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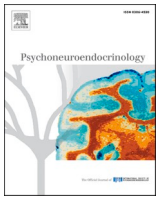

# Oxytocin modulates sensitivity to acculturation and discrimination stress in pregnancy

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ABSTRACT

*Background:* Latinas in the United States suffer disproportionately high levels of pre- and postnatal depression. However, little is understood regarding the biopsychosocial mechanisms linking socio-environmental factors to this increase in mental health risk. The oxytocinergic system, with its roles in the stress response, social behaviour and mood regulation, may be an important modulator of this sensitivity. We have previously reported prenatal discrimination to be a significant predictor of postnatal depression in Latinas; here we tested whether sensitivity to discrimination stress might depend on oxytocinergic system activity.

*Methods:* A sample of 148 Latina women residing in the US were assessed prenatally at 24–32 weeks' gestation and 46 weeks postnatally for perceived discrimination levels, acculturation, and depression and anxiety symptoms. Plasma oxytocin (OXT) levels and DNA methylation of the oxytocin receptor (*OXTR*) were measured prenatally together with genotyping for the *OXTR* SNP, rs53576.

*Results:* In mothers with low OXT levels and low *OXTR* methylation, acculturation level was associated with postnatal depression and anxiety symptoms. No such associations were found in those with higher OXT levels and higher *OXTR* methylation. We also found a significant relationship between prenatal psychosocial factors (discrimination and acculturation) and postnatal depression and anxiety in carriers of the G-allele at rs53576, but not AA genotypes. Finally, *OXTR* methylation positively correlated with mothers reports of experiencing affiliative social touch. Moreover, social touch mediated the relationship between discrimination and postnatal depression in those with low *OXTR* methylation.

*Conclusion:* These results support the hypothesis that the oxytocinergic system modulates sensitivity to prenatal stress in the development of postnatal mood and anxiety disorders in Latina mothers.

## 1. Introduction

During the perinatal period, 10–15% of United States women suffer mild to severe depression. In Latinas, such depression is even more common, with 12–59% prevalence (Blackmore and Chaudron, 2014). Systematic stressors disproportionately affecting Latina mothers, such as social and economic hardships, are linked to the development of depressive symptoms (Farina et al., 2021). On top of these, Latinas also face widespread discrimination, which is strongly linked with depressive symptoms during the pregnancy (Sluiter et al., 2020; Walker et al., 2012) and the early postpartum period (Ponting et al., 2020). Immigrant Latinas are also likely to experience stress from acculturation, the process of adopting beliefs and norms of the host culture and/or losing cultural heritage.

Latina maternal health trends demonstrate consistency with the Latina Paradox, a phenomenon wherein despite marked social disadvantages, foreign-born Latina mothers from some Latinx subgroups experience better birth outcomes than US-born mothers (DeSisto and McDonald, 2018; Osypuk et al., 2010). This disparity also appears to extend to mental health. For instance, studies have shown that Latinas who are more acculturated to mainstream US culture are more likely to experience prenatal and postpartum depressive symptoms than less

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acculturated counterparts (Alhasanat and Giurgescu, 2017; Ruiz et al., 2012). In fact, acculturation has been closely linked to origin and development of maternal-child health disparities in Latinas (Fox et al., 2015; Rubin, 2016). Although experiences of discrimination are embedded within the acculturation process for immigrants from ethnic minorities, the extent to which discrimination may be a key contributor to the trajectory of worsened mother-child health remains understudied (Fox et al., 2015; Schwartz et al., 2010). Not only is discrimination strongly linked to depressive symptoms during pregnancy, but self-reported discrimination may increase with longer residency in the US, suggesting a synergistic or dose-dependent relationship (Flippen and Parrado, 2015; Harris et al., 2022). Furthermore, greater acculturation, as measured by length of residency in the US or greater orientation to the host culture, has been linked to increased levels of immune dysregulation and inflammation (Scholaske et al., 2021). Recent evidence also suggests that acculturative stress in this group predicts indicators of accelerated cellular aging as indexed by telomere length (Incollingo Rodriguez, 2022). Importantly, these are the same preclinical indicators of disease tied to interpersonal discrimination (Cuevas et al., 2020).

