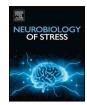
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# Parenting stress: A novel mechanism of addiction vulnerability

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# ABSTRACT

Addiction remains a significant public health concern. Despite numerous public health initiatives, many parents continue to use substances during the prenatal and postpartum period. While stress has been implicated in the maintenance of substance use disorders more generally, we propose that parenting stress specifically increases vulnerability to substance use in adults caring for young children. To explore this notion, we first consider the neurobiology of the adult transition to parenthood and the value of adopting a parenting-specific approach to understanding addictive processes. Next, we consider the neurobiology of addiction and parenting before directly addressing parenting stress in the context of addiction. Finally, we describe current interventions with parents that incorporate the management of negative affect to enhance caregiving quality and decrease substance use. Taken together, this article proposes that the unique demands of caring for a developing child may be more stressful above and beyond other forms of stress. As a consequence, intervention approaches that target stress in the parenting role hold promise for decreasing parental substance abuse.

## 1. Introduction

Addiction remains pervasive, with lifetime drug use disorder affecting 9.9% of adults in the United States (Grant et al., 2016). The recent sharp increases in opioid use and abuse have once more propelled addiction into the spotlight of societal discussion and concern (Compton et al., 2015). Parental substance use is particularly concerning, impacting at least two generations within families. Indeed, while there are the associated teratogenic effects of substance use on fetal development and neonatal outcomes (Banderali et al., 2015; Patra et al., 2011), consequences of maternal and paternal substance use extend beyond parturition. Sensitive maternal behavior may be compromised by addiction (Hatzis et al., 2017) and parental substance use is associated with childhood maltreatment, including neglect and abuse, and parental substance use is significantly implicated in child welfare cases (Ghertner et al., 2018; Kepple, 2018).

Given the importance of early caregiving relationships to children's socio-emotional and physical health and well-being, disruptions in early parenting may also be one mechanism through which vulnerability to later substance use in the child emerges (Alvarez-Monjaras et al., 2018; Mayes and Suchman, 2006), warranting addiction to be viewed through a lifespan developmental perspective (McCrory and Mayes, 2015). With this in mind, we propose a new approach to considering addiction vulnerability in adults, focusing on adult transition to parenthood. Our goal is to leverage knowledge on the neurobiology of parenting and addiction to provide new opportunities for interventions to decrease substance use in adults caring for children. Specifically in this article, we will review the role of parenting stress as being integral to addiction vulnerability in adults with young children.

## 2. Adult transition to parenthood

A central tenant of this article is the need to recognize adults as parents and parenting as a developmental process in understanding addiction vulnerability. Therefore it is necessary to first consider mechanistically how adults as parents differ from adults without children in the absence of addiction. At a behavioral level, caregiving has been differentiated between women with and without children. Specifically, when completing a simulated crying infant interaction, while basic behaviors (e.g., checking diaper, feeding) were comparable between mothers and non-mothers, the mothers engaged in more physical stimulation, talking, and ventral holding patterns with the infant simulator than the non-mothers (Gustafson and Harris, 1990). At a neurobiological level, accumulating research evidences structural and functional brain changes during pregnancy and the postpartum period (P. Kim, 2016). In particular, structural brain changes have evidenced decreased gray matter volume from pre-pregnancy to post-pregnancy in the anterior and posterior cortical midline, bilateral lateral prefrontal cortex, and temporal cortex (Hoekzema et al., 2017). Furthermore, structural gray matter volume increases have also been reported across

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the postpartum period in the prefrontal cortex, parietal lobes, as well as in midbrain regions (P. Kim et al., 2010). Functionally, parents (mothers and fathers) are more reactive to infant cries than non-parents in multiple brain regions, including the amygdala, insula, and ventral prefrontal cortex – with non-parents being more reactive to infant laughter in these same brain areas (Seifritz et al., 2003). Employing event-related potentials (ERPs), parents (mothers and fathers) also rapidly distinguish between different intensities of negative affect in infant faces (discomfort as compared to distress), a finding absent in nonparents (Proverbio et al., 2006). Finally, at a cognitive level, studies of visual attention have evidenced that infant distress faces preferentially engage attention in mothers to a greater extent than non-mothers (Thompson-Booth et al., 2014a, 2014b).

