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Prenatal cigarette exposure and infant learning stimulation as predictors of cognitive control in childhood

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Abstract

Prenatal exposures to neurotoxins and postnatal parenting practices have been shown to independently predict variations in the cognitive development and emotional-behavioral well being of infants and children. We examined the independent contributions of prenatal cigarette exposure and infant learning stimulation, as well as their inter-relationships in predicting variations in the proficiency of executive attention, a core element of cognitive control and self-regulation.

Participants were an ethnic-racially, socio-economically diverse sample of 249 children followed from birth in the Project on Human Development in Chicago Neighborhoods. We obtained histories of prenatal exposure to alcohol, cigarettes, and other drugs, and we assessed socio-economic status and learning stimulation during a home visit when the participants were infants. In childhood we utilized the Attention Networks Test to assess the proficiency of executive attention during two home visits, one year apart.

Accounting for age, SES, prenatal alcohol exposure, and baseline performance, we found that prenatal cigarette exposure impaired the speed of executive attention. Infant learning stimulation mitigated these effects, and predicted better accuracy of executive attention as well, suggestive of both protective and health promoting effects. Effect sizes for these relations, whether examined independently or by their inter-relationships, were comparable if not greater in magnitude to the effects of age on speed and accuracy, highlighting the importance of these very early experiences in shaping the proficiency of self-regulation.

Since executive attention is central to cognitive control and self-regulation, previously described relations between prenatal cigarette exposure, parenting practices, and some forms of childhood psychopathology, may be contingent on how early learning stimulation contributes to the proficiency of executive attention through direct and indirect effects. Furthermore, considering the prolonged developmental trajectory of executive attention, interventions to support provision of learning stimulation may mitigate poor outcomes for some at-risk children by promoting development of more proficient executive attention.

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Keywords

Prenatal cigarette exposure; infant learning stimulation; childhood executive function

The developing child is an integral part of open, dynamic systems, and is highly receptive to experiential influences that encompass the impact of the physical and social environments. Paramount in this process is the child's earliest experiences in the form of caregiver – offspring transactions, pre- and postnatal, that contribute to the development of self-regulation. The National Research Council report (2000) on early child development contends that, " … development may be viewed as an increasing capacity for self-regulation, seen particularly in the child's ability to function more independently in a personal and social context." (p. 94)

The proficiency of higher cortical functions critical to effective self-regulation matures well into the second decade of life, while the preponderance of physical brain growth and maximal brain plasticity occur during the prenatal period and the first two years of postnatal life (Huttenlocher & Dabholkar, 1997; Knickmeyer, et al., 2008; Matsuzawa, et al., 2001; Webb, Monk, & Nelson, 2001). Cognitive control involves the capacity to resolve competing demands by inhibiting prepotent responses and activating less dominant, more effortful ones instead. A common example of cognitive control can be seen whenever a child inhibits the impulse to blurt out in class to gain a teacher's attention, and raises his or her hand and waits to be recognized. This capacity to inhibit prepotent responses and substitute more effortful ones first emerges around 30 months of age (Baken-Jones, Rothbart, & Posner, 2003; Diamond & Taylor, 1996; Rennie, Bull, & Diamond, 2004) coincident with neurobiological evidence for peak production of gray matter in frontal lobe regions believed to subserve cognitive control (Huttenlocher & Dabholkar, 1997; Knickmeyer, et al., 2008; Matsuzawa, et al., 2001; Webb, et al., 2001). The proficiency of cognitive control improves over the next two decades of life as older children, adolescents and young adults manifest increasing capacity to deal with the ever more complex competing demands encountered in every day life (Bunge, Dudukovic, Thomason, Vaidya, & Gabrielli, 2002; Durston, Thomas, Yang, Ulu, Zimmerman, & Casey, 2002; Poggi-Davis, Bruce, Snyder, & Nelson, 2003; Segalowitz& Davies, 2004; Tamm, Menon, & Reiss, 2002).

In this study, we utilized a model of cognitive control elaborated by Posner and colleagues referred to as executive attention. Key structures in the mature neural network underlying executive attention, a dopaminergic network, form an integral part of the cingulo-opercular network, and include the ventral tegmental area, the basal ganglia (caudate nucleus and globus pallidus), the anterior cingulate cortex, and the dorsolateral and ventrolateral prefrontal cortex (Botvinik, Braver, Barch, Carter, & Cohen, 2001; Fan, McCandliss, Sommer, Raz, & Posner, 2002; Posner & Rothbart, 2009). Functional neuroimaging studies comparing the performance of children and adults on skills requiring the executive attention network show maturational changes in the architecture of this network that proceed in a caudal to rostral direction. Furthermore, when children activate executive attention network structures, they do so more intensely and diffusely than adults, findings that are taken to mean more immature, less efficient functioning in children as well (Bunge, et al., 2002; Durston, et al., 2002; Tamm, et al., 2002).