Despite these risk factors, little is known about molecular mechanisms that may underlie the psychosocial stress-depression relationship during pregnancy and the early postpartum period. The oxytocinergic system plays a well-established role in stress, mental health, and critical functions pursuant to pregnancy, childbirth, and lactation. Oxytocin (OXT) has anxiolytic properties; negatively regulates hypothalamic-pituitary-adrenal axis stress response; and moderates psychosocial stress, social interactions, and perinatal depression (Ellingsen et al., 2016). Moreover, studies investigating epigenetic alterations in the oxytocin receptor (*OXTR*) gene, particularly at CpG site − 934, have identified associations between reduced methylation and prenatal and postnatal depression (Kimmel et al., 2016). There is also evidence suggesting that common variations in the *OXTR* gene are associated with different degrees of stress reactivity (Rodrigues et al., 2009), while other studies document interactions with the *OXTR* genotype. For example, one study found an interaction between *OXTR* rs53576 genotype and child maltreatment on emotional dysregulation and disorganised attachment in adults with GG genotype but not in those with AA genotype (Bradley et al., 2011). In fact, genotypes that confer biological sensitivity to the social environment may engender *either* emotional resilience or vulnerability across human development (Ellis et al., 2011; Homberg and Jagiellowicz, 2021). In other words, those who are most likely to benefit from socially supportive environments may also be the most likely to suffer from socially adverse environments, such as discrimination.

Perceived discrimination is a robust, often daily (Cobb et.al. 2017) social stressor that is strongly linked to depression prevalence in Latinos (Ward et al., 2019). Reports of perceived discrimination predicts depression in Hispanic high school students (Basáñez et al., 2013) and a systematic review of the effect on discrimination on Latinx health confirmed the negative relationship between this social stressor and Latino mental health (Andrade et al., 2021). Furthermore, there is a dose response relationship between discrimination and increased risk of mood and anxiety disorders in Latinx populations (Cobb et al., 2021). The OXT system has been critically implicated in determining the salience of social cues, where it regulates the attention to and perception of both positive and negative cues, including those related to discrimination (Shamay-Tsoory and Abu-Akel 2016; Averbeck, 2010, Egito et al., 2020), and is associated with the monitoring of potential social threats (Olivera-Pasilio, 2020). In direct support of this social salience hypothesis of OXT, a study of healthy African Americans revealed that those with a genotype indicative of greater OXT receptivity reported greater perceived discrimination than those with a genotype indicative of less OXT receptivity (Drolet, 2021).

Considering these links, this study investigated the role of the oxytocinergic system in the response to acculturation and discrimination stress to specifically assess relationships between psychosocial stress, affiliative social behaviours and mental health in Latinas mothers. We aimed to understand how interactions between variations in oxytocinergic functioning and socio-environmental factors may mediate risk for postpartum depressive symptom severity.

## 2. Material and methods

### 2.1. Participants

Healthy pregnant Latinas (n = 150) living in North Carolina participated in this study. Eligibility criteria and full recruitment procedures are available elsewhere (Santos et al., 2018). Briefly, women were recruited during their prenatal clinical appointments. Data collection was completed in English or Spanish, depending on participants preference, at the prenatal (24–32-weeks' gestation) and postnatal (4–6 weeks postpartum) visits. Measures used in this study had validated versions in English and Spanish (Santos et al., 2018). The University of North Carolina at Chapel Hill Institutional Review Board approved this study (#15–3027).

### 2.2. Measures

All measures have been described in detail, previously (Santos et al., 2021, 2018; Sluiter et al., 2020) Discrimination was measured using the Everyday Discrimination Scale (EDS), a nine-item questionnaire used to measure routine, day-to-day experiences of discrimination at the prenatal and postnatal time points, as previously described (Santos et al., 2018). This is a widely used measure of subjective experiences of discrimination (Williams et al., 1997), with a validated Spanish translation (Campo-Arias and Herazo, 2015). Sample items include: "You are treated with less courtesy than other people are," "People act as if they think you are dishonest" and, "You are called names or insulted." It correlates with measures of institutional racial discrimination and interpersonal prejudice (Krieger et al., 2005) and does not prime the subjects to think about race, which limits cues to prejudice prior to responding to the questions (Deitch et al., 2003). The 9-item Likert response scale for frequencies ranged from 0 ("never") to 5 ("almost every day"). An additional question asks the respondent to select a reason to which they attribute their experiences of discrimination (e.g., skin colour, ethnicity). As previously described (Santos et al., 2018), we constructed a mean summary that ranged from 0 to 5, with a higher score indicating a higher frequency of perceived discrimination. Cronbach's alpha for item consistency for the EDS in our sample was 0.86 for T1 and 0.89 for T2.

