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Association between maternal childhood maltreatment and mother-infant attachment disorganization: Moderation by maternal oxytocin receptor gene and cortisol secretion

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ABSTRACT

This study examined maternal oxytocin receptor (*OXTR, rs53576*) genotype and cortisol secretion as moderators of the relation between maternal childhood maltreatment history and disorganized mother-infant attachment in the Strange Situation Procedure (SSP). A community sample of 314 mother-infant dyads completed the SSP at infant age 17 months. Self-reported maltreatment history more strongly predicted mother-infant attachment disorganization score and disorganized classification for mothers with more plasticity alleles of *OXTR* (G), relative to mothers with fewer plasticity alleles. Maltreatment history also more strongly predicted mother-infant attachment disorganization score and classification for mothers with higher SSP cortisol secretion, relative to mothers with lower SSP cortisol secretion. Findings indicate that maltreatment history is related to disorganization in the next generation, but that this relation depends on maternal genetic characteristics and cortisol.

Disorganized mother-infant attachment is one of the earliest measurable risk factors for maladaptive developmental trajectories in biologically normal individuals (Lyons-Ruth and Jacobvitz, 2016), having been linked to physiological stress reactivity (Bernard and Dozier, 2010; Luijk et al., 2010), attention and information processing (Claussen et al., 2002; Dykas and Cassidy, 2011), hostility and dissociation (Sroufe, 2005), and psychopathology (Fearon et al., 2010). Despite the importance of disorganization for child development, the origins of disorganized attachment are not completely clear (Lyons-Ruth and Jacobvitz, 2016). It is therefore “essential” (Bernier & Meinz, 2008, pp. 969) to study the factors contributing to disorganized mother-infant attachment. The current study addresses this issue by examining maternal maltreatment history, cortisol secretion, and *OXTR* genotype.

1. Attachment disorganization

Main and Solomon (1990) identified disorganized attachment based on the observation that some infants did not meet criteria for any of Ainsworth's (Ainsworth et al., 1978) organized attachment classifications (avoidant, secure, resistant), as assessed in the Strange Situation Procedure (SSP). These disorganized infants tended to engage in i) sequential displays of contradictory behaviors; ii) simultaneous displays of contradictory behaviors; iii) undirected, misdirected, incomplete, and interrupted movements and expressions; iv) stereotypies, asymmetrical movements, mistimed movements, and anomalous postures; v) freezing, stilling, and slowed movements or expressions; vi) direct indices of apprehension of the parent; and vii) direct indices of disorganization and disorientation. These disorganized behaviors are thought to reflect an approach/avoidance conflict as a result of mother-infant interactions in which maternal behavior evokes fear in the infant, or infant behavior evokes fear in the mother (Lyons-Ruth and Jacobvitz, 2016; Main and Hesse, 1990). In other words, infants are thought to exhibit these behaviors because their mother is simultaneously their source of comfort and fear.

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To account for the development of this fear, Main and Hesse (1992) proposed that when a mother's traumatic experiences are "unresolved", the memories and emotions associated with the trauma are reactivated by the infant's attachment cues, thereby triggering a dissociative state during which the mother displays inappropriate behavior while interacting with her infant. Supporting this idea, meta-analytic data found an effect size of $r = 0.32$ ($k = 6$; $n = 325$) linking "frightened or frightening" (FR) behaviors (e.g., aggressive facial expressions, dissociative expressions, submissive parental behavior) to disorganized mother-child attachment (Madigan et al., 2006). Building upon FR behaviors, Lyons-Ruth et al. (1999) identified disrupted communication behaviors (e.g., mocking infant, eliciting reassurance from infant) that can provoke unmodulated infant fear and contribute to disorganized attachment over and above FR behaviors. The effect size linking disrupted communication behaviors to disorganized mother-child attachment is $r = 0.35$ ($k = 4$; $n = 384$, Madigan et al., 2006). Direct child maltreatment (e.g., abuse, neglect) also contributes to disorganization (van IJzendoorn et al.'s, 1999), with a large effect size of $r = 0.74$ ($k = 10$; $n = 456$, Cyr et al., 2010).

Importantly, the presence of maternal childhood maltreatment history alone is enough to confer significant risk for disorganization (e.g., even when considering mother's unresolved state of mind, Berthelot et al., 2015). About 15% of middle-class, nonclinical dyads are classified as disorganized in the SSP (van IJzendoorn et al., 1999), but this number triples in the context of maternal childhood maltreatment history, regardless of the dose of maltreatment (i.e., any maltreatment constitutes substantial risk, Berthelot et al., 2015). As such, researchers have suggested that a mother's history of childhood maltreatment is one of the most important causes of disorganization, and that it is sufficient in and of itself to give rise to disorganization in the next generation (Bernier and Meins, 2008).

On the other hand, a substantial proportion of mothers with histories of childhood maltreatment do not develop disorganized attachment relationships with their infants (Berthelot et al., 2015), pointing to the role of moderating factors. Bernier and Meins (2008) proposed a threshold model for the development of disorganization that can account for such moderating factors. According to this model, certain maternal characteristics can both alter the dyad's threshold level for developing disorganization, and potentially induce the atypical parenting behaviors that can breach the threshold. As Bernier and Meins (2008) suggest, two such moderating factors may be genetic characteristics and maternal stress reactivity. To our knowledge, the current study is the first to examine these factors as moderators of the relation between maternal childhood maltreatment history and mother-infant disorganization in the SSP.