Prenatal cigarette exposure occupies a prominent position in behavioral teratology due to its widespread occurrence and the manifold deleterious effects that have been associated with it, including lower birth weight, smaller head circumference, lower IQ, attentional dysfunction, hyperactivity and other conduct problems, as well as school failure (Brent & Weitzman, 2004; DiFranza, Aligne, & Weitzman, 2004; Fried, 2002; Fried, Watkinson, &

Gray, 2003; Herrmann, King, & Weitzman, 2008; Wakschlag, Leventhal, Pine, Pickett, & Carter, 2006; Weitzman, Byrd, Aligne, & Moss, 2002; Williams, et al., 1998).

Most notable among the many toxins contained in cigarette smoke are carbon monoxide and nicotine. Carbon monoxide leads to formation of carboxyhemoglobin resulting in diminished oxygen carrying capacity of maternal and fetal blood, thereby contributing to relative fetal hypoxia. Nicotine causes vasoconstriction, resulting in diminished placental blood flow. The combined effects of hypoxia and placental vasoconstriction during gestation are presumed responsible for the observed reductions in birth weight and head circumference in human infants (Herrmann, et al., 2008; Slotkin, 2004).

Animal studies have demonstrated that nicotine is a potent cholinomimetic agent that can influence early brain development in at least two ways: through its trophic signaling effects on the cellular processes of replication, migration and differentiation, axono- and synaptogenesis, and apoptosis; and through its communicative signaling effects on the regulation of acetylcholine receptors. Both these effects occur at low levels of exposure even in the absence of somatic growth retardation. Prenatally then, the effects of nicotine are largely disruptive to the developing brain; with evidence for reductions in cell numbers and synapses, and altered reactivity of cholinergic receptors. Because of the diffuse representation of cholinergic neurons in the brain, these effects ultimately also impinge on the development of other systems, including those involved in noradrenergic and dopaminergic neurotransmission (Herrmann, et al., 2008; Slotkin, 2004; Slotkin, Pinkerton, & Seidler, 2006; Slotkin, MacKillop, Rudder, Ryde, Tate, & Seidler, 2007).

Human studies have in fact demonstrated a range of cognitive deficits related to prenatal cigarette exposure that cut across neurotransmitter systems. These include problems with auditory and visual attention, as well as working memory (Fried, et al., 2003; Jacobsen, Slotkin, Westerveld, Mencl, & Pugh, 2006; Jacobsen, Slotkin, Mencl, Frost, & Pugh, 2007). Correlated with these behavioral observations is evidence for disruption of anterior subcortical white matter in brain regions known to be involved with attention and working memory (Jacobsen, Picciotto, Heath, et al. 2007; Klingberg, 2006). Little is known however of the impact of prenatal cigarette exposure on executive attention; although it is reasonable to assume deleterious effects here as well, given the higher risk in exposed children for hyperactivity and conduct problems (Wakschlag, et al., 2006; Weitzman, et al., 2002; Williams, et al., 1998).

Prenatal cigarette exposure is frequently accompanied by factors during and after pregnancy, including poverty and problematic parenting practices, that may themselves contribute to many of the same adverse outcomes attributable to cigarette exposure (Atzaba-Poria, Pike, & Deater-Deckard, 2004; Pachter, Auinger, Palmer, & Weitzman, 2006). Nonetheless, the contributions of prenatal cigarette exposure to such adverse outcomes are affirmed by studies that controlled for relevant risks, and by others that demonstrated dose-response relations, where greater exposure predicted worse outcomes (Hermann, et al., 2008; Wakschlag, et al., 2006; Weitzman, et al., 2002; Williams, et al., 1998; Slotkin, 2004). What has not been demonstrated is whether relevant co-occurring risks and protective factors, such as those related to parenting practices, may magnify or mitigate the deleterious effects of prenatal cigarette exposure on cognitive control. This was a central goal of our study.

Where postnatal experiences are concerned, nowhere is the importance of early parenting to healthy development more apparent than in the accounts of children raised in orphanages under conditions of extreme psychosocial deprivation. Many of these children show global cognitive impairments and social-emotional development reminiscent of autism and mental retardation. Some subsequently experience placement in foster care or adoptive homes.

Depending on when this transition occurs, and the quality of the foster/adoptive care, children may show varying degrees of recovery in the cognitive and social-emotional realms (Beckett, et al., 2006; Nelson, Zeanah, Fox, Marshall, Smyke & Guthrie, 2007). Collectively studies such as these speak not only to the centrality of early parenting for the developing child, but to the plasticity of very young children as they respond to variations in their caregiving environments as well.