Acculturation was measured using the Bidimensional Acculturation Scale (BAS), a 24-item questionnaire to assess acculturation within both Hispanic (12 questions) and Non-Hispanic (12 questions) cultural domains and includes three subscales language use (6 questions), language proficiency (12 questions), and electronic media (6 questions). The BAS asks participants to report the frequency with which they experience events or their ability to use technology with 1–4 Likert scale, with higher scores indicating higher frequency or better ability (1 =Almost Never to 4 =Very Well). Participants responses from each cultural domain are summed and averaged resulting in a Hispanic BAS score as well as a Non-Hispanic BAS score between 1 and 4, with an overall score of 4 indicating a higher degree of acculturation. The BAS has been validated in both English and Spanish (Marin and Gamba, 1997).

Anxiety and depressive symptoms were assessed with the Generalised Anxiety Disorder Assessment (GAD, 7-item), and the Edinburgh Postnatal Depression Scale (EPDS, 10-item), respectively., as previously described (Santos et al., 2018). To measure social touch, pregnant participants were asked: *Over the last week, how often did you hold hands? How often did you exchange neck rubs, back massages or any other warm touching activities with someone else? How often did you give someone hugs lasting for more than a few seconds?* Reponses varied from "never", "sometimes", "often", "always".

### 2.3. OXT measurement

Venous blood samples were collected into pre-chilled 6 mL K2 EDTA BD Vacutainer® Blood Collection Tubes and Aprotinin (9000 KIU) added. Samples were centrifuged at 2000× g/10 min/4 C. Plasma and buffy coats were aliquoted into barcode-labeled cryovials and stored at − 80 C until assay in the UNC Biobehavioral Laboratory using the ELISA kit (Enzo Life Sciences). Solid-phase extraction of samples (600 μL) was performed using 200 mg C18 Sep-Pak Vac 3cc columns (Waters Corporation, Milford, MA) and evaporated using a Speed Vac. Samples were reconstituted in 250 μL of Assay Buffer and assayed in triplicate per the manufacturer's protocol.

### 2.4. DNA methylation

DNA, extracted from buffy coat, was transported to Manchester Metropolitan University for DNA methylation analysis using bisulphite pyrosequencing as previously described (Sluiter et al., 2020). Primers used to amplify and sequence CpG site − 934 of *OXTR* using PyroMark were: Forward, 5'-GGGGGGAGTTAATTTTAGGTT-3'; Reverse 5'-Biotin-CTCAATCCCCAAAAATCACTTTACAATCT-3'; Sequencing 5'-TTTT GTTTTTGGAGGAG-3'. All analyses use the average of three separate assays.

### 2.5. Genotyping

Genotyping for *OXTR* SNP rs53576 was performed using KASP Assay mix from LGC using the Stratagene PCR system. We combined subjects with GG and GA genotypes, in line with previous studies (Choi et al., 2019).

## 3. Results

### 3.1. Sample characteristics

Participants were on average 27.7 (SD 6.4) years old upon assessment and the majority (125 of 148) were foreign-born with 75% of those arriving from Mexico. 74.4% of the participants were either living together with a partner or married (Table 1). 44.2% reported experiencing discrimination; most attributed these experiences to their race and ancestry (Santos et al., 2018).

**Table 1**
Baseline characteristics of the cohort (n = 147).

| Age, years | |
|---|---|
| Mean (SD) | 27.6 (6.35) |
| **Marital status** | |
| Married | 34.7% |
| Not married but living with partner | 39.5% |
| Single | 25.8% |
| **Education** | |
| High school or less | 85.0% |
| Some college | 8.2% |
| Other | 6.8% |
| **Household income (Yearly)** | |
| < $25,000 | 79.6% |
| $25,000–39,999 | 19.7% |
| > $40,000 | 0.7% |
| **Nativity** | |
| Non-US born | 83.7% |
| US-born | 16.3% |
| **Years living in US** | |
| Mean (SD) | 12.0 (7.27) |
| **Sex of the infant** | |
| Male | 46.3% |
| Female | 53.7% |
| **Parity** | |
| 0 children | 35.1% |
| 1–2 children | 41.6% |
| ≥ 3 children | 20.4% |
| **Country of Origin** | |
| Mexico | 56.3% |
| Honduras | 17.2% |
| El Salvador | 13.2% |
| Other | 13.4% |
| **Gestational Age at T1** | |
| Mean (SD) | 28.81 (1.28) |
| **Postpartum weeks at T2** | |
| Mean (SD) | 4.9 (1.01) |
| **Depression Symptoms (IDAS-GD T1)** | |
| Mean (SD) | 30.77 (6.31) |
| **Depression Symptoms (IDAS-GD T2)** | |
| Mean (SD) | 29.87 (7.20) |

### 3.2. OXT levels and OXTR methylation are not related to psychosocial and symptom measures

There were no significant differences in *OXTR* methylation between *OXT* genotypes, G-carriers (GG/GA) and AA ($p > .05$), and no correlation between *OXTR* methylation and plasma OXT levels ($r = 0.14$, $p = .112$).