Taken together, these initial findings suggest differential responses to infant stimuli at behavioral, neural, and cognitive levels. Critically, while the heightened salience of infant affective cues in women may reflect physiological changes as a function of pregnancy or parturition; other studies suggest that there may be neurophysiological commonalities amongst fathers, as well as women who parent children that they did not deliver themselves (Abraham et al., 2014; Grasso et al., 2009). Thus, biological and experiential (or exposure) components are likely to contribute in the transition to parenthood and behavioral, neural, and cognitive differences between parents and non-parents. Nevertheless, irrespective of the origins of these parent and non-parent differences observed across multiple levels of analysis, these findings provide a compelling motivation to study adults as parents with respect to psychopathology generally, and addiction specifically, given the context of this article.

## 3. A neurobiological approach to parenting and addiction

Recent efforts to generate a more nuanced understanding of the pathophysiology of addiction and its impact on parenting have adopted a neurobiological perspective. Given the variability in compromised caregiving reported in parents with addiction (Hatzis et al., 2017), a neurobiological approach is valuable in the identification of mechanisms that might underscore differences in observed parenting behavior (Maupin et al., 2015). An initial review of the human and animal studies examining the neurobiology of addiction and maternal behavior suggested that key neural circuits implicated in stress and reward processes in parenting are dysregulated in addiction, including the central amygdala, medial prefrontal cortex, and nucleus accumbens (Rutherford et al., 2011). Thus compromised caregiving observed in many parents with substance use disorders may be secondary to an existing dysregulation of neural circuits in addiction, a hypothesis incorporated within the reward-stress dysregulation model of addiction and parenting (Rutherford and Mayes, 2017).

In adults without addiction, research has evidenced that the presentation of infant cues (infant faces, infant vocalizations) recruits a host of neural regions implicated in reward-related processes in nonparents as well as parents, including the ventral striatum, ventral tegmental area, prefrontal cortex, and orbitofrontal cortex (Feldman, 2015; Glocker et al., 2009). Notably, decreased neural responses to infant affective cues have been reported in substance-using mothers as compared to non-substance-using mothers, including in prefrontal, sensory, and limbic areas (Landi et al., 2011). Furthermore, delayed and attenuated ERP responses to infant faces have been observed in tobacco-smoking mothers compared to non-smoking mothers (Rutherford et al., 2017). Finally, mothers recruited from an inpatient facility for addiction treatment evidenced a decreased response in reward-brain regions (ventral medial prefrontal cortex, hypothalamus, and ventral striatum) when viewing their own infant's smiling face as compared to an unfamiliar infant's smiling face (S. Kim et al., 2017). Consequently, infant cues may be less rewarding and pleasurable for parents with addiction, which may underscore the passive and disengaged behaviors that have been observed during some behavioral interactions between substance-using mothers and their children (Gottwald and Thurman, 1994; Mayes et al., 1997). Therefore, while infant cues are usually rewarding, there may be a deficit in their reward salience in addiction.

Recognizing the role of reward salience in parenting and addiction is important and may suggest clear pathways for interventions designed to increase the pleasure of parenting in mothers and fathers with addiction. However, it is unlikely that this reward deficit alone is sufficient to maintain addictive behaviors despite salient infant needs, but instead such deficits may speak to broader behavioral difficulties parents with substance use disorders face when caring for their child (Hatzis et al., 2017). Given the implications of stress neural circuitry in parenting and addiction, we propose it is also critical to examine the role of stress in the maintenance of addiction in parents, which may be a second mechanism through which we can understand compromised caregiving behavior in families with addiction, including hostile and intrusive mother-child interactions (Johnson et al., 2002).

#### 4. Parenting stress and addiction

Stress dysregulation has been repeatedly implicated in addiction. Substance use has been well associated with stress-related symptomatology (Sinha, 2001), and increased exposure to stress heightens vulnerability to addiction (Goeders, 2004). Furthermore, exposure to stress increases subjective reports of craving that are associated with neural correlates of stress reactivity, specifically in the dorsal striatum and caudate (Sinha et al., 2005). Stress and negative affect have also been observed as primary motivators underscoring substance use in the general population, in particular in tobacco-smoking (Buchmann et al., 2010; Kassel et al., 2003). Stress-induced craving also predicts craving in cocaine abstinent individuals (Sinha et al., 2006). Therefore, addiction can be considered in part as a disorder of stress regulation, consistent with negative reinforcement models of addiction that posit substance-using behaviors continue given the relief the drug affords to the negative affective states of craving and withdrawal (Koob and Le Moal, 2001; Koob and Volkow, 2009). Over time, substance use becomes a more general, albeit maladaptive, means of stress regulation (Sinha, 2001, 2008). Consistent with this notion, higher levels of stress lead to an increase consumption of substances (Steptoe et al., 1996) and cortisol levels have been found to be positively correlated with measures of craving (Buchmann et al., 2010). Consequently, stress dysregulation is an important factor in the maintenance of addiction.

