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The Relation of Low-level Prenatal Lead Exposure to Behavioral Indicators of Attention in Inuit Infants in Arctic Quebec

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Abstract

The aim of this study was to investigate the association between prenatal exposure to lead (Pb) and several aspects of behavioral function during infancy through examiner ratings and behavioral coding of video recordings. The sample consisted of 169 11-month old Inuit infants from Arctic Quebec. Umbilical cord and maternal blood samples were used to document prenatal exposure to Pb. Average blood Pb levels were 4.6 µg/dL and 5.9 µg/dL in cord and maternal samples respectively. The Behavior Rating Scales (BRS) from the Bayley Scales of Infant Development (BSID-II) were used to assess behavior. Attention was assessed through the BRS and behavioral coding of video recordings taken during the administration of the BSID-II. Whereas the examiner ratings of behaviors detected very few associations with prenatal Pb exposure, cord blood Pb concentrations were significantly related to the direct observational measures of infant attention, after adjustment for confounding variables. These data provide evidence that increasing the specificity and the precision of the behavioral assessment has considerable potential for improving our ability to detect low-to-moderate associations between neurotoxicants, such Pb and infant behavior.

Keywords

lead; infant behavior; prenatal exposure; direct observation; Bayley Behavior; Rating Scales

1. Introduction

Although 10 to 15 µg/dL has long been considered the lower bound threshold for lead (Pb) neurotoxicity in children [13], recent improvements in study design have provided empirical evidence that there may be no safe level of Pb exposure [15,30,76]. Indeed the use of computerized neurobehavioral tasks, advances in electrophysiological or neurobiological

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studies, and the use of prospective longitudinal studies have provided the opportunity to assess more subtle developmental changes following low-level lead exposure. During gestation, Pb from the mother is transferred across the placenta [34], putting the developing fetus at risk. The fetal stage is thus considered a very susceptible period to Pb insult even from lowest exposure levels [32,67].

Results from prospective cohort studies have provided evidence that low-level *in utero* Pb exposure can impair infant growth and development. Cord blood Pb levels below 10 µg/dL have been associated with decreased birth weight [22], weight gain [64] and decreased body mass index [54]. In neonates from the Cleveland study, abnormal reflexes and neurological soft signs scales were related to cord Pb levels ($M = 5.8$ µg/dL) and the muscle tonicity scale was related to maternal blood Pb concentration ($M = 6.5$ µg/dL) [28]. Results from the Mexico City cohort showed associations between maternal blood Pb level at mid-pregnancy ($M = 7.7$ µg/dL) and brainstem auditory evoked responses in newborns, 3-month-old infants, and children at 67 months of age [60,61]. Deficits in visual function were also seen at cord blood Pb concentrations as low as 10.5 µg/dL [63]. In the Boston cohort in which cord blood Pb levels were lower than 16 µg/dL for 90% of participants, higher exposure was linked to decreased scores on the Mental Developmental Index of the Bayley Scale Infant Development at 6, 12, 18 and 24 months of age [5,6,8,9]; similar associations were observed at 3 and 6 months of age in the Cincinnati cohort [21,23]. Recent results from a Mexican cohort, based on maternal plasma levels obtained during pregnancy, suggest that the adverse effect of fetal lead exposure on neurodevelopment may be most pronounced when exposure occurs during the first trimester of pregnancy [40].

In spite of the likely relation among early growth and development, few studies have examined the relation of low-level prenatal Pb exposure to infant behavior. In the relatively few studies that have examined effects on behaviour in childhood, low-level prenatal Pb exposures have not been associated with detectable adverse effects [4,55,75]. By contrast, a large literature has documented adverse effects of low-level postnatal Pb exposure on various aspects of preschoolers and school-age behavior including activity, attention, anxiety, sleep disturbances, and conduct disorders [11,15,19,31,35,55,66,74,75]. In most studies, the postnatal exposures are substantially higher than the prenatal exposures [55] which may make it more difficult to detect the possibly subtler effects of the lower level prenatal exposure. Examining the effects of prenatal exposure on behaviors that occur very early in development using highly sensitive direct behavioural observation measures may make it possible to detect these subtler effects. To our knowledge, only one study, that of Tang et al. [71], has focused on the association between low-level prenatal Pb and behavioral development in infants before 18 months of age. These authors reported adverse effects of prenatal Pb exposure (mean cord blood level = 3.9 µg/dL) on sociability in 9 month-old children, assessed through a neurodevelopmental examination using the Brunet Lézine Scale.