*OXTR* methylation did not predict prenatal (b = 0.06, $p = .180$) or postnatal (b = −0.04, $p = .415$) depressive symptoms (EPDS), anxiety symptoms (GAD), acculturation (BAS) scores (all $p$'s > 0.05). OXT plasma levels were also not associated with prenatal (b = 0.06, $p = .224$) or postnatal (b =. 0.05, $p = .351$) depressive symptoms. There were no significant differences in any measures of stress and depression, prenatally or postnatally, based on genotype (GG/AG vs AA; $p$'s > 0.05).

### 3.3. OXTR methylation modulates sensitivity to stress

Our previous work suggests that discrimination predicts postnatal depressive symptoms (Sluiter et al., 2020). We therefore tested whether *OXTR* activity moderates sensitivity to discrimination stress. Participants were grouped into *OXTR* methylation tertiles (boundaries at 41% and 48% methylation) and plasma OXT tertiles (boundaries at 8.10 and 12.13 pg/mL). Tertiles reflected the distribution of scores with low, average, and high clusters. Prenatal acculturation and discrimination (EDS) were then tested as continuous predictors of postpartum depressive symptoms in each tertile (Table 2).

For both *OXTR* methylation and plasma OXT level, prenatal acculturation significantly predicted postnatal depressive symptoms in the lowest tertile but not in the two higher tertiles. Prenatal exposure to discrimination predicted depressive symptoms scores in the lowest and the highest methylation tertiles, but not the middle tertile. For OXT plasma levels, prenatal discrimination predicted depressive symptoms scores in only the lowest tertile.

Testing for gene-environment interactions, we compared the relationships between psychosocial factors (acculturation and discrimination) and postnatal depressive symptoms between G-carriers (GG/GA) and AA genotypes. Acculturation was a significant predictor of postnatal depressive symptoms in G-carriers (b = 2.70, $SE = 1.11$, $\beta = 32$, $p = .010$) but not AA genotypes (b = −0.03, $SE = 1.06$, $\beta = -0.00$, $p = .978$). The same pattern of significance was observed for discrimination: a significant predictor of postnatal depressive symptoms in G-carriers (b = 0.26, $SE = 0.07$, $\beta = 0.42$, $p = .001$), but not AA genotypes (b = 0.10, $SE = 0.11$, $\beta = 0.12$, $p = .374$).

### 3.4. Affiliative behaviour, OXTR methylation, and postnatal symptoms

Pregnant mothers' reported touch-related affiliative behaviours significantly correlated with *OXTR* methylation ($r(151) = 0.20$, $p = .022$) but not OXT levels ($r(148) = 0.04$, $p = .600$). Acculturation significantly predicted social touch (b = 1.02, $SE = 0.48$, $\beta = 0.17$, $p = .034$), as did discrimination (b = 0.09, $SE = 0.42$, $\beta = 0.17$, $p = .036$). Moreover, social touch significantly predicted postnatal depressive symptoms (b = 0.25, $SE = 0.11$, $\beta = 0.18$, $p = .033$) and anxiety symptoms (b = 0.21, $SE = 0.09$, $\beta = 0.19$, $p = .026$) scores.

**Table 2**
Regression analyses for psychosocial stress variables predicting EPDS scores by tertile of *OXTR* methylation and OXT plasma levels.

| Acculturation (BAS) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *OXTR* Methylation | | | | | OXT Plasma | | | | |
| Tertile | *n* | *B* | *SE B* | *β* | *p*-value | *n* | *B* | *SE B* | *β* | *p*-value |
| 1 | 36 | 3.72 | 1.80 | .33 | .046 | 43 | 3.70 | 1.34 | 0.39 | .009 |
| 2 | 48 | -0.44 | 0.67 | -0.10 | .512 | 46 | -0.69 | 0.54 | -0.19 | .209 |
| 3 | 42 | 0.85 | 1.10 | .12 | .443 | 49 | -0.19 | 1.29 | -0.02 | .886 |
| Everyday Discrimination (EDS) | | | | | | | | | | |
| | *OXTR* Methylation | | | | | OXT Plasma | | | | |
| Tertile | *n* | *B* | *SE B* | *β* | *p*-value | *n* | *B* | *SE B* | *β* | *p*-value |
| 1 | 36 | 0.48 | 0.18 | .42 | .010 | 43 | 0.59 | 0.12 | .62 | < 0.001 |
| 2 | 48 | 0.09 | 0.06 | .21 | .144 | 46 | 0.02 | 0.05 | .06 | .703 |
| 3 | 42 | 0.21 | 0.08 | .38 | .013 | 49 | 0.04 | 0.11 | .05 | .707 |

*Note.* Methylation tertile cuttoffs were set at 41% and 48%. Extracted level tertiles were set at 8.10 and 12.13.

