Pre- and postnatal exposure to PCBs and dioxins and cognitive development of Dutch children at 3½ years of age.

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Abstract

The effect of pre- and postnatal exposure to PCBs and dioxins on cognitive development at 3½ years of age was investigated. We studied 395 of the original 418 mother-infant pairs recruited for the "Dutch PCB/dioxin study". Their cognitive development was assessed with the Dutch version of the Kaufmann Assessment Battery for Children (K-ABC). After adjustment for covariates, prenatal PCB exposure, estimated from maternal plasma PCB levels measured during pregnancy, was significantly associated with a lower score on the cognitive scale of the K-ABC. Postnatal PCB and dioxin exposure measured from maternal milk samples, and PCB exposure at 3½ years measured from PCB levels in plasma of children, were not related to the cognitive development at 3½ years. We conclude that prenatal exposure to 'background' PCB levels influences the cognitive development of Dutch pre-school children negatively.

Introduction

Polychlorinated biphenyls (PCBs), chlorinated dibenzo-para-dioxins (PCDDs), -di-benzo-furans (PCDFs) are widespread and persistent environmental pollutants. The Netherlands belong to countries with high environmental levels of PCBs and PCDD/Fs (dioxins) as measured for instance in human milk. The "Dutch PCB/dioxin" project was therefore initiated to investigate possible adverse effects of background exposure to PCBs and dioxins on growth and neuro-development of young children. Healthy term newborns were studied until pre-school age. We have reported previously that subtle signs of neurological dysfunctioning, small delay in psychomotor development, alterations in thyroid hormone and immunological status are associated with perinatal PCB and dioxin exposure[1]. We report results of background PCB and dioxin exposure in relation to cognitive development of Dutch children at 3½ years of age.

Methods

At 3½ years of age we examined 395 children, 94 % from the original 418 mother-infant pairs recruited in the period from 1990-1992. At that time healthy pregnant women were asked to volunteer for a prospective follow-up study in Rotterdam and Groningen. Subjects were included in the study, if they met the following criteria: (1) Pregnancy and delivery had to be without complications or serious illnesses. (2) First or second term born infants (37-42 wks of gestation). (3) No congenital anomalies or diseases. (4) Caucasian race. Women were included who intended to breast-feed their child for at least 6 weeks (breast-fed group) next to women who intended to give formula-feeding (formula-fed group). The medical ethics committees of both University Hospitals approved the study protocol.

Maternal and umbilical cord plasma samples were obtained in the last month of pregnancy and shortly after delivery. Plasma samples of children were collected at 3½ of age. Four PCB congeners, IUPAC n's 118, 138, 153 and 180 were analysed in maternal, cord and 3½-year plasma samples. The PCB sum (∑PCB) was calculated by adding up the 4 congeners in each plasma sample. Maternal milk samples were collected 2 weeks after delivery and analysed for 17 dioxin and 26 PCB congeners. The total toxic potency of all dioxins and 8 dioxin-like PCBs (IUPAC n's. 77, 126, 169, 105, 118, 156, 170 and 180) was calculated using the toxic equivalent factor (TEF) approach. The toxic equivalent (TEQ) was calculated by multiplying the concentration and the TEF value. The sum of all TEQ values yielded the total PCB/dioxin TEQ. Prenatal PCB exposure was estimated from PCB levels measured in maternal or cord plasma. Postnatal PCB and dioxin exposure was estimated by PCB and dioxin TEQ levels measured in breast milk multiplied by the number of weeks of breast-feeding. PCB levels at 3½ years of age are a measure of current exposure.

The cognitive abilities at 3½ years of age were assessed with the Dutch version of the Kaufmann Assessment Battery for Children (K-ABC). The Dutch version is standardized on a large sample of normal children, ages from 2.5 to 4.5 years of age[2]. This battery yields standard scores in 11 subtests measuring Sequential and Simultaneous processing. The scores of the sequential (SEQ) and simultaneous (SIM) scale result in an overall score the Cognitive scale (COG). These scores have a mean of 100 and a SD of 15.

Potential confounding variables for developmental outcome at pre-school age were selected from a list pertaining data on study centre, socio-economic background, maternal age, parents' educational level, birth order, gender and fetal exposure to alcohol and cigarette smoking, feeding type and period of breast-feeding. The child's home environment was assessed by the Dutch version of the home observation for the measurement of the environment[3]. The verbal IQ of the mother was assessed by 2 subtests of the verbal scale of the Wechsler Adult Intelligence Scale[4].

To investigate the effect of pre- and postnatal and current exposure to PCBs (and dioxins) on developmental outcome at 3½ years of age, we performed a multiple linear regression analysis. Each outcome variable was evaluated in three regression analyses, one for prenatal, one for postnatal, and one for current exposure, after adjustment for confounding variables. Results were significant if $p \leq 0.05$.

Results and Discussion

At 3½ years of age 395 children (94%) were examined from the original cohort of 418 children. From the remaining group, 203 were breast-fed (BF) and 193 were formula-fed (FF) in infancy. Finally, 380 children completed the Dutch version of the K-ABC test battery. None of the children had an abnormal score, below the -2 SD, all scores are within the normal range (Table). Mean scores were significantly, higher in the breast-fed group, however after adjustment for maternal education and HOME score, this effect did not remain significant.

In the final model all potential confounding variables mentioned in the methods section were entered as covariates next to the exposure variable. Results from multiple regression analyses showed that, prenatal PCB exposure, measured from maternal plasma ∑PCB levels, was significantly associated with lower scores on the Cognitive scale (n=373; β (SE) = -4.6 (1.6), $p<0.01$). This was also true for the Sequential as well as the Simultaneous scale of the Dutch K-ABC. Postnatal exposure to PCBs and dioxins measured from PCB- and dioxin-TEQs in breast milk and breast feeding period, and current exposure estimated from 3½-year plasma ∑PCB levels, were not associated with poorer performances on the three outcome variables.

Table: Test results at 3½ years of age, given for both feeding groups

	All n=380		Formula-Fed Group n=183		Breast-Fed Group n=197	
Dutch version K-ABC*	Mean	(SD)	Mean	(SD)	Mean	(SD)#
Cognitive Scale	111	(14)	108	(15)	114	(13)
-Sequential Scale	109	(14)	107	(14)	111	(14)
-Simultaneous Scale	109	(13)	106	(14)	112	(12)

*: Dutch version of the Kaufmann Assessment Battery for Children (Z&Z)
#: Student t-test, significantly higher than the formula-fed group, all p-values < 0.01.

These findings are in accordance to what Jacobson and colleagues have found in the "fish exposure cohort"[5,6], and are consistent with the reports of reduced IQ scores in children born from mothers exposed to accidental high levels of PCBs (and PCDFs) in Taiwan (Yucheng incident)[7]. However, when we compare our results with those of the North Carolina cohort by Gladen and Rogan, who also studied background exposure to PCBs, we found an effect of in utero exposure to PCBs on cognitive development at 3½ years, whereas the effects they found until 2 years of age was no longer apparent at 3, 4 and 5 years[8]. This difference could be due to higher background PCB levels found in the Netherlands compared to the USA[9], or due to different laboratory techniques used in measuring PCB exposure.

In conclusion, prenatal exposure to background PCB levels, is significantly associated with lower scores on cognitive abilities in Dutch pre-school children. Postnatal exposure to

PCBs and dioxins as well as current exposure to PCBs measured at 3½ years were not related with the cognitive outcome. Future studies in "background" exposed cohorts are needed to investigate what the long-term implications for later intellectual functioning will be.

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