There is additional evidence that the development of cognitive control and related processes is shaped in part by experience (Belsky, Pasco-Fearon, & Bell, 2007; Eisenberg, Zhou, Spinrad, Valiente, Fabes, & Liew, 2005; Groot, de Sonneville, Stins, & Boomsma, 2004; Grossman, Churchill, McKinney, Kodish, Otte, & Greenough, 2003); although the need for further study in this area is considerable (Dawson, Ashman, & Carver, 2000; Posner & Rothbart, 2000). The relevance of broad contextual influences captured by socio-economic status (SES) for example, is noted in several studies where executive function was investigated (Farah, et al., 2006; Mezzacappa, 2004; Nobles, McCandliss, & Farah, 2007). These studies are consistent in reporting that children from more disadvantaged backgrounds demonstrate less proficient executive function.

Studies conducted by the Early Childcare Research Network of the National Institute of Child Health and Human Development (NICHD, 2005) demonstrated that maternal responsiveness and learning stimulation predicted the competence of children's sustained attention and inhibitory control, as well as their school readiness, defined by academic and social competence. These investigators also observed that children's capacity for sustained attention and inhibitory control mediated the relations between parenting quality and school readiness (NICHD, 2003). Farah and colleagues recently (Farah, et al., 2008) described differential relations between maternal nurturance and memory development on the one hand, and learning stimulation and language development on the other, suggesting some specificity in the links between the nature of early experiences and the development of particular cognitive functions. Finally, early coercive and rejecting parenting practices have been linked to later problems with conduct, emotion regulation, and hyperactivity (Hill, 2002; Morrell & Murray, 2003). This area in particular is one where cognitive control would be expected to play an important role in observed symptomatology (Posner & Rothbart, 2000).

Given all these considerations, we examined the independent contributions of prenatal cigarette exposure and infant learning stimulation, as well as their interrelationships in predicting variations in the proficiency of executive attention, a core element of cognitive control necessary for regulation of goal-directed behavior. We expected that prenatal exposure to the neurotoxins in cigarette smoke, and lower levels of learning stimulation during infancy, would independently predict poorer executive attention; and that higher levels of learning stimulation would be associated with greater proficiency of executive attention, as well as mitigating influences on the effects of cigarette exposure.

Method

The institutional review boards of Children's Hospital Boston and Harvard Medical School approved this study. Informed consent was obtained from parents or guardians, and assent was obtained from children.

Sample

Participants were 249 children (47% female; 54% Hispanic, 24% African-American, 22% Caucasian) from a wide range of SES backgrounds who were followed from infancy in the Project on Human Development in Chicago Neighborhoods (PHDCN) (Earls & Buka,

1997). PHDCN participants were sampled from 88 neighborhood clusters that were proportionally representative of the 343 neighborhood clusters encompassing the full ethnic-racial and socio-economic variations found in the City of Chicago at the time of the study. The ethnic-racial composition of our subsample was very similar to that for the PHDCN as a whole (48% Hispanic, 31% African American, 21% Caucasian). Our participants were randomly drawn from a larger cohort of 386 children who received in-depth assessments during a home visit when they were around 6 months of age. Resource limitations precluded attempts to assess all 386 children.

Prenatal Exposure to Neurotoxins

Histories of prenatal exposure to cigarettes, alcohol, cannabis, cocaine, and heroine were obtained from maternal reports during the infant home visit. For those mothers who endorsed using substances during pregnancy, distinctions were made if they stopped when they discovered they were pregnant, or if they continued use throughout pregnancy.

Forty-five mothers endorsed smoking during pregnancy. Twenty-two of these mothers reported smoking throughout pregnancy. Mothers who smoked throughout pregnancy consumed on average one pack of cigarettes per day (Mean 20.4; Median 18). Those who reported smoking for only part of their pregnancy also reported consuming far fewer cigarettes per day while they smoked (Mean 6.1; Median 7).

Seventy-three mothers endorsed consuming some amount of alcohol before discovering they were pregnant. Nine endorsed consuming some alcohol throughout pregnancy. Eleven mothers endorsed both drinking and smoking until they discovered they were pregnant; and only one endorsed drinking and smoking throughout pregnancy. Endorsement of prenatal use of marijuana, cocaine, and heroine was extremely low. Given the low endorsement of persistent alcohol consumption and our intent to examine inter-relationships between pre- and postnatal experiences, any degree of prenatal alcohol exposure was treated as a confounding covariate rather than a main effect.

Infant Learning Stimulation

The Home Observational Method of the Environment (HOME) (Caldwell & Bradley, 1984; Bradley, Corwyn, McAdoo, & Garcia-Coll, 2001; Bradley, Corwyn, Burchinal, & Garcia-Coll, 2001) formed the basis for assessing children's early parenting experiences during the infant home visit. We utilized the scale `Learning Stimulation' from the Infant-Toddler HOME (Fuligni, Han, & Brooks-Gunn, 2004; Linver, Martin, & Brooks-Gunn, 2004) which captures observed mother-child interactions, the presence of materials in the home intended to provide age-appropriate stimulation to infants, as well as maternal reports of their own behaviors intended to provide learning stimulation.