In a recent study conducted with the Inuit population of Nunavik (Arctic Quebec, Canada), prenatal exposure to lead, mercury and organochlorine compounds was documented from analyses conducted in umbilical cord blood samples. Pb concentration averaged 4.1 µg/dL (SD = 3.5), which is two times higher than that found in the general population from Southern Quebec [50], but lower than that found in the U.S. cohorts described above. In the Nunavik study, the infants were assessed at 11 months of age in multiple domains, including the Behavior Rating Scales (BRS) from the Bayley Scales of Infant Development, second edition (BSID-II) [2]. Furthermore, video recordings were made during the administration of the BSID-II, enabling us to perform the innovative direct assessments of infant behaviors described below. The research protocol also included the assessment of multiple potential confounding variables to be taken into account in the analysis.

The first aim of this study was to investigate the association between prenatal exposure to Pb and several aspects of infant behaviour assessed by examiner ratings. Infant attention, one aspect of behaviour that has frequently been linked to Pb exposure was also assessed by direct observational coding of video recordings.

2. Methods

2.1 Procedures and participants

This prospective study was conducted between 1995 and 2002 in three Nunavik communities inhabited by Inuit and located along East Hudson Bay coast: Puvirnituq, Inukjuak, and Kuujuarapik. The Nunavik region is located in eastern Canada, in the northern portion of the province of Quebec. Pregnant women were recruited at their first or second prenatal medical examination. Prenatal exposure was assessed by measuring lead concentration in two blood samples: one collected from the umbilical cord and the other obtained from the mother at delivery or within a few weeks thereafter. Data collection, which involved testing infants and interviewing mothers was performed by trained clinical psychologists during several 1-month trips to Nunavik. A total of 169 infants were tested at the local government nursing station in their village at 11-months of age on the Bayley Scales of Infant Development, second edition (BSID-II; [2]). This paper reports data for Bayley Behavior Rating Scales and behavioral observation coding from videotapes recorded during the BSID-II testing. The Bayley was administered at 11 months because visual attention is fully developed at this age [17] and stable individual differences in reactivity towards new situations or objects can be detected [44] but language is still rudimentary. During the BSID-II, the examiner's directions to the infant were translated by the mother or a professional translator. This procedure worked well for sensorimotor and gross motor items, but administration of a large number of language items through a translator would have been very difficult. Maternal interviews were conducted at mid-pregnancy and at 1, 6.5 and 11 months postpartum by trained research assistants to document potential confounding variables pertaining to demographic background, fetal exposure to other drugs and quality of parental cognitive stimulation provided to the infant. Medical charts were reviewed to document pregnancy and perinatal medical complications. Among the 417 Nunavik women invited to participate in this study, 47 were excluded because a newborn from the same mother had previously been recruited, 9 could not be contacted by our research assistants to schedule the prenatal interview, and 110 (30%) refused to participate. Among the 251 women interviewed prenatally, 11 were subsequently excluded due to miscarriage, perinatal or postnatal mortality; 8, due to failure to obtain at least one biological sample for exposure assessment; 7, due to relocation to another village; 7, due to the adoption of the newborn by residents of another village; and 8 chose to withdraw from the study at the postnatal interview. Pb concentration in cord blood was available for 110 children whereas maternal blood Pb concentration was available for 169 children (blood sample collected within 30 days following child birth). In order to assess potential bias, t-tests were performed to compare participants whose lead exposure was known ($n=169$) to the other subjects ($n=82$). Results revealed no significant differences between groups on the following variables: age of the mother at delivery, parity, number of cigarettes smoked per day during pregnancy, child's weight at birth (g), duration of gestation (no. of days), cord blood concentrations of polychlorinated biphenyls (PCBs) and mercury (Hg). Thus this sample was representative of the population from which it was drawn. The research procedures were approved by Laval University and Wayne State University ethics committees, and an informed consent was obtained from each participating mother.

2.2 Assessment of prenatal Pb exposure

Umbilical cord blood and maternal blood samples were analysed to document prenatal exposure to Pb at the Laboratoire de Toxicologie de l'Institut National de Santé Publique du Québec, which is accredited by the Canadian Association for Environmental Analytical Laboratories. Pb concentrations were determined by graphite furnace atomic absorption with Zeeman background correction (Perkin Elmer model ZL4100). Detailed laboratory and quality control procedures have been described previously [50,58]. The detection limit was 1.04 µg/dL, which corresponds to 0.05 µmol/l. We used cord blood lead level as the principal biomarker of exposure in our study because we believe that it reflects fetal exposure better than maternal blood or plasma lead level. The concentration of lead in venous cord blood is on the fetal side of the circulation. While some authors have argued that maternal plasma might be better than maternal blood for reflecting the fraction of lead available to cross the placental barrier [16], we believe that a direct measure on the fetal side (cord blood level) is preferable. Furthermore, plasma lead levels are very low and difficult to measure reliably.