Therefore, social touch was tested as a mediator of the established relationship between prenatal discrimination and postpartum symptoms (Sluiter et al., 2020). A hierarchical linear regression revealed that social touch was not a significant mediator when accounting for the direct effect of EDS (b = 0.19, *SE* = 0.11, $\beta = 0.14$, $p = .092$). It similarly did not mediate the relationship between prenatal depressive symptoms and postnatal anxiety symptoms(b = 0.16, *SE* = 0.09, $\beta = 0.15$, $p = .076$). Given the association between social touch and *OXTR* methylation, we also tested these models in the lowest methylation tertile. Here, social touch was a significant mediator of the relationship between discrimination and postnatal depressive symptoms (b = 0.67, *SE* = 0.29, $\beta = 0.33$, $p = .028$). The same was found for anxiety symptoms (b = 0.62, *SE* = 0.20, $\beta = 0.45$, $p = .004$).

Across all analyses, no sociodemographic factors (income, relationship status, age, education, or country of origin) were related to outcomes of interest (all $p$'s $> 0.228$) and therefore were not included in our models for the sake of preserving parsimony in our analyses of this relatively small sample when stratified.

## 4. Discussion

In this sample of Latina mothers, greater prenatal acculturation, exposure to discrimination, lower *OXTR*methylation, lower OXT levels, or having the G allele in the *OXTR* gene increased sensitivity to developing postnatal depressive symptoms. These mothers also reported higher levels of social touch, which was also associated with higher *OXTR* methylation. These results support the hypothesis that the oxytocinergic system modulates sensitivity to prenatal stress in the development of postnatal mood and anxiety disorders in this underserved population.

Low *OXTR* methylation levels in Latina mothers predicted increased sensitivity to postpartum depressive symptoms in more acculturated mothers and those who experienced higher levels of discrimination. This suggests higher *OXTR* levels and elevated oxytocinergic activity may drive stress vulnerability. Some work indicates high OXT levels in relation to postpartum depression and risk of posttraumatic stress disorder following recent stress (Donadon et al., 2018). Our data suggest that relationships between OXT levels and *OXTR* methylation and mood are also context-dependent. Namely, interactions with environmental factors, such as greater acculturation and discrimination exposure are critical. For instance, OXT activity may exacerbate or buffer social stress by strengthening both positive and negative emotional memories. We found associations between low *OXTR* methylation and postnatal depression symptoms alone with moderation of the relationship between discrimination and postnatal EPDS by *OXTR*methylation status. This may indirectly support the hypothesis of increased susceptibility to social stress in individuals who are more sensitive to social stimuli. While high levels of social touch may indicate decreased risk of depression in many less-challenging contexts, the present contrary observation in this Latina sample exposed to high levels of discrimination stress may be related to increased sensitivity to social stress.

We also found elevated postnatal depression symptoms in mothers with higher levels of social touch and *OXTR* methylation (and presumably low *OXTR* levels). This may be driven by a subset displaying symptoms of depression and receiving higher levels of social support and associated social touch. While we could not directly evaluate this hypothesis because of lack of data on social support, it is an important protective factor in similar populations (Xie et al. 2009) and future studies should explore social support factors in detail in a longitudinal study with additional sampling points. These results in combination with the associations between low *OXTR* methylation and postnatal depression symptomology, suggest a bimodal role for *OXTR*-related risk in this population. Women with low *OXTR* levels and less OXT receptivity may be at risk due to deficits in maternal bonding and/or the rewarding aspects of social support and maternal care (Nephew et al., 2015). Mothers with high *OXTR* levels and greater OXT receptivity may be more sensitive to adverse effects of discrimination on maternal mood (Drolet et al. 2021).

Finally, we found an interaction between rs53576 genotypes and depression where mothers with the G-allele were sensitive to stress. Meta-analytic evidence shows the G-allele is associated with greater sociality (Li et al., 2015). In the Latina cohort, *OXTR* and sociability may increase sensitivity to prenatal discrimination in the development of postnatal depression. Because the G-allele is associated with greater recognition of social cues and desire to form social connections, discrimination stress may exacerbate emotions from negative social interactions and social exclusion in these women. In fact, increased social sensitivity in G-allele carriers has been linked to increased vulnerability to depression and anxiety among adults with early life stress (Dannlowski et al., 2016).

