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Developmental pathways from prenatal tobacco and stress exposure to behavioral disinhibition

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ABSTRACT

Prenatal tobacco exposure (PTE) and prenatal stress exposure (PSE) both have been linked to externalizing behavior, although their effects generally have been considered in isolation. Here, we aimed to characterize the joint or interactive roles of PTE and PSE in early developmental pathways to behavioral disinhibition, a profile of cognitive and behavioral under-control that presages severe externalizing behavior. As part of a prospective, longitudinal study, 296 children were assessed at a mean age of 5 years. Exposures were assessed via repeated interviews across the prenatal period and bioassays of cotinine were obtained. Behavioral disinhibition was assessed using temperament measures in infancy, performance-based executive control tasks and measures of disruptive and inattentive behavior. PSE was associated with a higher probability of difficult temperament in infancy. Each exposure independently predicted poorer executive control at age 5 years. Difficult temperament and executive control difficulties in turn predicted elevated levels of disruptive behavior, although links from PTE and PSE to parent-reported attention problems were less robust. Children who experienced these prenatal exposures in conjunction with higher postnatal stress exposure showed the lowest executive control and highest levels of disruptive behavior. Findings highlight the compounding adverse impact of PTE and PSE on children's behavioral trajectories. Given their high concordance, prenatal health campaigns should target these exposures in tandem.

1. Introduction

There is growing recognition that the prenatal environment shapes health and disease across the lifespan (e.g., Barker, 1998). Two prenatal exposures that have been linked independently to externalizing behavior are maternal smoking and psychosocial stress during pregnancy. Often disregarded in studies of their impact, however, is the fact that prenatal tobacco exposure (PTE) often accompanies a high degree of stress. Women who smoke during pregnancy on average experience higher levels of financial stress, reduced social and partner support, more negative life events and trauma, and increased levels of psychological distress and anxiety (Bullock et al., 2001; Goedhart et al., 2009; Holtrop et al., 2010; Lynch et al., 2011). Moreover, high stress levels increase the likelihood of persistent smoking during pregnancy and are associated with reduced cessation self-efficacy (Weaver et al., 2008; Pickett et al., 2009; Prusakowski et al., 2011). PTE and prenatal stress exposure (PSE) therefore are intertwined and likely operate additively or interactively to shape children's outcomes. A veridical understanding of the impact of these exposures demands consideration of their effects in the context of one another. Here, we aim to integrate measures of PTE and PSE and consider their mutual or interactive roles in shaping pathways to externalizing behavior.

Children with PTE are 2 to 4 times more likely to meet criteria for oppositional defiance disorder and conduct disorder beginning in early childhood and also are more likely to exhibit substance use disorders and severe antisocial behavior in adolescence and adulthood (Wakschlag and Hans, 2002; Gatzke-Kopp and Beauchaine, 2007; Monshouwer and Huizink, 2011; Ellis et al., 2012; Goldschmidt et al., 2012). Reported links to ADHD have been less consistent: while some studies have demonstrated associations between PTE and ADHD symptoms (Mick et al., 2002; e.g., Linnet et al., 2003), others suggest that there is no association or that PTE predicts only co-morbid ADHD and conduct problems as opposed to ADHD symptoms per se (Wakschlag et al., 2006a; Huijbregts et al., 2007; Ball et al., 2010). Studies using continuous outcome measures compliment those that have used clinical cut-offs, reporting elevated levels of aggression, impulsivity, hyperactivity and rule-breaking in preschoolers, children and adolescents with PTE relative to their non-exposed peers (Martin et al., 2006; Carter et al., 2008; Galera et al., 2011; Cornelius et al., 2012).

Similar to PTE, PSE has been linked to a higher likelihood of aggression, conduct disorder and ADHD in children and, more recently, to externalizing behavior in young adults (Talge et al., 2007; Li et al., 2010; Bekkhus et al., 2011; Blair et al., 2011; Glover, 2011; Ronald et al.,

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2011; Grizenko et al., 2012; Class et al., 2014; Betts et al., 2015). In the Raine study, the number of maternal stressors experienced during pregnancy and PTE were two of the strongest predictors of psychiatric morbidity in early childhood, over and above several measures of postnatal psychosocial adversity (Robinson et al., 2008, 2011). Externalizing behavior problems were almost 2-fold more prevalent in children whose mothers reported 3 or more negative life events during pregnancy relative to those whose mothers reported fewer than 3 negative life events (Robinson et al., 2011).

Taken together, these studies suggest that PTE and PSE may contribute to the developmental origins of behavioral disinhibition, a risk phenotype that has been implicated in life-course persistent antisocial behavior and substance dependence (Tarter, 2002; Tarter et al., 2003; Iacono et al., 2008; Zucker et al., 2011; Lester et al., 2012). Behavioral disinhibition is characterized by trait-like deficits in cognitive and behavioral self-control, which manifest as high levels of behavioral sensation seeking, impulsivity, aggression and early substance use initiation. Behavioral disinhibition is thought to reflect disruptions to prefrontal cognitive networks in the brain, including abnormal reactivity of thalamic and limbic neural structures that feed input to the prefrontal cortex or a deficiency in the prefrontal modulation of these inputs or both (Zucker et al., 2011). These neural networks modulate core executive control processes, which develop rapidly over the course of early childhood, and allow for greater goal-directed control over attentional resources (Clark et al., 2012; Wiebe et al., 2012).

