempts, then a null result was assigned. This test yielded a call rate of 99.6% overall. Among the current sample, 54.8% were G/G homozygotes, 38.0% were A/G heterozygotes, and 7.2% were A/A homozygotes. To facilitate analyses, A/A and A/G individuals were combined.

CD38: The SNP rs3796863 is found in an intronic region of the CD38 gene at Chr.4: 15848363 on GRCh38 (NC000004.12:g.15848363G>T). This test yielded a call rate of 99.6% overall. Among the current sample, 45.2% were C/C homozygotes, 39.2% were C/A homozygotes, and 15.6% were A/A homozygotes. To facilitate analyses, C/A and AA individuals were combined.

African ancestry.—To validate self-reported race, ancestral proportion testing was conducted. DNA from study participants was subjected to SNP genotyping of the Burchard et al panel of 106 SNPs (Lai et al., 2009; Yaeger et al., 2008), known to be informative for ancestry from Africa, Europe, and Native America. The SNPs were genotyped using the iPLEX platform from Sequenom Bioscience, Inc which uses the Sequenom MassArray. Samples are subjected to single base primer extension (SBE) with fluorophore labeled nucleotides from primers designed for SNPs of interest. The samples including the SBE products were placed on the iPLEX platform and MALDI-TOF was used to identify the allele based on the fluorophore passing the detector at the expected time associated with the mass of the SBE primer. The SNP genotyping results were then recoded and uploaded into STRUCTURE v2.3.4 which uses algorithms developed by Pritchard and colleagues (Falush et al., 2007, 2003; Hubisz et al., 2009). Three SNP tests were excluded based on high allele call rates of the non-DNA containing wells. The data from remaining 103 loci were uploaded into the software and set to analyze with an Admixture model of ancestry and initialization of the simulation on the GALA cohort (initialize of POPINFO). The simulation was set to run with a Burn-in of 10,000, MCMC Reps of 1,000 and assuming 3 populations within the group. The results of the simulations were subsequently identified as percent association to each ancestry group based on the known ancestry of the GALA cohort. Among this sample of self-identified African-American participants, the mean proportion of African-Ancestry was .90, thus validating the self-report measure of race and supporting genotypic homogeneity.

Results

The three maltreatment groups (i.e., nonmaltreated (NM), infancy onset maltreated (IO), and later onset maltreated (LO)) did not differ in genotype distributions (OXTR: χ^2 (2)=3.61, p>.05; CD38: χ^2 (2)=.13, p>.05) or lifetime depression (χ^2 (2)=.61, p>.05). Among NM young adults, 29.1% endorsed lifetime depression, compared to 34.3% of IO maltreated individuals and 27.7% of LO maltreated individuals.

Statistically significant differential rates of suicide ideation (SI) were found among maltreatment groups (χ^2 (2)=11.03, p=.004). Specifically, 25.7% of IO maltreated individuals endorsed SI, compared to 10.9% of NM individuals, and 5.7% of LO maltreated individuals. IO maltreated individuals reported significantly greater SI than LO maltreated individuals (χ^2 (1)=11.13, p=.002), and marginally significantly greater SI than NM individuals (χ^2 (1)=4.70, p=.05). NM and LO groups did not differ in SI (χ^2 (1)=1.95, p=.22). Table 1 presents the percentage of individuals who endorsed SI by maltreatment group and genotype. Results did not support statistically significant differences in rates of SI across OXTR polymorphism (χ^2 (1)=1.31, p=.31) or across CD38 polymorphism (χ^2 (1)=.81, p=.42).

Two separate binary logistic regressions were conducted to determine whether maltreatment timing effects on young adult SI (binary outcome variable) depend on oxytocin-related polymorphisms for the following genes: 1) OXTR, and 2) CD38. For these analyses, the infancy onset maltreatment group (n=35) was compared to the non-maltreated group (n=110) for a total sample size for the logistic regressions of N=145. The decision was made

to conduct this specific comparison given our aim to examine early maltreatment effects on suicide ideation moderated by genotypic variation. For the 2 logistic regressions, gender and lifetime depression were included as covariates.

Results of the OXTR logistic regression are presented in Table 2. Individuals with lifetime depression were more likely to endorse SI than were those without a history of depression (B=3.08, p<.001). Men and women did not differ in their endorsement of SI (B=−.70, p=.27) and neither did maltreatment groups (B=1.06, p=.27). There was not a significant main effect of OXTR genotype on SI, nor was there a significant interaction of OXTR and maltreatment.