2.3 Behavioral assessment

2.3.1 Examiner ratings—The Bayley Scales of Infant Development (BSID-II) provides three developmental scales: the mental developmental index (MDI), the psychomotor developmental index (PDI) and the Behavior Rating Scale (BRS). We have previously reported that no association was found between prenatal lead exposure and MDI or PDI in this cohort [42,43]. The BRS is a revised version of the Infant Behavior Record (IBR) used in the original Bayley Scales of Infant Development (BSID; [1]). Reliability studies of the BRS have shown excellent internal consistency and good-to-excellent test-retest stability and inter-rater agreement [2]. Each of the 28 BRS scales is a five-point Likert scale, based on the child's behavior in the testing situation. At the end of the testing situation, examiners have to rate children on 28 scales such as “adaptation to change in test materials: from (1) consistently resists relinquishing materials and/or refuses to accept new materials, to (5) consistently relinquishes materials and accepts new materials”, or “energy: from (1) consistently lacks animation or energy; tired and lackluster, to (5) consistently animated or energetic”. The instrument provides a global score as well as, when administered after 5 months of age, summary scores for orientation and engagement, emotional regulation and motor quality scores. As described by Engle et al. [27], “*the orientation and engagement subscale includes nine items which clustered together in factor analytic studies, and reflect the child's willingness to look at and engage both the tasks at hand and the examiner. The emotional regulation factor includes 10 items reflecting the child's ability to adjust emotionally and adapt to the challenges of the testing situation, such as negative affect, ability to adapt to change in materials, attention, frustration, and cooperation*”. During the course of our study, BRS data from 54 infants were coded by two independent examiners and inter-rater agreements within one point of discrepancy on the Likert scale ranged from 79% to 100% across the BRS scales.

2.3.2 Observed attention—The administration of the Mental Development Index (MDI) from the BSID-II was videotaped. Since the BSID-II consists of successive standardized presentations of novel objects to the child, it provides an opportunity to document objectively visual inattention through video coding. This method is inspired from classical ethological works that continue to inform our understanding of behavioral development in children [10,38,68,70]. The BSID-II is considered a natural challenging situation during which children express their behavioral tendencies. The coding was performed using specialized computer program (The Observer©, Noldus). Two research assistants reviewed the videotapes and coded looking transitions: every 1 second the observer noted, whether the infant was looking at the test material, was looking at the tester or was looking away from

test material and tester. The two research assistants were blind with respect to exposure to environmental contaminants, including lead. During the MDI (mean duration: 32.3 minutes per child), 17 objects are presented to the infant. The video recordings of 159 children were coded for looking behaviour. Data were not obtained from the remaining 10 infants due to technical failure (poor quality video image or bad framing). Behavioral coding requires an acceptable inter-observer agreement (usually 80%). An agreement is counted when both observers code the same looking transition at the same time (with a tolerance windows of 2 seconds). To reach this acceptable inter-observer agreement, looking transitions of 81 children were coded by two independent research assistants. During this stage of training, each disagreement on looking transitions was reviewed and consensus was achieved. Inter-observer agreement was also monitored periodically during the coding process and level of inter-observer agreement reached a kappa of 0.9.

Based on previous studies on the influence of Pb exposure on child behavior [35,36,55], two summary measures of visual attention were constructed: off task duration, which was defined as the proportion time the child looked away from the test material and tester during the task and off task latency, which was derived by summing the time (in sec.) that lapsed between the initial presentation of each object and the child's initial look away from the object and tester divided by the total number of objects presented. A shorter latency indicates poorer attention. Although in the context of infant paired comparison and habituation tasks, short average duration of looking has been shown to indicate more efficient information processing [17], in this context the infant must maintain attention to the examiner's demonstration of the task over a period of at least 5-10 sec. in order to perform it.

2.4 Potential confounding variables

A broad range of potential confounding variables were assessed. These variables were selected for their potential or documented associations with Pb exposure or child behavior. To document possible adverse effects of other environmental contaminants relevant in the population under study, concentrations of PCBs, chlorinated pesticides and Hg were obtained from laboratory analyses conducted on umbilical cord samples. Laboratory procedures were previously described in Muckle et al. [50]. The following potential confounders were documented through maternal interviews and medical files: socioeconomic status (Hollingshead Index; [39]), marital status, parity, highest grade achieved by the primary caregiver, number of children and adults at home, maternal psychological distress (Indices de détresse psychologique – Enquête Santé Québec (IDESPQ) [56]), maternal non verbal reasoning ability (Raven Progressive Matrices [57]) and Peabody Picture Vocabulary Test (PPVT [26]), domestic violence (Conflict Tactics Scales; [69]), quality of intellectual stimulation provided by the family (Home Observation for Measurement of the Environment (HOME) [12]), prenatal exposure to alcohol (frequency and quantity), illicit drugs such as PCP, cocaine, crack, sniffing (frequency) and tobacco (number cigarettes/day), birth characteristics (complication at delivery, gestational age, birth weight and head circumference) and child characteristics (age, sex, status of adoption, breastfeeding duration, and day care attendance). Hemoglobin levels were obtained from an infant blood sample collected at 6 months of age.