Despite only one blood collection sampling point and limited measurement of affiliative touch, the rich biopsychosocial dataset and longitudinal design in an underserved group are major strengths of this work. Together, these findings present novel evidence supporting the unique importance of the oxytocinergic system in the aetiology of postnatal depression in a high-risk population.

## Declaration of Competing Interest

All authors have no conflicts of interest to declare.

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## References


Alhasanat, D., Giurgescu, C., 2017. Acculturation and postpartum depressive symptoms among hispanic women in the United States: systematic review. MCN Am. J. Matern. Child Nurs. 42 (1), 21–28.

Andrade, N., Ford, A.D., Alvarez, C., 2021. Discrimination and latino health: a systematic review of risk and resilience. Hisp. Health Care Int. 19 (1), 5–16.

Averbeck, B.B., 2010. Oxytocin and the salience of social cues. Proc. Natl. Acad. Sci. USA 107 (20), 9033–9034. May 18.

Basáñez, Tatiana, et al., 2013. Perceived discrimination as a risk factor for depressive symptoms and substance use among Hispanic adolescents in Los Angeles. Ethn. Health 18 (3), 244–261.

Blackmore, E.R., Chaudron, L., 2014. Psychosocial and cultural considerations in detecting and treating depression in Latina perinatal women in the United States. In: Perinatal Depression Among Spanish-Speaking and Latin American Women: A Global Perspective on Detection and Treatment. Springer, New York, pp. 83–96. https://doi.org/10.1007/978-1-4614-8045-7_6.

Bradley, B., Westen, D., Mercer, K.B., Binder, E.B., Jovanovic, T., Crain, D., Wingo, A., Heim, C., 2011. Association between childhood maltreatment and adult emotional dysregulation in a low-income, urban, African American sample: moderation by oxytocin receptor gene. Dev. Psychopathol. 23 (2), 439–452.

Campo-Arias, A., Herazo, E., 2015. El complejo estigma-discriminación asociado a trastorno mental como factor de riesgo de suicidio. Rev. Colomb. De. Psiquiatr. 44, 243–250. https://doi.org/10.1016/j.rcp.2015.04.003.

Choi, D., Tsuchiya, K.J., Takei, N., 2019. Interaction effect of oxytocin receptor (OXTR) rs53576 genotype and maternal postpartum depression on child behavioural problems. Sci. Rep. 9, 1–8. https://doi.org/10.1038/s41598-019-44175-6.

Cobb, C.L., Xie, D., Meca, A., Schwartz, S.J., 2017. Acculturation, discrimination, and depression among unauthorized Latinos/as in the United States. Cult. Divers Ethn. Minor Psychol. 23 (2), 258–268.

Cobb, C.L., Salas-Wright, C.P., John, R., Schwartz, S.J., Vaughn, M., Martínez Jr., C.R., Awad, G., Pinedo, M., Cano, M.Á., 2021. Discrimination trends and mental health among native- and foreign-born latinos: results from national surveys in 2004 and 2013. Prev. Sci. 22 (3), 397–407 (Apr).

Cuevas, A.G., Ong, A.D., Carvalho, K., Ho, T., Chan, S.W.C., Allen, J.D., Chen, R., Rodgers, J., Biba, U., Williams, D.R., 2020. Discrimination and systemic inflammation: a critical review and synthesis. Brain Behav. Immun. 89, 465–479.

Dannlowski, U., Kugel, H., Grotegerd, D., Redlich, R., Opel, N., Dohm, K., Zaremba, D., Grögler, A., Schwieren, J., Suslow, T., Ohrmann, P., Bauer, J., Krug, A., Kircher, T., Jansen, A., Domschke, K., Hohoff, C., Zwitserlood, P., Heinrichs, M., Arolt, V., Heindel, W., Baune, B.T., 2016. Disadvantage of social sensitivity: interaction of oxytocin receptor genotype and child maltreatment on brain structure. Biol. Psychiatry 80, 398–405. https://doi.org/10.1016/j.biopsych.2015.12.010.

Deitch, E.A., Barsky, A., Butz, R.M., Chan, S., Brief, A.P., Bradley, J.C., 2003. Subtle yet significant: the existence and impact of everyday racial discrimination in the workplace. Hum. Relat. 56, 1299–1324. https://doi.org/10.1177/00187267035611002.