Of all the HOME scales, `Learning Stimulation' is the most closely associated with cognitive development (Bradley, et al., 2001). Psychometrically this scale functions similarly across socio-economic and ethnic-racial groups, as ascertained by Leventhal and colleagues in the PHDCN (Leventhal, Selner-O'Hagan, Brooks-Gunn, Bingenheimer, & Earls, 2004), an important consideration given the diversity of our sample. Like other scales of the HOME, `Learning Stimulation' is best construed as an indicator of higher or lower levels of developmental support, rather than a continuous measure of early childhood experiences (Bradley, et al., 2001; Leventhal, et al., 2004).

Socio-Economic Status

Socio-economic status (SES) was assessed concomitantly with early parenting during the infant home visit. SES was represented by a standardized composite of the highest

educational level, income, and occupational status ever achieved by the child's primary caregiver (PC) (mean 0.065, median −0.17, SD 1.48, minimum −2.30, maximum 3.49). For 99% of children the PC was biological mother.

Executive Attention

The Attention Networks Test (ANT) adapted for children was chosen for the assessments of executive attention (Rueda, et al., 2004; Mezzacappa, 2004). The childhood ANT consists only of pictures, and places no demands on language or reading competence. At time 1, children had to feed a hungry fish according to the direction the fish swam in. At time 2, children were asked to help a mouse outrun a cat according to the direction of the race. Left- and right-oriented targets were equally represented. A correct response was registered whenever children pressed the touch pad key corresponding to the direction of the target stimulus, and was followed by animation and positive sounds, while errors were followed by the sound of a buzzer and no animation.

On some trials `flanker' stimuli identical in appearance to the target stimulus appeared in equal numbers on either side of the target. Children were instructed to focus on and respond only to the orientation of the central target. Flankers, when they appeared, were oriented either in the same direction (congruent), or in the opposite direction (incongruent) of the target. In the incongruent condition, children had to inhibit the tendency to respond to the direction of flankers and choose the direction of the target instead.

There were equal numbers of trials with congruent, incongruent and no flankers. These three unique task conditions were presented in a pseudo-random order in order to prevent habituation or strategic responding to the recurrence of particular target-flanker stimulus combinations. The pseudo-random order was predetermined and fixed, and did not vary across children or over time, thereby eliminating the possibility that order effects contributed to differences in task performance.

Executive attention reaction time (RT) was derived by comparing median RT for correct responses on trials with congruent and incongruent flankers. Executive attention accuracy (ACC) or commission errors, was derived by comparing mean incorrect active responses across these same trials.

Procedure

Administration of the ANT occurred twice. Mean age at the time of the first assessment was 5.9 years (range 4.9 to 7.2 years). Mean time between assessments was 1.01 years (median 0.97, SD 0.14, minimum 0.85, maximum 1.43). Retention at Time 2 was 96% (n = 239). Of the 239 children assessed at both time points, 5 children were missing data either for prenatal exposure to neurotoxins or for observations of infant learning stimulation, leaving a final sample of 234 children.

The ANT was administered during home visits. The examiner requested a quiet place where she and the child could be alone. Children were first familiarized with the ANT in their primary language, English or Spanish, using a picture book that portrayed all the task conditions to be encountered. Only after children demonstrated a clear understanding of the task demands using the picture book did they move to the computer task, which consisted of 168 trials divided into four blocks. The first 24 trials formed a practice block, and could be repeated if necessary. The remaining three blocks consisted of 48 trials each. Children received a holographic sticker for each block they completed. All children completed the task at both assessments.

Statistical Analyses

We estimated the simultaneous, independent contributions of prenatal cigarette exposure and infant learning stimulation, as well as their inter-relationships in predicting the speed and accuracy of executive attention using mixed-effects models, with child age, SES, prenatal exposure to alcohol and cigarettes, and infant learning stimulation as the fixed between subjects effects, and time of assessment as the repeated within subject effect, controlling for task performance in the congruent flanker condition in order to account for individual differences in baseline performance and motor speed. Because we controlled for baseline performance, results for the predictors of interest were identical whether difference scores (congruent vs. incongruent) or raw indices in the incongruent flanker condition served as the outcomes. Raw indices, rather than difference scores, are presented here for clarity and ease of interpretation. In all instances, we reported Type 3 tests for fixed effects; i.e. those resulting after all other effects in the model are accounted for, based on the number of participants, not the number of data points.

Results

Preliminary Analyses

There were no differences between children from the original sample of 386 who were not tested and the 234 children in our sample who were assessed for executive attention in childhood in rates of prenatal cigarette exposure, or infant learning stimulation scores, whether we controlled for SES or not.

Children who were tested in childhood came, on average, from higher SES homes (tested mean = 0.065; not tested mean = −0.50; $F = 17.7$, $p < 0.0001$) than those who were not tested. SES was also correlated with task performance [RT: $F(1, 229) = 9.3$, $p = 0.003$; ACC: $F(1, 229) = 12.7$, $p = 0.0004$]. However, these SES effects on performance did not differ according to the levels of prenatal exposure to alcohol or to cigarettes, nor to the levels of infant learning stimulation, for either RT or ACC. Finally, among the children we tested, those who were exposed prenatally to cigarettes did not differ from those who were not exposed where gestational age, APGAR scores at birth, birth weight, or head circumference was concerned, whether we controlled for SES or not.