2.5 Statistical analyses

Pearson correlation analyses were performed to select from among the potential confounding variables those to be included in subsequent analyses. Any variable associated with a specific outcome at a p-value < .20 was included as a potential confounding variable in the initial multiple regression analysis assessing that outcome. Final regression models were computed for each behavioral outcome by entering prenatal exposure to Pb together with the initial set of potential confounders and then removing, one at a time, those variables

that were not significantly associated with the outcome (at $p \leq .10$) with the outcome. All variables were normally distributed except blood Pb concentrations (cord and maternal) and off task latencies. These variables followed log-normal distributions and their analyses were, therefore, conducted with natural log-transformed values. All statistical analyses were performed using the SPSS software (Statistical Package for Social Sciences) (Release 11.5.0, 6.09.02, ©SPSS Inc.).

3. Results

3.1 Exposure

Descriptive data for the 169 mother-infant pairs that constitute the sample examined in this paper are presented in Table 1. Data relating to methylmercury, organochlorine exposures and their association with lead levels in this cohort have been reported and described elsewhere [50]. Lead concentrations in cord and maternal blood samples are presented in Table 2. T-tests analyses indicated that blood Pb levels were similar for the two subsamples for whom the BRS and observational data are available, respectively (cord blood Pb, $t(163) = .08$, $p = .93$; maternal blood Pb, $t(255) = .15$, $p = .88$). The percentage of cord Pb concentrations exceeding $10 \mu\text{g/dL}$ was also similar in the two subsamples (10-11%). As seen in Figure 1, cord blood Pb concentrations were strongly associated with maternal blood Pb concentrations. To increase the sample size when conducting regression analyses, missing cord blood Pb concentrations (Cpb) were estimated from maternal blood Pb concentrations (Mpb) by regression analyses, using the following equation: $\text{Cpb} = 1.00 \times \text{Mpb} - 0.41$.

3.2 Intercorrelations among behavioral outcomes

The correlations between the 28 BRS items and the three summary scales indicated that within a scale, some of the items are not as highly correlated as others, suggesting that the BRS scale scores do not clearly identify distinct behaviors in this population (Table 3). This inference was corroborated in a principal components analysis, which showed that the BRS scales loaded on a single common factor. Off task duration was not related to any of the BRS summary scales, and off task latency was associated with only one (emotional regulation). This relation would indicate that the higher the child's ability to adjust emotionally to the testing situation was, the shorter off task latency the child had. But, off task latency was significantly related to only two of the specific BRS items (adaptation to change in test materials and frustration with inability to complete tasks); off task duration, to only one (energy). These data indicate that the two observationally-based indicators of visual inattention represent domains that are distinct from those documented in the BRS. Moreover, off task duration and off task latency were only moderately correlated with each other, indicating that they reflect different aspects of infant inattention.

3.3 Relation of cord Pb concentration to the infant behavioral outcomes

Cord Pb concentration was not significantly related to any of the BRS summary scales and was marginally related to only three of the BRS items: adaptation to change in test materials, persistence in attempting to complete tasks and frenetic movement (see Table 4). With respect to the observationally-based indicators of visual inattention, cord Pb concentration was marginally related to off task duration and significantly related to off task latency.

Multiple regression analyses were performed for the three BRS items whose correlations with prenatal lead exposure fell just short of the statistical significance, the BRS attention item (due to its direct relevance to the focus of this study), and the two observationally-based indicators of visual inattention. After controlling for confounders, cord blood Pb concentration was associated with only one BRS item—higher frequency of frenetic

movement. By contrast, cord blood Pb levels were related to both observationally-based measures—off task duration and off task latency (Table 4). Higher prenatal exposure was associated with an increased duration of the looking away from test material and tester during the task, and more immediate looking away from a novel object and the tester after a new object has been introduced.

3.4 Model validations with children for whom cord blood Pb concentrations were not missing

Due to the possibility that the estimation of missing cord blood Pb levels from maternal blood concentration may have decreased the precision of the exposure data thereby resulting in lower statistical power, the significant regression models in table 4 were validated by re-running them for the children for whom cord blood samples were not missing. The results obtained with this smaller subsample corroborated those obtained when the estimated cord blood Pb measures were examined. The relation of cord Pb to adaptation to change in test materials ($\text{std } \beta = -.18$) and persistence in attempting to complete tasks ($\text{std } \beta = -.15$) was slightly stronger for this subgroup but continued to fall short of statistical significance. The associations with frenetic movement ($\text{std } \beta = -.24$, $p = .04$), and off task duration ($\text{std } \beta = .28$, $p = .01$; Fig. 2) remained significant, and the relation with off task latency fell short of significance ($\text{std } \beta = -.19$, $p = .12$) presumably due to smaller sample size.

