Prenatal Exposure to Nicotine and Impaired Reading Performance

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Objective To investigate whether prenatal exposure to nicotine has an impact on several reading skill outcomes in school age children.

Study design Using a longitudinal sample of 5119 school age children in the Avon Longitudinal Study of Parents and Children, this study investigated specific reading skill outcomes in the area of speed, fluency, accuracy, spelling, and comprehension in relation to prenatal nicotine exposure, after adjusting for potential mediators and confounders. Prenatal nicotine exposure was divided into 3 categories: high (>17 mg per day), low (≤17 mg per day), and no exposure.

Results We found that prenatal nicotine exposure was associated with increased risk of underperformance in specific reading skill outcomes after adjusting for potential mediators and confounders ($P = .006$). The effect of poor performance in decoding single words was most pronounced among children with prenatal exposure to high levels of nicotine in conjunction with a phonological deficit. Overall, the results showed that maternal smoking has moderate to large associations with delayed or decreased reading skills of children in the Longitudinal Study of Parents and Children.

Conclusions High prenatal nicotine exposure has a negative association with reading performance in school age children. In addition, modeling showed that environmental factors significantly moderated the interaction between prenatal nicotine exposure and reading skill outcomes. *(J Pediatr 2013;162:713-8).*

Reading is a critical skill that has profound social, health, and economic implications for life-course development. A significant proportion of the population will have unexpected reading difficulty. Such difficulty (often set at 1.5 SD below developmental expectations) among children and adults who otherwise have the intelligence and instructional opportunities necessary for accurate and fluent reading is the primary identifier of reading disability (RD). Worldwide, the prevalence of RD ranges from 7%-17% among school age children.[1-3] Understanding factors that account for variability in reading performance is, therefore, critical to understanding and preventing RD. Cigarette smoking exposes the developing fetus to nicotine and may be an unexplored but significant environmental risk factor for variability in reading skill. Despite multiple studies that have validated the adverse consequences of smoking during pregnancy,[4] approximately 9% of pregnant women smoke although estimates as high as 37% have been reported.[5,6]

Numerous studies have investigated the relationship between maternal smoking during pregnancy and various cognitive and behavioral indices.[7] Maternal smoking has been associated with reduced performance on tests of intelligence, academic achievement, short-term and verbal working memory, long-term and immediate memory for auditory/verbal material, executive function, increased incidence of behavioral disorders during childhood and adolescence, hyperactivity, and attention deficit. Animal studies support biological evidence for accelerated motor activity, neurobehavioral, learning and memory deficits, and alteration of neurotransmitter function due to exposure to nicotine in utero.[8] In addition, a large human study[9] found decrements in reading ability attributed to maternal smoking. Observational studies in humans have shown mixed results because of bias from unmeasured and confounding factors and small, unrepresentative sample sizes.

To address the shortcomings in previous studies and to test the hypothesis that prenatal nicotine exposure has specific effects on reading, we investigated the association of prenatal nicotine exposure and specific reading skills measured at age 7 or 9 years among children in the Avon Longitudinal Study of Parents and Children (ALSPAC). The overall goal was to cover multiple dimensions of the reading construct (eg, decoding, single-word identification, fluency, and comprehension) with a rich set of social and environmental variables in modeling the association between maternal smoking and reading skills.

ADHD	Attention deficit-hyperactivity disorder
ALSPAC	Avon Longitudinal Study of Parents and Children
RD	Reading disability
WORD	Wechsler Objective Reading Dimensions

Methods

The ALSPAC is a large population cohort of 15 211 children born in 1991 and 1992 in Bristol, England. The core ALSPAC sample consists of 14 663 children.[10] Among children who had any reading assessments at age 7 and 9 years (n = 6823), we excluded those with Wechsler Intelligence Scale for Children total IQ score[11] equal to or below 75 (n = 876) to minimize potential confounding effects from comorbid cognitive syndromes. Although the diagnosis of Intellectual Disability requires an assessment of IQ below approximately 70, the SE of most relevant measures is 5. The cutoff for this study was chosen to ensure that individuals with IQ who may or may not meet the other criterion of Intellectual Disability (eg, adaptive functioning) were not over-excluded. We also excluded children who were born outside of the 2 main maternity wards (n = 717) because they had limited perinatal information, and twins (n = 111). Our final sample contained 5119 children. Ethical approval for the study was obtained from the ALSPAC Law and Ethics Committee, the Local UK Research Ethics Committees, and the Yale Human Investigation Committee.