The effects of the incongruent flankers on children's performance were readily apparent. Compared to the reference condition with congruent flankers, children were slower and less accurate when confronted with the competing demands created by incongruent flankers. Unadjusted performance for the entire sample combined over both assessments revealed a 13.2% increase in RT from 925 ms to 1047 ms ($t = −22.7$, $p < 0.0001$, $d = 0.81$), and a 2.7-fold increase in commission errors from 5.8% to 15.6% ($t = −13.5$, $p < 0.0001$, $d = 0.63$). As expected, RT and ACC were uncorrelated ($r = 0.071$, $p = 0.13$), consistent with the selection of RT for correct responses and commission errors as our primary outcomes.

Older children performed more proficiently than younger children. The age effect for RT was 42.2 ms/year [beta = 0.28; $F(1, 223) = 19.2$; $p < 0.0001$], and for ACC 6.4%/year [beta = 0.41; $F(1, 223) = 20.4$; $p < 0.0001$]. For any given age, children who completed the task for a second time performed no differently than children who were of similar age when they completed the task for the first time; indicating that practice effects after one year were not appreciable.

Analyses of Main Effects

The independent contributions of prenatal cigarette exposure and infant learning stimulation to the proficiency of executive attention are summarized in Tables 1 and 2. For these

analyses each main effect was trichotomized, the former according to level of prenatal exposure: none, partial, and throughout pregnancy, the latter into high (children above the median score), intermediate (children with the median score), and low (children below the median score) levels of learning stimulation. Both main effects were then entered simultaneously into the statistical models together with age, SES, prenatal alcohol exposure, and baseline performance.

Children exposed to cigarettes throughout pregnancy responded more slowly to the competing demands created by incongruent flankers than those who were not exposed (d = 0.26) or those who experienced only partial exposure (d = 0.28). Children who experienced only partial prenatal exposure did not differ from those who were not exposed at all. Prenatal cigarette exposure did not appear to influence executive attention accuracy.

Children who experienced higher levels of learning stimulation as infants responded more rapidly and more accurately to the competing demands created by incongruent flankers than those who experienced intermediate or lower levels of learning stimulation in infancy (RT: High vs. Intermediate d = 0.25; RT High vs. Low d = 0.20; ACC: High vs. Intermediate d = 0.34; ACC High vs. Low d = 0.38). Children who experienced intermediate or lower levels of learning stimulation as infants did not differ from each other, either in the speed or the accuracy of executive attention.

Analyses of Inter-relationships

The manner in which prenatal cigarette exposure and infant learning stimulation worked together to influence the proficiency of executive attention is summarized in Table 3. For these analyses cigarette exposure was dichotomized into exposed or not exposed, and learning stimulation was dichotomized into high (above the median score), and all others, to preserve sufficient statistical power in each comparison group. The sample distribution according to prenatal cigarette exposure and infant learning simulation constructed in this way did not differ from expected [chi-square (1) = 0.30; p = 0.58], and the infant stimulation score did not differ by level of prenatal cigarette exposure [F(2, 231) = 0.60, p = 0.55].

The interpretation of any observed inter-relationships between prenatal cigarette exposure and infant learning stimulation would therefore have to take into account their statistical independence, the potential bi-directional nature of the inter-relationships, as well as the temporal sequencing of these two early experiences (Kraemer, Stice, Kazdin, Offord, & Kupfer, 2001). Restated according to our expectations, and recognizing that any observed inter-relationships would represent effect modification (rather than mediation), prenatal cigarette exposure would interfere with an infant's ability to benefit from learning stimulation, and learning stimulation would mitigate the deleterious effects of prenatal cigarette exposure on the proficiency of executive attention.

We found that the effects of prenatal cigarette exposure on the speed of executive attention were contingent on the amount of learning stimulation children subsequently experienced as infants. In the most extreme contrast, children exposed to cigarettes prenatally who then experienced lower levels of learning stimulation as infants performed the poorest of all, while those who were not exposed and then experienced higher levels of stimulation performed the best (d = 0.34).

Higher levels of learning stimulation during infancy were protective for children exposed to cigarettes during pregnancy. Although these children demonstrated somewhat longer reaction times to incongruent flankers, they did not differ statistically from their counterparts who also experienced higher levels of learning stimulation as infants but were not exposed to cigarettes prenatally. Children were more vulnerable to the effects of prenatal cigarette

exposure if they subsequently experienced lower levels of learning stimulation, seen in the statistical trend indicating longer reaction times in the exposed group who experienced lower levels of infant learning stimulation, compared to the non-exposed group with similar experience in infancy (d = 0.14). Finally, children who experienced higher levels of learning stimulation as infants performed better than those who received lower levels, whether they were exposed (d = 0.25) or not exposed (d = 0.20) prenatally to cigarettes.