All parents, irrespective of whether they have an addiction, experience some stress with the arrival of a newborn, and the demands of caregiving extend across the lifetime (Abidin, 1990; Crnic and Greenberg, 1990; Webster-Stratton, 1990). While stress has been implicated as an important component of addiction, stress is multifaceted, including general and contextual factors. In laying the theoretical and empirical foundation for the study of stress, Lazarus (1993) cited the importance of understanding the relational meaning of the stressor; that is, not just recognizing a stressor exists, but the significance of that stressor to the individual. Here we advance this relational meaning to incorporate parenting-specific stressors, which are uniquely salient to adults with children and are important to understand in the context of addiction and maintenance of substance use - above and beyond other sources of stress. In preliminary support of this notion, personalized stressors are more closely associated with craving than standardized stressors, such as public speaking (Sinha et al., 1999). Presumably increased craving to the personalized stressor reflects a stronger affective experience when the stressor is especially salient to the individual.

Given that stress is a central tenant of addiction, for the purposes of this article it is necessary to distinguish between the stressed parent and parenting stress (Crnic and Ross, 2017). The term stressed parent encapsulates *general stressors* outside the parent-child relationship (e.g., housing, income, social support), with parenting stress encompassing the *specific stressors of parenting* a child. One of the challenges of

studying the impact of addiction on parenting is understanding the stressed parent element, that is identifying, quantifying, and controlling for the factors associated with more general stressors that may distinguish parents with and without addiction, even before assessments of the family begin. Nevertheless, we hypothesize that caregiving (i.e., parenting stress) increases craving and continued substance use above and beyond other sources of general stress (i.e., stressed parent) (Rutherford and Mayes, 2017). Although parents with addiction may be managing both forms of stress, evidence suggests that stress in the parenting role may be particularly problematic for substance-using women. Notably research in this area has largely focused on tobaccosmoking parents, providing an important empirical base to build upon. Tobacco-smoking mothers who relapsed postpartum reported higher levels of stress, depression, and anxiety, with mothers reporting episodes of infant crying and irritability as triggers of tobacco-using cognitions and behaviors (Correa et al., 2015; Gaffney et al., 2008; Solomon et al., 2007). Many mothers also described smoking as a source of relief during stressful interactions with their infants (Gaffney et al., 2008). Thus infant cries appear to be particularly salient to recent parents in driving substance use (and repeated exposure to infant cries is a central and unique experience of early parenting). In some of our own work we have started to examine how parenting stress may be different from other sources of stress and how this may be associated with different aspects of parenting. Specifically, we have examined how mothers tolerate infant cries as compared to tolerance of a non-infant related stressor (i.e., mental arithmetic) (Rutherford et al., 2015; Rutherford et al., 2013). In these distress tolerance studies, we observed that mothers who report higher levels of reflective functioning (referring to their capacity to understand their infant's emotions, thoughts, and feelings), tolerate infant cries for longer than mothers with lower levels of reflective functioning. Critically, levels of parental reflective functioning were not associated with tolerance of the non-infant related stressor - suggesting parenting context is critical to these associations.

Thus far we have considered parental stress as a potential factor maintaining substance use during early childhood. However, stress surrounding parenting is not unique to the postpartum period and may also be a factor during pregnancy. Even before birth, prenatal stress may shape children's neurodevelopment. Prenatal stress, including stress, depression, and anxiety, has been associated with infants being born low for their gestational birth weight and age, and may elevate the risk of children developing a host of socio-emotional, cognitive, and behavioral difficulties (Glover, 2015). Indeed, exposure to stress in utero is thought to program fetal brain development in preparation for the postpartum environment, which may have lasting consequences across development (Glover et al., 2016). Although the precise mechanisms underlying how maternal stress alters fetal neurodevelopment are unclear, one pathway may be through changes in gene expression of a placental enzyme that breaks down cortisol (Monk et al., 2016).

Given that stress may increase craving and substance use during pregnancy, the developing child may receive a dual stress and drug exposure effect. Qualitative research has evidenced that women continue to smoke during their pregnancy to facilitate management of their stress levels (Flemming et al., 2015). Consequently, pregnancy is a critical window of risk for mothers and their developing child to stress and substance use exposure. In the United States, rates of past month substance use during pregnancy were lower than rates of substance use in non-pregnant women (Smith and Lipari, 2017), consistent with the hypothesis that pregnancy may offer a protective benefit to motivate change away from substance use (Kendler et al., 2017). Empathy has been proposed as one mechanism that may be critical to spontaneous quitting of substance use in pregnancy (Massey et al., 2017), where spontaneous tobacco-smoking quitting in pregnancy was associated with increased maternal responsiveness during interactions with her child (Massey et al., 2018). Consequently, intervention efforts targeting parenting stress in substance-using mothers may be optimal during pregnancy as well as the postpartum period for parents as well as their developing child.