DeSisto, C.L., McDonald, J.A., 2018. Variation in birth outcomes by mother's country of birth among hispanic women in the United States, 2013. Public Health Rep. 133 (3), 318–328.

Donadon, M.F., Martin-Santos, R., Osório, F., de, L., 2018. The associations between oxytocin and trauma in humans: a systematic review. Front. Pharmacol. 9, 154 https://doi.org/10.3389/fphar.2018.00154.

Drolet, C.E., Lucas, T., 2021. The neurogenetics of racial injustice: oxytocin receptor (OXTR) gene rs53576 is associated with perceived discrimination and other-oriented justice beliefs in African Americans. Race Soc. Probl. 13, 102–109.

Egito, J.H., Nevat, M., Shamay-Tsoory, S.G., Osório, A.A.C., 2020. Oxytocin increases the social salience of the outgroup in potential threat contexts. Horm. Behav. 122, 104733.

Ellingsen, D.-M., Leknes, S., Løseth, G., Wessberg, J., Olausson, H., 2016. The neurobiology shaping affective touch: expectation, motivation, and meaning in the multisensory context. Front. Psychol. 6 https://doi.org/10.3389/fpsyg.2015.01986.

Ellis, B.J., Boyce, W.T., Belsky, J., Bakermans-Kranenburg, M.J., van Ijzendoorn, M.H., 2011. Differential susceptibility to the environment: an evolutionary–neurodevelopmental theory. Dev. Psychopathol. 23 (1), 7–28.

Farina, A.S.J., Kremer, K.P., Caldera Wimmer, S., Villarreal-Otálera, T., Paredes, T., Stuart, E., 2021. Anxiety, Depression, and Trauma Among Immigrant Mexican Women up to Two-Years Post-partum. J Immigr Minor Health 23 (3), 470–477. https://doi.org/10.1007/s10903-020-01096-1. Jun.

Flippen, C.A., Parrado, E.A., 2015. Perceived discrimination among Latino immigrants in new destinations: the case of Durham, NC. Socio Perspect. 58 (4), 666–685.

Fox, M., Entringer, S., Buss, C., DeHaene, J., Wadhwa, P.D., 2015. Intergenerational transmission of the effects of acculturation on health in Hispanic Americans: a fetal programming perspective. Am. J. Public Health 105, S409–423. Suppl 3(Suppl 3).

Harris, R.A., Chen, D., Santos Jr., H.P., 2022. Which roads lead to depression in Latinas? A network analysis of prenatal depressive symptoms, discrimination, acculturative stress, and low birth weight. Res. Nurs. Health. https://doi.org/10.1002/nur.22210. Jan 28, PMID: 35088896.

Homberg, J.R., Jagiellowicz, J., 2021. A neural model of vulnerability and resilience to stress-related disorders linked to differential susceptibility. Mol. Psychiatry 27 (1), 514–524. https://doi.org/10.1038/s41380-021-01047-8.

Incollingo Rodriguez, A.C., Polcari, J.J., Nephew, B.C., Harris, R., Zhang, C., Murgatroyd, C., Santos Jr, H.P., 2022. Acculturative stress, telomere length, and postpartum depression in Latinx mothers. Journal of psychiatric research 147, 301–306. https://doi.org/10.1016/j.jpsychires.2022.01.063.

Kimmel, M., Clive, M., Gispen, F., Guintivano, J., Brown, T., Cox, O., Beckmann, M.W., Kornhuber, J., Fasching, P.A., Osborne, L.M., Binder, E., Payne, J.L., Kaminsky, Z., 2016. Oxytocin receptor DNA methylation in postpartum depression. Psychoneuroendocrinology 69, 150–160. https://doi.org/10.1016/j.psyneuen.2016.04.008.

Krieger, N., Smith, K., Naishadham, D., Hartman, C., Barbeau, E.M., 2005. Experiences of discrimination: validity and reliability of a self-report measure for population health research on racism and health. Soc. Sci. Med. 61, 1576–1596. https://doi.org/10.1016/j.socscimed.2005.03.006.

Li, J., Zhao, Y., Li, R., Broster, L.S., Zhou, C., Yang, S., 2015. Association of oxytocin receptor gene (OXTR) rs53576 polymorphism with sociality: a meta-analysis. PLOS One 10, e0131820. https://doi.org/10.1371/journal.pone.0131820.

Marin, G., Gamba, R.J., 1997. Changes in reported awareness of product warning labels and messages in cohorts of California Hispanics and Non-Hispanic whites. Health Educ. Behav. 24, 230–244. https://doi.org/10.1177/109019819702400210.