Information on maternal cigarette smoking was obtained from self-reported postal questionnaires completed by mothers between gestational age 8-42 weeks, and 8 weeks post-delivery. Daily intake of nicotine was calculated by multiplying the number of cigarettes per day by the nicotine content of each brand of cigarettes smoked. On the basis of previous studies[12,13] and because there was not enough statistical power to divide smokers into 3 trimester time periods, we derived the prenatal exposure to nicotine variable by taking the maximum amount of nicotine from the 4 time points. Smoking was then classified into 3 groups: no exposure, low exposure ($\leq$17 mg of nicotine per day), and high exposure (>17 mg of nicotine per day).[14] The cutoff of 17 mg nicotine per day is the approximate minimum of 1 pack (20 cigarettes) of average strength cigarettes.[14]

We investigated the following 7 specific reading outcomes: reading speed, single-word identification, spelling, accuracy, real and nonword reading, and reading comprehension. The reading speed, accuracy, and comprehension scores were standardized measures at age 9 years from the revised *Neale Analysis of Reading Ability, 2nd revised British edition*.[15] The child read passages from a booklet or stories, then was asked a series of questions about the content of the story. The reading speed score was a standardized measure of the number of words read per minute, with comprehension questions asked as soon as the child had finished reading. Single-word identification was assessed at age 7 years with the reading subtest of the Wechsler Objective Reading Dimensions (WORD).[16] Pictures and words were used to assess decoding and word reading. The final reading score was obtained by computing the sum of the number of items the child read or responded to correctly. WORD spelling was assessed at ages 7 and 9 years with a series of 15 age-adjusted words. The final spelling score was the average of scores at age 7 and 9 years. The real

words and nonword reading scores were assessed by asking the child to read 10 real and ten nonwords out loud at age 9 years.[17] Both the words and nonwords were specifically chosen from a larger selection of words taken from research conducted by Nunes et al in Oxford.[17] As a secondary analysis, we also used the comprehension component of the Reynell Developmental Language Scale[18] at age 25 months to explore early language development factors. This measure focuses on the understanding or comprehension of spoken language.

We assessed the impact of several comorbid conditions previously associated with maternal smoking and maternal alcohol consumption during pregnancy,[19] and attention deficit-hyperactivity disorder (ADHD).[20] ADHD was assessed through the Development and Well-Being Assessment[21] *Diagnostic and Statistical Manual of Mental Disorders, 4th edition*, clinical diagnosis at 91 months. We also examined birth weight and gestational age because these have been associated with prenatal smoking. We adjusted for neonatal resuscitation due to the reported association of hypoxic/ischemic brain injury and cognition.[22] In addition, we included the following covariates in the multivariable model: mother's age at delivery, social class, alcohol consumption during pregnancy, marital status, general verbal interaction, specific interactions around literacy,[23] antenatal class attendance, child's sex, ethnicity, and type of school. The literacy- and verbal-based interaction terms were derived from information on frequency of mother or other caregivers reading (literacy) to the child during age 5-8 years and talking (verbal) to the child when doing another task during age 3-5 years.

Furthermore, we designed our analysis to include the effect of phonology because of strong evidence that identifies this skill as the core cognitive and linguistic ability that drives early acquisition of reading skills.[24] Children with RD underutilize temporoparietal structures, and those resistant to intensive phonologically-based interventions fail to show increased temporoparietal processing or connectivity with other involved regions.[25] As a result, our model prioritized phonology using the phoneme awareness score based on performance on the phoneme deletion task of the WORD. In addition, we considered this factor as a potential effect modifier of the relationship between prenatal exposure to nicotine and each individual reading skill outcome.

To assess and characterize covariates for potential confounding or mediating effects, we evaluated the total set of 15 covariates in 2 subsets. Subset 1 consisted of covariates that were independent of the timing of the nicotine exposure: mother's age, social class, marital status, literacy, and verbal interaction with the child, status of antenatal class attendance, child's sex, ethnicity, and type of school. Subset 2 consisted of covariates that were concurrent with or occurred after the time of prenatal exposure and may have been affected by the downstream biological impact of the exposure: ADHD, neonatal resuscitation, birth weight, alcohol consumption, phonology, and gestational age.