

# Prenatal exposure to tobacco and cannabis: Effects on autonomic and emotion regulation

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## ABSTRACT

Tobacco and cannabis are often used together in pregnancy and both have effects on children's regulatory system. Yet, little is known about the impact of co-use on the development of emotion regulation at the developmentally salient age of 2 years. One pathway linking co-exposure to tobacco and cannabis to toddler regulation may be via poor autonomic regulation in infancy. In addition, substance using mothers may be more dysregulated themselves, which may have direct effects on toddler regulation, but may also affect parenting, particularly maternal sensitivity during mother-child interactions. Thus, a second pathway linking exposure to toddler regulation may be via maternal dysregulation and low maternal sensitivity. We examined a conceptual model linking prenatal exposure to toddler regulation via these two pathways in a prospective sample ( $N = 247$ ) of mother-child dyads recruited in the first trimester of pregnancy. Results indicated significant effects of co-exposure on poor autonomic regulation in infancy, which in turn predicted poor toddler emotion regulation. Mothers who used both tobacco and cannabis displayed lower sensitivity during play interactions with their infants. Maternal sensitivity was modestly stable from infant to toddler period and was predictive of higher toddler emotion regulation. Continued postnatal exposure to tobacco was also a significant, unique predictor of lower toddler emotion regulation. Results highlight the importance of examining co-exposure effects and suggest that this common pattern of use may be associated with higher infant/toddler risks.

## 1. Introduction

Tobacco and cannabis are two of the most commonly used substances among pregnant women, with tobacco use rates ranging from 18% to 27% (USDHHS, 2014). These rates are even higher among young, low-income women (USDHHS, 2014). A large number of women who use tobacco also use cannabis with co-use rates as high as 45% (Chabarría et al., 2016), but little is known about the effects of co-occurring use. This is especially critical given changes in cannabis legalization and increases in cannabis potency in recent years (Calvigioni et al., 2014; Mehmedic et al., 2010).

Tobacco use in the form of cigarettes delivers significant amounts of chemical toxins to the fetus via maternal bloodstream (USDHHS, 2014). Prenatal tobacco exposure (PTE) also increases norepinephrine and dopamine concentrations (Lichtensteiger et al., 1988), as well as acetylcholine and serotonin (Slotkin et al., 2015) in the developing brain. Similarly, gestational cannabinoid exposure in rats interferes with neuronal wiring (pro-apoptotic brain signaling molecule changes, DNA fragmentation) and may cause subsequent impairments in regulatory

behaviors (Downer et al., 2007; Scott-Goodwin et al., 2016). Recent brain morphology studies indicated that tobacco exposed children had cortical thinning, especially in the frontal and superior parietal cortices (El Marroun et al., 2016; Toro et al., 2008), while cannabis exposed children had thicker frontal cortices indicating altered neurodevelopmental maturation in regions involved in higher order processing (El Marroun et al., 2016). Both these alterations may also result in deficits in regulation of emotions. Indeed, there is robust evidence of the association between PTE and arousal dysregulation in the neonatal period (Espy et al., 2011; Jacobson et al., 1984; Stroud et al., 2009), a smaller literature in infancy (Wiebe et al., 2014; Schuetze et al., 2017), and a larger literature on problem behavior in later childhood (USDHHS, 2014, review). Similarly, prenatal cannabis exposure was associated with deficits in sustained attention and lower self-regulation in later childhood (Day et al., 2006; Day et al., 2011; Day et al., 1994; Fried, 2002; Willford et al., 2012). However, little is known about effects of co-occurring use of tobacco and cannabis (PTCE) on emotion regulation in early childhood. This was the major goal of the current study.

Emotion regulation was defined as a process of modulating intensity

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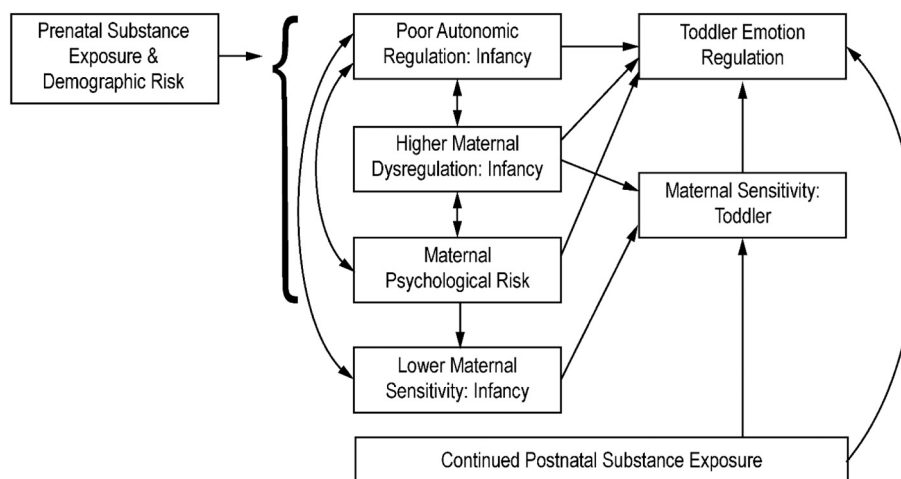


Fig. 1. Conceptual model.