4. Discussion

The purpose of this study was to examine whether prenatal exposure to Pb is associated with behavioral outcomes during infancy. Prenatal Pb exposure was not related to the BRS summary scales and was related to only one of the 28 ratings, frenetic movement, in spite of the broad range of behaviors evaluated on the BSID. The finding of an association between prenatal Pb exposure and a higher frequency of frenetic movement, is consistent with results reported on the NBAS measure of abnormal reflexes in human neonates [28,62]. In our study, “frenetic movement” is associated with the BRS “hyperactivity” item ($r = .30$, $n = 149$, $p < .001$). This finding is, therefore, consistent with data from primate studies that have identified agitation as an early behavioral effect of Pb [46], and reports of increased hyperactivity in childhood in relation to postnatal lead exposure [72,77].

The absence of other correlations with BRS ratings was not entirely surprising as examiner's ratings of children's behavior have seldom been related to low level Pb exposure in previous studies [25,36,47]. Moreover, the early behavioral effects of Pb are known to be specially reduced when control variables, such as the socioeconomic status, are included in the analyses [7]. The full impact of the Pb effect is thus difficult to isolate [15], and instruments designed to document behavioral outcomes are often near the limits of their discriminative ability. Because the specific domains reflected in many of the BRS scales are behaviorally heterogeneous, these scales may not be as sensitive to teratological effects as other measures that are focused on more narrowly-defined aspects of behavioral functions. Sensitivity is related to variability, and in our sample, there was little variability in examiner ratings on the 5-point-BRS Likert scales. The standard deviations ranged from .3 to 1.2, and the inter-quartile ranges never exceeded 1 for the 28 BRS scales by contrast to duration of off task attention, which ranged from 0 to 26.4% of the task administration period, with a mean of 12.1% ($SD = 5.3$), and off task latency, which ranged from 0 to 51.6 seconds after presentation of a novel object with a mean of 9.6s ($SD = 12.1$). As a consequence, the coefficient of variation C_V , which allows comparison of the variation of variables with different mean values, was markedly higher for the behavioral measures (C_V off task duration = .44; C_V off task latency = 1.26) than for the examiner ratings measures (average C_V BRS items = .17; average C_V BRS summary scales = .13). Moreover, the behavioral observation measures rely upon objective data while examiner-rated measures are more

subjective and may, therefore, be applied with less consistent criteria, thus reducing their sensitivity.

Thus, it is of interest that the effect of prenatal Pb on attention, which was not observed when attention was evaluated using examiner ratings, became evident when it was assessed from direct observation of video recordings. Other studies have also found observed behavioral outcomes from video recordings to be highly sensitive in detecting subtle effects of low-level Pb exposure [15,19,35,55]. In the structured settings of the BSID-II administration, our visual inattention measures appeared to provide a natural assessment of the inability to maintain focus and alertness over time, an aspect of behaviour often referred to as sustained attention [48]. Attention is known to be affected by Pb exposure at levels as low as 3 µg/dL [15,31,53]. Epidemiologic studies using teacher's ratings or neuropsychological testing also find that children with higher Pb burdens have reduced ability to sustain attention [29,37,52,73,78], although work by Bellinger et al. [3] found the clearest effects in the domains of focused attention and executive function. Relations between low level Pb exposure and impaired sustained attention have also been documented in experimental studies with rats [49] and in monkeys [46,59].

Davis et al [20] have suggested that impaired ability to maintain attention and regulate one's behavior could be one of the earliest signs of Pb neurotoxicity, and a possible basis for later cognitive dysfunction. Given that prenatal lead exposure was not associated with cognitive performance on the MDI in this cohort [42,43], the attentional effects reported here are presumably not attributable to difficulty in performing the task that might lead a child to disengage from the testing situation. Our study has demonstrated that a highly sensitive assessment of sustained attention through video recordings can be used to detect behavioral effects of low level prenatal Pb exposure during infancy. These data suggest that sustained attention may provide an early behavioral signature of low level Pb exposure and that early disruption of attention could mediate, at least partly, the Pb-induced cognitive impairments observed later in development. However, further studies using appropriate statistical modelling techniques are needed to test this hypothesis.