Nephew, B., Murgatroyd, C., Pittet, F., Febo, M., 2015. Brain reward pathway dysfunction in maternal depression and addiction: a present and future transgenerational risk. J. Reward Defic. Syndr. 01, 105. https://doi.org/10.17756/jrds.2015-017.

Olivera-Pasilio, V., Dabrowska, J., 2020. Oxytocin promotes accurate fear discrimination and adaptive defensive behaviors. Front. Neurosci. 14, 583878.

Osypuk, T.L., Bates, L.M., Acevedo-Garcia, D., 2010. Another Mexican birthweight paradox? The role of residential enclaves and neighborhood poverty in the birthweight of Mexican-origin infants. Soc. Sci. Med 70 (4), 550–560.

Ponting, C., Chavira, D.A., Ramos, I., Christensen, W., Guardino, C., Schetter, C.D., 2020. Postpartum depressive symptoms in low-income latinas: cultural and contextual contributors. Cult. Divers. Ethn. Minor. Psychol. 26 https://doi.org/10.1037/cdp0000325.

Rodrigues, S.M., Saslow, L.R., Garcia, N., John, O.P., Keltner, D., 2009. Oxytocin receptor genetic variation relates to empathy and stress reactivity in humans. Proc. Natl. Acad. Sci. USA 106, 21437–21441. https://doi.org/10.1073/pnas.0909579106.

Rubin, L.P., 2016. Maternal and pediatric health and disease: integrating biopsychosocial models and epigenetics. Pediatr. Res. 79 (1–2), 127–135. https://doi.org/10.1038/pr.2015.203.

Ruiz, R.J., Stowe, R.P., Brown, A., Wommack, J., 2012. Acculturation and biobehavioral profiles in pregnant women of Hispanic origin: generational differences. ANS Adv. Nurs. Sci. 35 (3), E1–E10. https://doi.org/10.1097/ANS.0b013e3182626199.

Santos, H.P.O., Adynski, H., Harris, R., Bhattacharya, A., Incollingo Rodriguez, A.C., Cali, R., Yabar, A.T., Nephew, B.C., Murgatroyd, C., 2021. Biopsychosocial correlates of psychological distress in latina mothers. J. Affect. Disord. 282, 617–626. https://doi.org/10.1016/J.JAD.2020.12.193.

Santos, H.P.O., Nephew, B.C., Bhattacharya, A., Tan, X., Smith, L., Alyamani, R.A.S., Martin, E.M., Perreira, K., Fry, R.C., Murgatroyd, C., 2018. Discrimination exposure and DNA methylation of stress-related genes in Latina mothers. Psychoneuroendocrinology 98, 131–138. https://doi.org/10.1016/J.PSYNEUEN.2018.08.014.

Scholaske, L., Wadhwa, P.D., Entringer, S., 2021. Acculturation and biological stress markers: a systematic review. Psychoneuroendocrinology 132, 105349. https://doi.org/10.1016/j.psyneuen.2021.105349.

Schwartz, S.J., Unger, J.B., Zamboanga, B.L., Szapocznik, J., 2010. Rethinking the concept of acculturation: implications for theory and research. Am. Psychol. 65 (4), 237–251. https://doi.org/10.1037/a0019330.

Shamay-Tsoory, S.G., Abu-Akel, A., 2016. The social salience hypothesis of oxytocin. Biol. Psychiatry 79 (3), 194–202. https://doi.org/10.1016/j.biopsych.2015.07.020. Feb 1.

Sluiter, F., Incollingo Rodriguez, A.C., Nephew, B.C., Cali, R., Murgatroyd, C., Santos, H.P.O., 2020. Pregnancy associated epigenetic markers of inflammation predict depression and anxiety symptoms in response to discrimination. Neurobiol. Stress 13, 100273. https://doi.org/10.1016/J.YNSTR.2020.100273.

Walker, J.L., Ruiz, R.J., Chinn, J.J., Marti, N., Ricks, T.N., 2012. Discrimination, acculturation and other predictors of depression among pregnant hispanic women. Ethn. Dis. 22, 497–503.

Ward, Julia B., et al., 2019. Perceived discrimination and depressive symptoms among US latinos: the modifying role of educational attainment. Ethn. Health vol. 24 (3), 271–286. https://doi.org/10.1080/13557858.2017.1315378.

Williams, D.R., Yan, Yu, Jackson, J.S., Anderson, N.B., 1997. Racial differences in physical and mental health. J. Health Psychol. 2, 335–351. https://doi.org/10.1177/135910539700200305.