Table 3 presents the results of the CD38 logistic regression. Again, women and men did not differ in SI (B=−1.00, p=.15). Individuals with a history of depression were more likely to endorse SI than were those without a history of depression (B=3.11 p<.001). There was not a significant main effect of CD38 polymorphism (B=1.56, p=.11). Infancy onset maltreated individuals evidenced a greater likelihood of SI than non-maltreated individuals (B=2.71, p<.003). Finally, a significant interaction was found between early maltreatment and CD38 (B=−3.76, p=.02). Probing the interaction revealed that among CD38 C-carriers, infancy onset maltreatment predicted greater likelihood of SI compared to non-maltreatment (p=.003). However, among CD38 AA homozygotes, there was no difference between infancy onset maltreatment and non-maltreatment in likelihood of SI (p=.32).

Given that OXTR and CD38 are both involved in the oxytocin system, we also tested a polygenic risk score model which combined both SNPs. The polygenic risk variable was coded such that individuals with a minor allele on both OXTR and CD38 were coded 2, individuals with a minor allele on either OXTR or CD38 were coded 1, and individuals with only major alleles on both SNPs were coded 0. Results of this logistic regression indicated that individuals with depression were more likely to endorse SI than were those without a history of depression (B=2.85, p<.001). Gender (B=−0.87, p=n.s), maltreatment timing (B=−0.97, p=n.s.), and the polygenic variable (B=−0.15, p=n.s.) did not significantly predict SI. The interaction of the polygenic risk score by maltreatment timing was also non-significant (B=1.73, p=n.s.).

It is worth noting that we also re-analyzed the OXTR and CD38 logistic regressions including the full sample (*N*=251). For these analyses we coded the three category maltreatment timing variable (i.e., infancy onset maltreatment (IO); later onset maltreatment (LO); nonmaltreated (NM)) into two dummy coded variables. Specifically, the following two dummy codes were used to compare the three maltreatment groups (D1: comparison of IO maltreated to NM; D2: comparison of IO maltreated to LO maltreated). Cross-product interaction terms were computed between the binary genotype variable and each dummy code separately (resulting in two interaction terms) to test genetic moderation. The pattern of results was the same for both the OXTR model and the CD38 model. Thus, our findings are robust to the inclusion or exclusion of later-onset maltreated individuals.

Discussion

Early onset child maltreatment predicted suicide ideation among this sample of African-American emerging adults. Specifically, we found that individuals who experienced maltreatment during infancy were more likely to report lifetime suicide ideation compared to individuals whose maltreatment began after infancy, as well as compared to their nonmaltreated counterparts. Our findings are consistent with those of Dunn and colleagues (2013) who showed that exposure to sexual abuse in early childhood was strongly associated with suicide ideation in early adulthood. To our knowledge, this is the first study to focus specifically on maltreatment during infancy. We selected this developmental stage for investigation because of the establishment of secure attachment very early in childhood as critical to adaptive development (Sroufe, 2005) and disruptions in attachment during this period may pose a unique risk for suicide ideation given that suicide is theorized to be a largely interpersonal process (Joiner et al., 2009; Van Orden et al., 2010). Moreover, it is worth noting that our measurement of infancy-onset maltreatment was based on the coding of Department of Human Services (DHS) records of maltreatment coded via the Maltreatment Classification System (Barnett et al. , 1993). Thus, we do not rely on retrospective reporting of early maltreatment which further buttresses our conclusions regarding the association between early maltreatment and later risk for suicide ideation.

We also examined oxytocin-related gene polymorphisms in relation to suicide ideation and as moderators of early child maltreatment risk for suicide ideation. We did not find evidence that variation in OXTR rs53576 differentially predicted suicide ideation. The lack of a main effect of this SNP on suicide ideation is consistent with prior literature that has not found an effect of OXTR polymorphism on suicide ideation, attempt, and completion (McQuaid et al., 2016; Parris et al., 2018; Wasilewska et al., 2017). Moreover, the current study did not find evidence that OXTR moderated the effect of early child maltreatment on suicide ideation. Thus, our findings add to a growing literature failing to show OXTR rs53576 moderation of early adversity risk for suicide ideation and behavior (McQuaid et al., 2016; Parris et al., 2018) and do not lend support to the social sensitivity hypothesis with regards to this OXTR SNP. The current study advances this literature by using child maltreatment record data in the prospective investigation of suicide ideation moderated by OXTR. Although prior work has shown OXTR gene polymorphism moderates childhood adversity risk for negative outcomes including emotion dysregulation, perceived social support, and internalizing symptoms (Bradley et al., 2011; Hostinar et al., 2014; McQuaid et al., 2013), our study suggests that this does not extend to suicide ideation.