The accuracy of executive attention was contingent only on the degree of learning stimulation children received as infants. Those who received higher levels of learning stimulation performed better than those who received lower levels, regardless of whether prenatal cigarette exposure occurred or not.

Similar to our observations for RT, for executive attention accuracy children exposed to cigarettes prenatally who then experienced lower levels of learning stimulation as infants performed the poorest of all, while those who were not exposed and then experienced higher levels of stimulation performed the best (d = 0.46). Furthermore, children exposed to cigarettes prenatally who experienced higher levels of learning stimulation as infants performed comparably to unexposed children who experienced similar levels of learning stimulation, as well as more accurately than those exposed prenatally to cigarettes who then experienced lower levels of learning stimulation as infants (d = 0.43).

A similar pattern was observed for children not exposed to cigarettes in utero, who then experienced higher or lower levels of stimulation as infants, respectively. Once again, those experiencing more stimulation as infants performed more accurately (d = 0.35). Finally, the mitigating effects of infant learning stimulation on prenatal cigarette exposure were also apparent in the contrast between children exposed to cigarettes prenatally who then experienced higher levels of learning stimulation as infants, and those not exposed to cigarettes who then experienced lower levels of learning stimulation. The former performed more proficiently than the latter (d = 0.32).

Taken together, the inter-relations of prenatal cigarette exposure and infant learning stimulation in predicting the proficiency of executive attention were entirely consistent with their independent effects; and highlighted the mitigating effects of learning stimulation on cigarette exposure.

Secondary analyses involving the inter-relations of prenatal cigarette exposure and infant learning stimulation in predicting the proficiency of executive attention were conducted comparing children who were not exposed to cigarettes prenatally and those who were exposed throughout pregnancy. These results are summarized in Table 4, and should be interpreted with caution given the smaller numbers of exposed children involved in the contrasts.

Conducted in this manner the contrasts for RT revealed larger effect sizes (*d*), ranging from 0.4 to 0.6, where differences involving children exposed to cigarettes throughout pregnancy were concerned. This approach also clarified the statistical trend for the differences in RT noted in Table 3 between children who were exposed to cigarettes and the non-exposed group, when both groups subsequently experienced lower levels of infant learning stimulation. The former were now significantly slower in response to incongruent flankers (d = 0.41), and clearly more vulnerable to the effects of this exposure. The contrasts for ACC also revealed larger effect sizes, now in the 0.5 to 0.6 range where differences involving children exposed to cigarettes throughout pregnancy were concerned; but without any further changes in the pattern of the findings.

Summary of Findings

Accounting for age, SES, prenatal alcohol exposure, and baseline performance, we found that prenatal cigarette exposure impaired the speed of executive attention. Infant learning stimulation mitigated these effects and predicted better accuracy of executive attention as well, suggestive of both protective and health promoting effects. Furthermore, effect sizes for these relations, whether examined independently or according to their inter-relations, were comparable if not greater in magnitude to the observed effects of age on the speed and accuracy of executive attention, highlighting the importance of these very early experiences in shaping the proficiency of self-regulation.

Discussion

We examined the contributions of prenatal cigarette exposure, infant learning stimulation, and their inter-relations, to variations in the proficiency of executive attention in a diverse, population-based sample of young children using a prospective design. Our findings indicated that prenatal cigarette exposure was deleterious to the speed of executive attention, and that infant learning stimulation exerted protective, modifying influences on the effects of cigarette exposure, in addition to its own health promoting effects on the speed and accuracy of executive attention. It also bears mentioning that the effects we observed for prenatal smoking on the speed of executive attention occurred in the absence of any measurable differences in gestational age, birth weight, or head circumference that may be associated with this type of exposure; and as such, are entirely consistent with the animal literature previously cited. By linking prenatal cigarette exposure and infant learning simulation to the proficiency of executive attention, a core element of cognitive control, this study contributes to an emerging body of literature regarding how the development of components critical to self-regulation unfolds according to variations in early experience.

Our sample was population-based and reasonably representative of the composition of the City of Chicago at the time our study was conducted. Therefore our findings may be expected to generalize to other children of similar socio-demographic backgrounds living in other large, densely populated urban centers in the United States. The prospective, longitudinal nature of the overall study design meant that variations in prenatal and early parenting experiences were assessed at or very near the time of their occurrence, by self-report as well as through direct observations. Our key predictors would therefore be less subject to the limitations of recall inherent in data that rely only on self-reports obtained years after salient events have occurred.

Our measure of socio-economic status was a composite comprising the highest educational level, income, and occupational status ever achieved by the child's primary caregiver; thereby covering a number of key domains known to be associated with early cognitive development. Our assessment of infant learning stimulation was relevant to early cognitive development and psychometrically appropriate for use in a diverse, population-based sample. Our outcome, variations in the proficiency of executive attention, is reliably elicited throughout the lifespan; making it a useful performance index for developmental studies of self-regulation.