To our knowledge, our study is the first to show a significant relation between prenatal cord blood Pb concentrations and observed behavioral outcomes in infancy. These effects were seen in a population whose cord blood Pb levels averaged only 4.8 µg/dL. Moreover, when children with cord blood Pb levels higher than 10 µg/dL were removed from the analysis, observed attention continued to be associated with Pb exposure ($F = 2.94$, $r^2 = .10$, $p = .03$, $n = 69$; std β for Pb = .22, $p = .06$). One limitation is that only prenatal level of exposure was available in our cohort, whereas most of the behavioral effects found in the literature originate from postnatal exposure [4,15,19,25,35,47,53,55,66,74,75]. Blood Pb isotope studies indicate that sources of Pb in the southern population of Quebec include a mixture of atmospheric Pb coming from southern Ontario and the USA and urban Pb found in paint, dust, tires, etc [58]. By contrast to the southern population, the main source of Pb exposure in Nunavik is game hunting, and Pb gunshot or Pb-bearing fragments from game meat were in a large part responsible for the Pb levels found in Nunavik Inuit newborns [45]. At 1 year of age, Pb exposure in Inuit infants comes thus mainly from a prenatal source. Thus, our cohort may be regarded as unique in providing an opportunity to study the effects of low level prenatal Pb exposure independently from postnatal exposure.

In conclusion, our results provide evidence linking early behavioral effects with prenatal Pb exposure. After control for confounders, Pb accounted for 8% of the variance in observed attention. The magnitude of the Pb effect is thus very small, as stressed in many other studies [24,66,75]. Nevertheless, small disturbances in behavior at such an early age, in conjunction with the documented adverse effects of prenatal Pb exposure on cognitive

abilities [65], may compound over time, contributing to more substantial difficulties by school age. One noteworthy feature of these data is the absence of confounding effects from the other environmental contaminants. In fact, mercury and polychlorinated biphenyls are not known to specifically impair attention [18,33,51] but do have documented effects on activity [14,41,51]. Given the evidence from this study that behavioral coding of video recordings is sensitive enough to detect early behavioral effects associated with low level Pb exposure, an important next step will be to develop observed assessments of other behavioral functions, such as activity. In addition, a 10-year follow-up assessment of this cohort currently in progress will provide an opportunity to evaluate the implications of early Pb exposure for attentional, social, and cognitive adaptation in the school years and to test the hypothesis that early deficits in attention may mediate the adverse impact of Pb exposure on cognitive function in childhood.

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Figure 1.
Pearson correlation between cord blood lead and maternal blood lead concentration ($\mu\text{g}/\text{dl}$).

Figure 2.

Correlation between cord blood lead and offtask duration after adjustment for confounders.

^a by removing this outlier, the regression models remained significant ($F=4.08, r^2=.14, p<.005, n=77$) and cord blood Pb was still associated with offtask duration ($\text{std}\beta=.25, p=.03$)

Table 1

Characteristics of participants^a

	Total no.	Percent	Mean	SD	Range
Age (days)	167 / 86		354.2 / 350	40.3 / 38.7	215-517 / 302 - 478
Sex (% female)	169 / 87	40.2 / 35.6			
Adopted (%)	168 / 87	11.9 / 9.2			
Breastfeeding duration (days)	168 / 87		154.6 / 168.8	133.4 / 127.5	0.0-465.5 / 0.0-401.3
Day care attendance	161 / 82	15.5 / 12.2			
Primary caregiver's characteristics					
Language (% english or french)	169 / 87	83.4 / 82.8			
Socioeconomic status ^b	169 / 87				
Unskilled laborer		34.9 / 33.3			
Semiskilled workers		21.9 / 20.7			
Skilled craftsmen, clerical and sales		24.3 / 28.7			
Technical, small business		18.9 / 17.2			
Raven (standard progressive matrices)	165 / 85		34.7 / 34.1	7.4 / 7.9	13-52 / 13-47
Highest grade achieved	169 / 87		8.7 / 8.6	2.0 / 2.1	0-14.2 / 0-14.2
PPVT	169 / 87		68.2 / 63.7	31.2 / 29.3	13-146 / 13-129
IDESPQ depression scale	166 / 86		8.5 / 8.7	2.5 / 2.5	5-15 / 5-15
IDESPQ anxiety scale	166 / 86		4.5 / 4.4	1.6 / 1.7	3-9 / 3-9
% with at least one episode of reported domestic violence	169 / 87	60.9 / 60.9			
HOME total score	163 / 83		31.5 / 31.6	5.1 / 5.3	17-42 / 19-41
Maternal age at delivery (years)	169 / 87		24.9 / 24.7	5.8 / 5.8	14.6-40.9 / 15.4-39.2
Married or living with a partner (%)	169 / 87	69.2 / 67.8			
Nb of live birth	169 / 87		1.9 / 2.1	1.7 / 1.9	0-9 / 0-9
Nb of children in house	169 / 87		3.5 / 3.6	1.8 / 1.8	1-9 / 1-9
Birth characteristics					
At least one delivery complication (%)	169 / 87	20.7 / 16.1			
Gestational age (weeks)	169 / 87		38.8 / 39.2	1.8 / 1.5	32-42 / 36-42
Prematurity (%<37 wks)	169 / 87	23.1 / 12.6			
Birth Weight (g)	169 / 87		3469.9 / 3580.2	584.1 / 472.4	1620-4870 / 2420-4560