There is accumulating evidence that children with PTE have impairments in executive control, including discrepancies in processing speed, sustained attention, response inhibition and working memory, relative to non-exposed controls in childhood and adolescence (Fried and Watkinson, 2001; Willford et al., 2010; Mezzacappa et al., 2011; Cornelius et al., 2012). While research examining the impact of prenatal maternal stress on child executive control generally is lacking, one study of school-aged children reported dose–response reductions in working memory and inhibitory control performance with increasing maternal pregnancy-specific stress (Buss et al., 2011), while another found that sustained attention was reduced in boys, but not girls, whose mothers reported high levels of anxiety during pregnancy (Van den Bergh et al., 2006). Deficits in these core control processes have repeatedly been implicated in pathways to externalizing behavior, including ADHD, oppositional defiance and aggression (Hughes et al., 2000; Séguin et al., 2004; Hughes and Ensor, 2008; Raaijmakers et al., 2008; Espy et al., 2011b). As youngsters approach kindergarten age and most children have gained some proficiency in executive control, delays or deficits in these key skills will likely become increasingly evident to caregivers in the form of behavior problems.

Less is known regarding the early features of behavioral disinhibition, although both theory and empirical work suggests that temperament may play an important role. Biological variations in infant temperament, evident as early as age 4 weeks, are thought to shape responses from others in the environment, exerting long-term influence on behavior and personality (Clark, 2005; Thomas and Chess, 1977). Difficult temperament in infancy, characterized by irregular feeding and sleeping patterns, high levels of withdrawal from environmental stimuli, difficulties adjusting to new experiences or routines, and intense expression of negative emotion, places children at increased risk of externalizing behavior problems later in childhood, particularly when paired with environmental stress (Sanson et al., 1993; Wright Guerin et al., 1997; Fanti and Henrich, 2010). PTE and PSE each have been linked to higher negative reactivity, higher activity levels and less adaptable temperament in infants (Martin et al., 2006; Wakschlag et al., 2006a; Willoughby et al., 2007; Carter et al., 2008; Pickett et al., 2008). Moreover, Lester et al. (2009) found evidence for a mediated pathway from prenatal substance exposure via early difficult temperament to behavioral disinhibition problems at age 7 years. It is possible, therefore, that there is an underlying heterotypic continuity to behavioral disinhibition that is evident even in the earliest phases of development among children with PTE and PSE.

Despite suggestions of parallel outcomes from PTE and PSE to behavioral disinhibition, most studies have treated the variance associated with one of these factors as 'nuisance' variance to be minimized through matching or statistical control. While this approach may help to isolate specific effects, it has limited applied value and does not elucidate potentially synergistic effects of these exposures. Further, studies often lack prospective, high quality measurement of one if not both of these exposures. As an exception, Rodriguez and Bohlin (2005) found that self-reported smoking and maternal stress during pregnancy each accounted for significant variance in child ADHD symptoms at age 7 years. Their findings suggest that a combination of high prenatal stress and PTE may place children at 'double jeopardy' for later externalizing problems. Given that PTE and PSE often occur concurrently, there is a need for high-quality, prospective studies that jointly model the additive or interactive contributions of these prenatal exposures for children's development over time.

Another important concern is the role of ongoing stress in the lives of children with adverse prenatal experiences. Research and theory suggest that the postnatal environment may amplify or exacerbate prenatal exposure effects. For instance, Fisher et al. (2011) found that prenatal substance exposure predicted neurobehavioral disinhibition in adolescence, but that early cumulative adversity also showed unique, additive effects. Similarly, Bekkhus et al. (2011) reported considerable stability ($B = .86$) in latent measures of pre- and postnatal maternal distress. There are conflicting findings as to whether prenatal, postnatal or cumulative effects are most important. Clearly, then, consideration of the postnatal environment will be important in pinpointing the role of exposure timing. Studies have also varied in their definition and approach to the measurement of stress during pregnancy (Nast et al., 2013). In this study, we drew upon decades of research in the developmental literature indicating that the effects of psychosocial stress are cumulative, where an increasing number of stressors increases the likelihood of poor functional outcome in a dose–response manner and the accumulation of these risk factors is a stronger predictor of cognitive and behavioral outcome than any single factor (Rutter, 1979; Sameroff et al., 1987; Doan et al., 2012; Evans et al., 2013).

The specific aims of this study were to:

1) Describe the unique or interactive relations of PTE and PSE to infant temperament, executive control, and disruptive and inattentive dimensions of externalizing behavior in the late preschool period.
2) Test a sequenced developmental model, which links PTE and PSE indirectly to dimensions of externalizing behavior late in the preschool period via difficult infant temperament and poorer executive control.
3) Examine the roles of postnatal stress and postnatal tobacco exposure in these pathways.

Based on a behavioral disinhibition framework, we posited that PTE and cumulative PSE each would be linked to difficult temperament in infancy and that these temperamental difficulties would show developmental continuity, manifesting as deficits in executive control and higher levels of externalizing behavior in the late preschool period.

2. Method

2.1. Participants

Participants were recruited through fliers distributed at local obstetrics clinics in two sites: a 5-county rural area in Southern Illinois and a small city in Nebraska. Interested women were carefully screened via telephone interviews to assess study eligibility. Those who reported illegal substance use or alcohol use >4 drinks on a single occasion were deemed ineligible. Mothers who reported smoking during pregnancy