Other aspects of our findings warrant further consideration. The absence of any observed relations between prenatal cigarette exposure and executive attention accuracy was unexpected. While children exposed to cigarettes throughout pregnancy responded more slowly to incongruent flankers than all others, they nonetheless achieved similar levels of accuracy to those exposed only partially or not at all (see Table 1). This pattern of slower RT and comparable accuracy suggests the possibility of a speed-accuracy trade off in children who were exposed to cigarettes throughout pregnancy. Future studies may include

more formal examination of speed accuracy relations to test for this possibility. Furthermore, a task where speed was inherently emphasized, or a more complex task, might reveal differences in accuracy outright.

If accuracy is indeed achieved at the expense of speed in children who experience persistent prenatal exposure to cigarettes, then under `real-life' conditions of higher demands on speed, as might occur for example during timed tests in school, one might expect to see compromises in performance in the form of more inaccurate responding among these children when compared to those who have not experienced such extensive prenatal cigarette exposure.

It also remains to be determined how much of the relations we found between prenatal cigarette exposure and the speed of executive attention represent direct effects, and how much is the result of influences on selective visual attention (staying focused on the central target), or working memory (keeping active the instructions to respond only to the central target when flankers were present), such that executive attention may have operated with `faulty input' for regulating task behavior.

The animal literature reports disruptions in neuronogenesis, synaptogenesis, and myelination in relation to prenatal exposure to nicotine alone. Cigarette smoke on the other hand contains many putative neurotoxins besides nicotine. We cannot directly address questions concerning neurotoxicity per se with our data, but we may speculate in the following manner about the neurodevelopmental implications of our findings.

The influences we studied in relation to executive attention occurred prenatally and during infancy, while the age range of our participants when we studied them was 4 to 8 years old. Hence the timing of these early experiences and the age of the children when they were tested came respectively during or on the heels of a major spurt in gray matter development that begins in utero and peaks by around 3 years of age; but before the intense myelination of cingulo-opercular and fronto-parietal regions critical to executive function that begins later in childhood, and proceeds through adolescence and into young adulthood. This suggests that the differences we noted between children who were and those who were not exposed prenatally to cigarettes, at least at this stage in their development, were more likely to result from differences in the maturation of gray matter, which was then subject to modification by subsequent parenting influences.

Our findings resonate with those of other investigators in highlighting observations that prenatal exposure to neurotoxins and other early biological insults do not operate alone in shaping child outcomes. Caregiver characteristics and early interventions have been shown to modify the deleterious effects on infant development of prenatal exposure to cocaine (Frank, et al., 2002), and lead (Surkan, et al., 2008), as well as the effects of prematurity (Als, et al., 2004; Landry, Smith, & Swank, 2003). Our findings extend the reach of inter-relationships between pre- and postnatal experiences on specific aspects of cognitive development into childhood.

The involvement of executive attention by prenatal cigarette exposure is consistent with observations of heightened risk for conduct problems and hyperactivity in children exposed to cigarettes in utero. Similarly, the involvement of executive attention by early parenting is consistent with reports linking parenting with the self-regulatory capacities needed for school readiness, and with conduct problems and hyperactivity in children. Since executive attention is fundamental to the regulation of goal-directed behavior, and the cingulo-opercular network has been implicated in the pathogenesis of disruptive behavior disorders (Blair, 2004; Posner & Rothbart, 2009), from the perspective of developmental psychopathology important questions remain concerning the possibility that executive

attention mediates relations between early experiences such as prenatal cigarette exposure and infant learning stimulation, and later adaptive functioning or psychopathology such as ADHD and Conduct Disorder (Posner & Rothbart, 2000; Dawson, et al., 2000).

Some additional limitations of our study design bear mentioning. We could not examine gender differences in the contributions of prenatal cigarette exposure and infant learning stimulation to the proficiency of executive attention due to the small cell sizes that would result in order to examine these inter-relations. This is important since males are generally considered to be more susceptible to poor outcomes when exposed to risk factors than females. Furthermore, the age difference between the youngest child at Time 1 (4.9 years) and the oldest child at Time 2 (8.2 years) was 3.3 years. This meant our window for assessing executive attention was narrow, especially when considering its prolonged developmental trajectory. In addition, with only two data points, we were not able to examine growth trajectories of executive attention in relation to our key predictors. Further speculation from the perspective of growth trajectories also leads us to the possibility that what we reported may very well represent relations between parenting practices throughout pregnancy, infancy and childhood, and proficiency of executive attention. For instance, parents who stimulate more in infancy may also stimulate and instruct more in childhood, and do so in ways that are relevant to the daily challenges for which executive attention is required. Similarly, mothers who smoked throughout pregnancy, as well as those who smoked but stopped during pregnancy, might have continued or resumed smoking once their children were born; adding the burden of second-hand smoke to prenatal exposure (Slotkin, 2004).