2. Maternal genetics and mother-infant attachment disorganization

There has been increasing interest in examining gene × environment (G × E) interactions as they predict disorganization, although with limited replication and inconsistent results (Lyons-Ruth and Jacobvitz, 2016). For example, maternal unresolved loss was found to only be associated with mother-infant attachment disorganization for infants with the *long* allele of *DRD4* (i.e., 7-repeat) (van IJzendoorn and Bakermans-Kranenburg, 2006), and maternal affective communication was found to only be associated with disorganization for infants with the *short* allele of *DRD4* (Gervai et al., 2007). A notable limitation of G × E studies as they predict mother-infant attachment disorganization is their neglect of *maternal* genotypes. This oversight is important because maternal genotype is related to maternal features pertinent to mother-child interactions (Mileva-Seitz et al., 2016), and these are reflected in attachment classification.

In this regard, a probable maternal genetic candidate is the *OXTR* gene. Animal models support the role of *OXTR* in impacting parental behavior and susceptibility to early life adversity. For example, Keebaugh et al. (2015) found that suppressing *OXTR* expression in female prairie voles reduced alloparental behavior (i.e., time spent licking and grooming pups). The impact of *OXTR* on alloparental behavior appears to be "organizational" early in development, as adults over-expressing *OXTR* in the nucleus accumbens from weaning (but not from adulthood) display increased alloparental behavior (Keebaugh and Young, 2011). Furthermore, early life adversity (i.e., social isolation) reduces the pair bonding of female prairie voles as adults, but only among those with low nucleus accumbens oxytocin receptor densities (Barrett et al., 2015). In other words, female prairie voles are differentially susceptible to early life adversity, depending on variation in oxytocin function.

Consistent with such animal research, a single nucleotide polymorphism (SNP) in the third intron, rs53576 (G/A), of the *OXTR* gene, located on chromosome 3p25, containing four exons and three introns, has been found to impact maternal interactive behavior in humans. For example, in a low-risk community sample, mothers with *OXTR* genotypes that signify more efficient oxytocin function (i.e., GG genotypes) display more observable sensitivity to their toddlers (Bakermans-Kranenburg and van IJzendoorn, 2008). Bradley et al. (2011) examined childhood maltreatment history, *OXTR*, and self-reported attachment on the Adult Attachment Prototype Questionnaire in a sample of 284 low-income African American men and women. They found that individuals with the GG genotype, relative to individuals with other genotypes, had higher levels of disorganized attachment in the context of more maltreatment. Thus, given the role of *OXTR* in maternal bonding, and susceptibility to the influences of early life adversity (specifically the influences of childhood maltreatment on self-reported attachment), the *OXTR* gene is an excellent candidate for moderating the degree to which maternal history of maltreatment impacts mother-infant disorganization in the next generation, as assessed with the gold standard measure of attachment, the SSP.

Relevant to this hypothesis are the definitions of G × E interaction models. *Diathesis-stress* refers to genetic characteristics exclusively conferring vulnerability to the adverse effects of negative rearing environments. *Differential susceptibility* refers to genetic characteristics conferring susceptibility to the adverse effects of negative rearing environments *and* the positive effects of enriched rearing environments (Belsky and Pluess, 2009). Finally, *vantage sensitivity* refers to genetic characteristics exclusively conferring susceptibility to the positive effects of enriched rearing environments. It is currently unknown how differential context associates with each of the three G × E models (Del Giudice, 2017; Ludmer et al., 2015). However, to address this issue, Roisman et al. (2012) proposed statistical criteria for differentiating between the models, including: i) *Regions of Significance on environmental factors* (*RoS on X*)*:* demonstration that the outcome variable and the plasticity genotype are correlated at high and/or low ends of the environmental variable bounded by ± 2SD from the mean; ii) *Proportion of interaction index* (*PoI*)*:* ratio of improved outcomes for the plasticity genotype over the sum of improved outcomes and harmful outcomes (this criterion was recently revised by Del Giudice, 2017); and iii) *Linearity:* repeating analyses when introducing quadratic effects (i.e., the environmental variable squared, and the product of the environmental variable squared and the moderator). Although these statistics are an important step toward clarifying the contexts in which each G × E model occurs, the RoS on X test is biased by sample size, sample characteristics, power, and environmental ranges, and the PoI index lacks clear cut-off guidelines (Del Giudice, 2016, 2017). Thus, it appears that, at this time, the most crucial piece of information is the fact that there is an interaction, as opposed to the type of interaction.

In addition to the Roisman criteria, we also present the current results without "binning" alleles. Binning alleles is the typical method in G × E research and it involves creating dichotomous groups of "plasticity genotype" and "non-plasticity genotype" individuals. This is problematic because this unjustifiably assumes allele dominance in heterozygous individuals (Ludmer et al., 2015). To avoid such