	Total no.	Percent	Mean	SD	Range
Low birth weight (% < 2500g)	169 / 87	5.3 / 1.1			
Head circumference (cm)	157 / 85		34.4 / 34.8	1.7 / 1.4	29.40 / 31.5-38
Infant Health					
Hemoglobin in 6 months blood (g/L)	155 / 79		108.4 / 109.2	12.5 / 11.3	82-148 / 85-148
Anemic children at 6 months (%)	155 / 79		10.3 / 12.7		
At least one health problem at testing time (%)	161 / 80	32.9 / 30.0			
At least one medication at time of testing (%)	160 / 79	35.6 / 31.6			
Prenatal exposures					
Average AA/day at conception ^c	168 / 87		0.3 / 0.4	1.2 / 1.5	0-12.7 / 0-12.7
Average AA/drinking day at conception	168 / 87		1.1 / 1.3	2.2 / 2.2	0-12.7 / 0-12.7
At least one type of drug (marijuana, PCP, Coke)	169 / 87	38.5 / 41.4			
Marijuana exposure during pregnancy (%)	169 / 87	37.9 / 41.4			
Sniffing during pregnancy (%)	169 / 87	2.4 / 2.3			
Nb Cigarettes per day	169 / 87		9.5 / 10.3	6.7 / 7.0	0-27.5 / 0-27.5
> 10 cigarettes / day (%)	169 / 87	45.6 / 52.9			
PCB congener 153 in cord plasma (µg/Kg)	86 / 85		111.9 / 108.1	96.1 / 90.0	15.7-550.9 / 15.7-550.9
Cord blood Hg (µg/L)	85 / 85		22.1 / 22.1	16.5 / 16.5	2.4-97.4 / 2.4-97.4
Maternal hair Hg (µg/g)	163 / 85		4.3 / 4.8	2.7 / 2.9	0.3-15.1 / 0.7-15.1

^aValues are given first for participants whose prenatal lead exposure was assessed either with cord blood lead or maternal blood lead. Other values are given for participants whose prenatal lead exposure was only assessed with cord blood lead.

^bHollingshead index;

^cOne standard drink of alcohol corresponds to 0.5 oz of absolute alcohol (AA), which is the equivalent of 350 ml of beer (12 oz), 175 ml of wine (6 oz), or 44 ml of liquor (1.5 oz)

Table 2

Blood lead concentrations (µg/dL)

Lead concentrations	No.	Arithmetic mean	Median	SD	Range	IQR ^c
Cord blood	110	4.64	3.52	3.54	0.52-17.80	2.07-5.38
Maternal blood	169	5.86	5.17	3.59	0.52-25.88	3.11-8.07
<i>in the BRS sub-sample^a</i>						
Cord blood	86	4.81	3.52	3.59	0.52-17.80	2.28-5.43
Maternal blood	135	5.95	5.17	3.60	1.04-25.88	3.10-8.07
<i>in the OBS sub-sample^b</i>						
Cord blood	79	4.84	3.52	3.73	0.52-17.80	2.07-5.59
Maternal blood	122	5.87	5.17	3.57	1.04-25.88	3.10-7.56

^a children rated by the examiners with the BRS

^b children coded through observation of video recordings

^c Interquartile range

Table 3

Pearson correlations between behavioral outcomes

	<i>BRS summary scales</i>			<i>Observed attention</i>	
	Orientation/engagement	Emotional regulation	Motor quality	Total score	Off task latency
<i>Observed attention</i>					
Offtask duration	-	-	-	-	-
Offtask latency	-	-	-	-	-.29***
<i>BRS summary scales</i>					
Orientation/engagement	-				
Emotional regulation	.29***	-			-.22**
Motor quality	.19**	.61***	-		
Total score	.40***	.26***	.27***	-	
<i>BRS items</i>					
Predominant state	.36***	.26***	.18*	.22**	
Lability of state of arousal	.35***	.20**	.15 [†]	.19*	
Positive affect	.63***	.20**	.16*	.26***	
Energy	.63***	.32***	.34***	.42***	.19*
Interest in test materials and stimuli	.66***	.39***	.35***	.32***	
Initiative with tasks	.58***	.30***	.32***	.27***	
Exploration of objects and/or surroundings	.62***	.32***	.32***	.32***	
Enthusiasm toward tasks	.64***	.49***	.36***	.32***	
Fearfulness	.53***	.37***	.32***	.30***	
Social engagement	.60***	.26***	.18*	.31***	
Orientation to examiner	.62***	.59***	.30***	.31***	
Persistence in attempting to complete tasks	.50***	.56***	.42***	.25***	
Negative affect	.32***	.61***	.29***	.30***	
Hypersensitivity to test materials and stimuli	.34***	.57***	.44***	.25***	
Adaptation to change in test materials	.37***	.64***	.20*	.22**	-.19*