In accordance with recent research on oxytocin-related genes, we also examined the role of CD38, a gene central to the secretion of oxytocin (Jin et al., 2007). In the current study, CD38 genotypic variation did not differentially predict suicide ideation. However, CD38 significantly moderated the link between infancy-onset child maltreatment and suicide ideation. Among C-carriers, early onset maltreatment predicted a greater likelihood of suicide ideation compared to nonmaltreated individuals. However, among AA homozygotes, there was no difference between infancy onset maltreatment and non-maltreatment in likelihood of suicide ideation in emerging adulthood. Thus, our results suggest that C-

carriers may be more vulnerable to the development of suicide ideation as a result of early experiences of child maltreatment.

Prior research on CD38 and suicide ideation and behavior is limited and results are inconsistent (McQuaid et al., 2016; Parris et al., 2018). A number of significant methodological differences between studies are noteworthy. First, the distribution of genetic polymorphisms can differ across ancestral groups and the current study involved a sample of African-American youth, in contrast to the Caucasian samples used in prior studies. Moreover, there is variation in definitions and measurement of traumatic experiences, and the coding of the gene polymorphism. Future research is necessary to clarify the complex role of CD38 gene polymorphism and the development of suicide ideation among individuals who have experienced various negative life events.

Limitations of this study include the small sample size which necessitated the combination of genotypes into binary groups (i.e., combining OXTR rs53576 AA and A/G individuals and combining CD38 GG and G/T individuals). Future research with larger samples will allow for more specificity in the examination of specific genotypes and their interaction with maltreatment. This study is also limited by the reliance on a two-item measurement of lifetime suicide ideation. Our focus on infancy onset maltreatment clearly establishes temporal order such that onset of maltreatment precedes suicide ideation in all cases. However, we were unable to determine how timing of any subsequent maltreatment, as well as chronicity and severity of maltreatment may influence suicide ideation. Furthermore, the current study did not assess suicide attempts. Additional research is necessary to further clarify the role of oxytocin-related genes and their potential interactions with maltreatment onset and timing in predicting suicide ideation and attempts.

In conclusion, results of the current study indicate that individuals who experience child maltreatment during infancy are at increased risk for the development of suicide ideation, compared to both later onset maltreated individuals, and those without a maltreatment history. Moreover, we found that CD38 gene variation moderated this association such that early onset maltreatment was related to suicide ideation among C-carriers only. Together these findings highlight the vulnerability of individuals who have experienced early childhood maltreatment and suggest that this risk is heightened for those with specific oxytocin-related genotypes.

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Highlights

- Infancy onset child maltreatment predicted suicide ideation among a sample of African-American young adults.
- Individuals with a certain CD38 gene variant were more vulnerable to the development of suicide ideation as a result of early experiences of child maltreatment.
- The OXTR gene did not moderate infancy onset maltreatment suicide ideation risk.

Table 1.

Frequency of suicide ideation among maltreatment and genotype groups

	Overall	OXTR		CD38	
		AA/AG	GG	CC/CA	AA
Nonmaltreated	10.9%	12.8%	9.7%	8.3%	14.3%
IO maltreated	25.7%	33.3%	14.3%	40.0%	6.7%
LO maltreated	5.7%	4.4%	6.6%	7.0%	4.1%

Note. IO maltreated = infancy onset maltreated, LO maltreated = later onset maltreated

Table 2.

Logistic regression predicting suicide ideation from maltreatment and OXTR polymorphism

Predictor	β	SE β	Wald χ^2	Odds ratio
$B_{intercept}$	−3.09			
Gender	−.70	.63	1.22	.50
Depression	3.08***	.70	19.39	21.76
Maltreatment	1.06	.81	1.71	2.90
OXTR	−.87	.71	1.51	.42
Maltreatment X OXTR	.15	1.33	.01	1.16

Note: β = unstandardized logistic regression coefficients. Maltreatment is coded 0=nonmaltreated, 1=infancy onset maltreatment.

*** p<.001

Table 3.

Logistic regression predicting suicide ideation from maltreatment and CD38 polymorphism

Predictor	β	SE β	Wald χ^2	Odds ratio
$B_{intercept}$	−4.08			
Gender	−1.00	.70	2.04	.37
Depression	3.11	.72	18.83	22.41
Maltreatment	2.71**	.90	9.10	14.95
CD38	1.16	.72	2.56	3.18
Maltreatment X CD38	−3.76*	1.60	5.50	.02

Note: β = unstandardized logistic regression coefficients. Maltreatment is coded 0=nonmaltreated, 1=infancy onset maltreatment.

* p<.05,

** p<.01