#### 5. Targeting parental stress in addiction through intervention

Building on the work discussed thus far, focusing on the transition to parenthood may be a valuable time window to implement intervention approaches that address parenting stress generally, and specifically in parents struggling with addiction. Critically, interventions that have targeted parents with addiction show little to no efficacy for improvements in caregiving (Suchman et al., 2006), with many more generalized programs focusing on decreasing substance use rather than recognizing the role of adults as parents that may contribute to maintaining substance use and abuse.

One intervention approach, Mothering from the Inside Out (MIO) (Suchman et al., 2012), adopts an individualized therapeutic approach with substance-using mothers that recognizes adults as parents and places the demands of parenting first and foremost even before, or equally weighted to, the mothers' ongoing substance use. In MIO, clinicians work with parents to facilitate their capacity to recognize and understand their own emotions, thoughts, and feelings, as well as those of their child, and how these emotions and cognitions may be reflected in their own and their child's behaviors (i.e., parental reflective functioning). MIO is designed to support mothers learning to regulate their emotions, particularly distress, to optimize their own well-being, as well as the well-being of their developing child. In the first randomized control trial of MIO (as compared to parent education), improvements were observed in levels of parental reflective functioning and caregiving that were sustained at follow-up (Suchman et al., 2011). Furthermore, although not the direct focus of the intervention, improvements were also observed in changing patterns of substance use in the MIO sample. A second randomized trial also showed promising benefits to mother-child outcomes with respect to caregiving and substance use (Suchman et al., 2017). Consequently, there may be significant value to the implementation of intervention programs that recognize adults as parents and interactions with parenting stress and addictive processes. It may also be that such an approach positively impacts substance use (as well as parenting behaviors) through facilitating regulation of the stress associated with caregiving, which lessens the reliance on substance use as a means of regulation. Concurrently, focusing on the mother-child relationship, rather than the substance use itself, may increase the salience and reward of caregiving and perhaps lessen the salience of substances. We may also posit that focusing on the motherchild relationship also provides earlier positive impact for the child in contrast to standard substance abuse treatment that rarely includes the family or children in the therapeutic lens. Finally, it is worth considering that placing the emphasis on these women as mothers, rather than as women with addiction, may improve the acceptability, and the retention of women, in intervention programs.

Approaches such as MIO work with mothers after birth. This is particularly important given that while many women are able to abstain from substance use during their pregnancy, following delivery and the initial months postpartum, relapse rates are high (Park et al., 2009). However, given extant literature on prenatal consequences of stress and substance use for child development, interventions during pregnancy would be valuable. In particular, prenatal interventions can capitalize on pregnancy being a critical window for risk (i.e., to fetus as well as mother) and a window for opportunity where women may be motivated to decrease substance use (Kendler et al., 2017). Concurrently, given the evidence that infant cues are also salient to non-parents (Glocker et al., 2009), and that substance-using parents do respond to infant cues, just at a decreased level (S. Kim et al., 2017; Landi et al., 2011; Rutherford et al., 2017), taking advantage of the neurobiology of motherhood may present a protective opportunity to address both the decreased salience and increased stress of caregiving when working with parents with addiction (Rutherford and Mayes, 2017). In particular, hormonal shifts during pregnancy and the postpartum period

may sensitize neural circuitry implicated in reward processing leading to the increased salience of infant affective cues and motivation towards them (Ferrey et al., 2016). Therefore, increasing the pleasure and reward of caregiving may also prove valuable in this process as well as targeting stress specifically. Given the integration of stress and reward neural circuitries in maternal behaviors (Rutherford et al., 2011), optimal intervention approaches, particularly in the perinatal period, may benefit incorporating stress regulation strategies as well as approaches to facilitate increasing the pleasure of caregiving.