A longer period of observation of both our predictors and outcomes would have allowed us to construct individual growth trajectories and to study the contributions of a range of experiences and influences occurring at different points during development, as well as the impact of the duration of those experiences. This approach is particularly relevant when studying trajectories for skills like executive attention and other aspects of self-regulation that develop over prolonged periods lasting decades.

The possibility that there are dose-response relations between prenatal cigarette exposure and the speed of executive attention is suggested by the differences between children who experienced partial exposure and those who were exposed throughout pregnancy. In order to fully explore this possibility it would have been helpful to quantify cigarette exposure more precisely by monitoring maternal cotinine levels throughout pregnancy. This would have also circumvented the possibility that prenatal cigarette exposure was underestimated due to underreporting. Similarly, our observations of the home environment and of parenting practices could have been affected by mothers' efforts to put their best foot forward during home visits. This would attenuate variations we observed in early parenting practices.

Research involving the executive attention network and genes relevant to dopaminergic neurotransmission indicates that heritability plays an important role in the observed competence of this network as well (Fan, Fossella, Sommer, Wu, & Posner, 2003; Rueda, Rothbart, McCandliss, Saccomanno, & Posner, 2005). Assessment of parental executive attention, along with screening for candidate genes could shed light on the interplay of genetic and environmental contributions to children's proficiency in executive attention.

Despite the limitations of our study design, the implications of our findings support the notion that variations in early life experiences can influence the proficiency of developing neural networks that are critical to self-regulation. The effects on those networks, and by implication self-regulation, will depend on the nature of the experiences, the timing and duration of their occurrence, and how these experiences interact to shape observable

outcomes. Considering the prolonged developmental trajectory of executive attention and its centrality to self-regulation, interventions designed to support provision of learning stimulation may mitigate the risk for poor outcomes in some children by promoting more proficient development of cognitive control.

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Table 1

Relations of executive attention RT and ACC to prenatal cigarette exposure

Prenatal Cigarette Exposure	Mean	95 % Confidence Interval	N
RT (ms – correct responses) F(2, 223) = 6.4; p = 0.002			
None	1053.3	1035.8 – 1070.7	189
Partial	1050.5	1012.7 – 1088.4	23
Throughout	1093.2	1068.0 – 1118.4	22
ACC (% commission errors) F(2, 223) = 0.31; p = 0.73			
None	14.6	12.5 – 16.7	189
Partial	15.6	10.9 – 20.3	23
Throughout	15.7	12.3 – 19.2	22

Table 2

Relations of executive attention RT and ACC to infant learning stimulation

Infant Learning Stimulation	Mean	95 % Confidence Interval	N
RT (ms – correct responses) $F(2, 223) = 8.0$; $p = 0.0004$			
High	1043.4	1019.2 – 1067.6	98
Intermediate	1080.5	1052.9 – 1108.1	41
Low	1073.1	1049.7 – 1096.5	95
ACC (% commission errors) $F(2, 223) = 10.9$; $p < 0.0001$			
High	11.6	8.6 – 14.5	98
Intermediate	16.8	12.9 – 20.7	41
Low	17.5	14.5 – 20.5	95

Table 3

Relations of executive attention RT and ACC to prenatal cigarette exposure and infant learning stimulation (full sample)

Prenatal Cigarette Exposure / Infant Learning Stimulation	Mean	95 % Confidence Interval	N
RT (ms – correct responses) F(3, 225) = 5.1; p = 0.002			
None / Higher	1027.7	1013.5 – 1041.9	78
Exposed / Higher	1041.1	1016.1 – 1066.0	20
None / Lower	1057.2	1045.2 – 1069.3	111
Exposed / Lower	1078.5	1050.6 – 1106.5	25
ACC (% commission errors) F(3, 225) = 7.3; p = 0.0001			
None / Higher	11.5	9.7 – 13.4	78
Exposed / Higher	12.0	8.7 – 15.3	20
None / Lower	17.0	15.1 – 18.9	111
Exposed / Lower	18.6	15.1 – 22.1	25

Table 4

Relations of executive attention RT and ACC to prenatal cigarette exposure throughout pregnancy and infant learning stimulation (reduced sample)

Prenatal Cigarette Exposure / Infant Learning Stimulation	Mean	95 % Confidence Interval	N
RT (ms – correct responses) $F(3, 202) = 11.7$, $p < 0.0001$			
None / Higher	1028.8	1014.5 – 1043.2	78
Exposed / Higher	1041.3	1022.7 – 1059.8	10
None / Lower	1058.0	1045.9 – 1070.1	111
Exposed / Lower	1120.3	1092.4 – 1148.2	12
ACC (% commission errors) $F(3, 202) = 9.1$, $p < 0.0001$			
None / Higher	11.6	9.7 – 13.4	78
Exposed / Higher	10.7	6.2 – 15.2	10
None / Lower	17.2	15.3 – 19.1	111
Exposed / Lower	20.5	16.3 – 24.6	12