	BRS summary scales			Observed attention		
	Orientation/engagement	Emotional regulation	Motor quality	Total score	Off task duration	Off task latency
Attention to tasks	.42 ***	.46 ***	.37 ***	.31 ***		-.15 †
Frustration with inability to complete tasks	.45 ***	.53 ***	.17 *	.22 **		-.16 *
Cooperation	.48 ***	.60 ***	.31 ***	.30 ***		-.14 †
Hyperactivity	-.14 †	.17 *				
Frenetic movement		.27 ***	.21 **			
Gross-motor movement required by tasks	.27 ***	.36 ***	.69 ***	.27 ***		
Fine-motor movement required by tasks	.19 **	.25 ***	.56 ***	.19 *		
Control of movement	.21 **	.39 ***	.73 ***	.26 ***		
Hypotonicity	.27 ***	.20 **	.58 ***	.21 **		
Hypertonicity	.17 *	.45 ***	.46 ***	.20 *		
Tremulousness	.14 †					
Slow and delayed movement	.40 ***		.39 ***	.22 ***		
Soothability when upset	.31 ***	.44 **	.15 *	.24 **	.13 †	

† .05 < p < .10;

* p < .05;

** p < .01;

*** p < .001

Note: Outcomes correlated with age at testing (p < .05) were age-adjusted.

^a dotted boxes identified items of each BRS sub-scale.

Simple and multiple linear regression on behavioral outcomes - models with children whose prenatal lead exposure was assessed either with cord blood lead or maternal blood lead ^a

Table 4

Behavioral outcome (univariate correlation with prenatal Pb)	Independent variable	Standardized coefficients				
		β	s.e.	β	t	p Value
Adaptation to change in test materials ($r = -.13, p = .10$)	Language	0.36	0.76		0.47	0.64
	IDESPQ depression scale	-0.15	0.08	-0.15	-1.86	0.06
	Socioeconomic index	-0.06	0.02	-0.20	-2.47	0.01
	Infant hemoglobin in 6 months blood	-0.01	0.01	-0.13	-1.71	0.09
	PCB congener 153 in cord plasma ^b	0.01	0.00	0.16	2.03	0.04
	Prenatal lead exposure	-0.19	0.09	-0.17	-2.15	0.03
		-0.13	0.10	-0.11	-1.33	0.19
	$F=3.61, R^2=0.08, p<0.004, n=150$					
	At least one delivery complication	-0.78	0.26		-3.06	0.00
	Home organization	0.23	0.10	0.17	2.18	0.03
Persistence in attempting to complete tasks ($r = -.13, p = .09$)	Low birth weight (<2500g)	0.11	0.04	0.19	2.48	0.01
	Prenatal lead exposure	-0.60	0.20	-0.23	-3.05	0.00
		-0.11	0.06	-0.13	-1.74	0.08
	$F=5.79, R^2=0.11, p<0.000, n=164$					
	Nb of ear infections since birth	4.66	0.13		37.04	0.00
Frenetic movement ($r = -.13, p = .09$)	Prenatal lead exposure	-0.07	0.02	-0.25	-3.23	0.00
		-0.13	0.06	-0.16	-2.14	0.03
	$F=6.89, R^2=0.07, p<0.001, n=160$					
Attention to tasks ($r = -.11, p = .14$)	Maternal age at delivery	-3.04	0.83		-3.64	0.00
	Gestational age	-0.03	0.01	-0.30	-3.95	0.00
	Infant Hemoglobin in 6 months blood	0.07	0.02	0.25	3.52	0.00
	Medication at testing time	0.01	0.00	0.20	2.81	0.01
	Average AA/drinking day at conception	0.22	0.08	0.20	2.73	0.01
	Prenatal lead exposure	-0.20	0.05	-0.28	-3.76	0.00
		-0.06	0.06	-0.08	-0.99	0.32

Behavioral outcome (univariate correlation with prenatal Pb)	Unstandardized				Standardized coefficients			
	β	s.e.	β	t	β	t	p	Value
$F=10.24, r^2=0.28, p<0.000, n=144$								
OFF TASK duration ($r=.13, p=.11$)								
$F=4.11, r^2=0.08, p<0.003, n=148$								
OFF TASK latency ($r=-.22, p<.01$)								

^a missing cord blood Pb concentrations were estimated from maternal blood Pb concentrations through regression analyses.

^b missing cord blood PCB concentrations were estimated from maternal blood PCB concentrations through regression analyses.