and duration of affective states and related physiological processing (Morris et al., 2017). Indeed, physiological processing of affective states may play a critical predictive role in behavioral manifestations of emotion regulation. One particularly useful measure of physiological regulation is respiratory sinus arrhythmia (RSA), a measure of the high-frequency portion of heart rate variability that occurs within the frequency range at which respiration occurs (approximately 0.24–1.04 Hz for infants; Porges et al., 1996). Although RSA is multiply determined, it is believed to index activity of the parasympathetic nervous system in autonomic control of heart rate via the vagus nerve. Two commonly used indices of autonomic regulation (Porges, 1996) include RSA at rest (baseline RSA) and changes in RSA during environmental demands (RSA regulation; Bornstein and Suess, 2000; Calkins, 1997). Baseline RSA is a measure of the infant's ability to maintain physiological homeostasis during periods of minimal external stimulation. During exogenous challenges to homeostasis, activity of the parasympathetic nervous system is often reduced, allowing HR to increase, which, in effect, releases the parasympathetic brake on HR (Porges et al., 1996). RSA regulation during periods of environmental challenge is believed to reflect the infant's ability to appropriately engage or disengage with the environment (Bornstein and Suess, 2000; Porges, 1996), such that RSA is suppressed during stressful or negative emotional situations. Thus, the measurement of change in RSA from baseline in response to stress or negative affect situations may be an important index of autonomic regulation in infants and be predictive of emotion regulation at later ages.

Theories of emotion regulation highlight the importance of autonomic regulation of arousal as an important predictor of children's ability to effectively modulate emotions in challenging contexts (Beauchaine, 2001). Indeed, RSA suppression in response to affective challenges were associated with higher levels of emotion regulation and lower problem behavior, while maladaptive RSA increases in these contexts were predictive of higher behavior problems (Calkins et al., 2007; Calkins and Keane, 2004; Cho et al., 2017). Thus, one mechanism linking PTE and PTCE to toddler emotion regulation may be autonomic regulation (Baseline RSA and RSA suppression) in infancy. One major goal of this study was to examine the association between prenatal substance exposure (particularly co-exposure to tobacco and cannabis) and toddler emotion regulation (at 24 months of child age) via poor autonomic functioning in infancy (at 9 months of child age).

Although few studies examined the role of autonomic regulation as an explanatory mechanism linking co-exposure to tobacco and cannabis (PTCE) to toddler emotion regulation, there is a small, but robust literature on PTE and autonomic regulation. During early infancy, studies found higher heart rates during quiet and active sleep, lower long-term heart rate variability, and lower baseline RSA during rest among

tobacco exposed infants (Franco et al., 2000; Schuetz and Zeskind, 2001; Schuetz and Eiden, 2006; Schuetz et al., 2013; Zeskind and Gingras, 2006). In later infancy, one study reported significant RSA suppression in response to negative emotion among control infants, but not among tobacco exposed infants (Schuetz et al., 2013). Thus, it is unclear if dual exposure to both tobacco and cannabis is associated with poor autonomic regulation, but given the small but robust literature on tobacco effects on infant autonomic regulation, we hypothesized this as a mediating pathway.

In addition to autonomic variables, parents are one of the most critical influences on development of emotion regulation. Mothers using tobacco and cannabis not only experience greater demographic risks, such as younger age, lower income, and single status (Chabbaria et al., 2016; USDHHS, 2014), but are also at higher risk for emotional dysregulation and are at higher risk for symptoms of depression and anger/hostility (Eiden et al., 2011; Ludman et al., 2000; Massey et al., 2016). Mothers' own emotion regulation abilities and psychological risk may impact child emotion regulation via social learning processes, by impacting parenting, or through potential heritability of dispositional facets of emotion regulation. However, despite theoretical support, few studies examined parents' emotion regulation as a predictor of child emotion regulation, although studies examined the role of parents' emotion socialization of their children and psychological symptoms as predictors of child outcomes (Eisenberg and Fabes, 1992; Eisenberg et al., 1996). Parents' own emotion regulation and psychological symptoms may also impact quality of parenting, the most proximal predictor of child emotion regulation. Indeed, the capacity to regulate emotions is strongly rooted in dyadic parent-infant interactions (Schore, 1994). Empirical evidence points to the critical protective role of maternal sensitivity in the infant toddler period, which includes warmth, support, and acceptance of children and contingent responsiveness to child cues, as a proximal predictor of children's emotional and behavioral regulation across development (Feldman et al., 2011; Feldman et al., 1999; Kochanska et al., 2008). Thus, a second goal of this study was to examine the role of maternal sensitivity as an additional predictor of toddler emotion regulation (see Fig. 1).

There is some evidence that boys are more vulnerable to PTE, including stronger PTE effects on lower birthweight among boys (Tayie and Powell, 2012), lower positive mood (Pickett et al., 2008), higher peak cortisol reactivity (Schuetz et al., 2008), lower attentional response (Schuetz et al., 2013), and lower delay of gratification at preschool age (Wiebe et al., 2015) compared to exposed girls. A few studies also reported stronger associations between PTE and behavior problems among boys compared to girls, although these results are not consistent and many studies did not examine the role of child sex as a moderator (see Coles et al., 2012; review). In contrast, few studies examined sex as

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