Stress does appear to play some role during pregnancy in continuation of substance use (Flemming et al., 2015) and novel approaches to targeting levels of stress in substance-using women during pregnancy have been proposed (O'Hair et al., 2018). However, most prenatal intervention approaches have focused more on infant salience to the mother as a way of improving substance use and parent-child outcomes. For instance, one intervention employed a similar therapeutic approach to MIO during pregnancy, sharing three-dimensional ultrasounds with expectant mothers to reinforce the relationship forming between these women and their developing child - with preliminary findings suggesting that enrollment in this prenatal intervention may decrease maternal substance use (Pajulo et al., 2016). This finding resonated with reports that greater maternal-fetal attachment as being associated with decreased tobacco-smoking consumption during pregnancy (Magee et al., 2014; Massey et al., 2015). Early postpartum approaches that have focused on the mother-newborn relationship have also been beneficial. One study reported that promoting maternal-child bonding when infants were in the Neonatal Intensive Care Unit resulted in longer tobacco-smoking abstinence in recent mothers (Phillips et al., 2012). Furthermore, when mothers with opioid addiction were empowered in their role for caring for the infant as part of a non-pharmacological treatment approach, decreased lengths of hospital stays, reduced morphine treatment for the newborns, and decreased hospital costs were reported (Grossman et al., 2017). Although these studies do not focus on stress regulation per se, they do suggest that prenatal interventions capitalizing on the changing neurobiology of motherhood (i.e., the increased salience of infant cues) are beneficial. Taken together, these initial findings suggest significant benefit of introducing intervention approaches in parents with addiction both prenatally and during the initial months postpartum; specifically, with the focus of these interventions being on stress regulation and reward processes surrounding the parent-child relationship.

#### 6. Limitations and future directions

Accumulating animal and human research led to a reward-stress dysregulation model of addiction and parenting (Rutherford and Mayes, 2017). This model proposed that parenting was less rewarding and more stressful to caregivers struggling with addiction. To date, neurobiological research in parents with addiction have primarily focused on reward responses in mothers with substance-use disorders (S. Kim et al., 2017; Landi et al., 2011; Rutherford et al., 2017), overlooking the role of stress in the maintenance of addiction. Here we propose a specific need to investigate parenting stress as a salient and relational stressor in the caregiving role, which may increase craving and motivate continued substance use. This can be assessed empirically through examining exposure to parenting stressors, including infant cries, parenting stress self-report measures (Abidin, 1990), as well as guided imagery approaches tailored to the parenting experience, an approach which has been successfully implemented to study the impact of personalized stressors in the study of addiction (Sinha and Tuit, 2011).

Repeated assessment of stressors, parenting and non-parenting, measured systematically across pregnancy and the postpartum period is also warranted to characterize the extent to which these stressors are elevated in parents, mothers and fathers, with and without addiction. It will also be important to address other sources of psychosocial stress, including socioeconomic status and social support, number of other children as well as other vulnerability factors, including fatigue, to disentangle the stressed parent from parenting stress. Many of these studies could begin with behavioral and physiological (including hormonal) measures before introducing neuroimaging methodologies to identify potential mechanisms of interest and their overlap of studies of addiction in non-parents. Furthermore, understanding the contribution of distal risk factors for stress regulation difficulties and addiction in adulthood will be valuable, including the exposure to early stress and adversity during key periods of development (McCrory and Mayes, 2015).

Measuring trajectories of substance use across pregnancy and the postpartum period might also provide insight into the identification of relapse risk in abstaining parents based on parental stress assessments. Our focus has also been on parenting in early infancy, and it will be important to establish the extent to which parenting stress changes when caring for children across early childhood, adolescence, and adulthood. In the development of interventions, it will also be important to examine whether combined programs incorporating stress regulation and increasing the joys of parenting are more effective than focusing on parenting stress in isolation. Similarly, increased parenting stress has been reported in families caring for children with developmental disabilities (Estes et al., 2009; Gupta, 2007), highlighting the importance of studying parenting stress beyond addiction to other clinically-relevant contexts. Finally, it will be important to incorporate studies of mothers and fathers, as well as non-parents, to establish the parental specificity of these effects.

## 7. Conclusion

Accumulating evidence recognizes an adult's transition to parenthood, differentiating parents from non-parents at behavioral, cognitive, and neurobiological levels. Such findings warrant the recognition of adults as parents in our understanding of psychopathology, including addiction. We considered the neurobiology of addiction and parenting and the focus of current empirical research to reward processing and parenting, with less focus on the stressors of being a parent. Given the documented role of stress in the maintenance of addiction, as well as the increased affective experience of personalized stressors, we have proposed a novel direction for parenting and addiction research and clinical work that specifically examines parenting stress. In particular, we hypothesize that parenting stress, above and beyond other sources of stress (i.e., the stressed parent), will be associated with increased craving and substance use in recent parents. This hypothesis is testable, and if supported, will necessitate new directions for interventions and substance use treatment programs that explicitly recognize adult transition to parenthood and the specific role of parenting stress in the maintenance of addiction.

### **Declarations of interest**

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