A COHORT STUDY OF BEHAVIORAL PROBLEMS AND INTELLIGENCE IN CHILDREN WITH HIGH PRENATAL PCB EXPOSURE

Te-Jen Lai 1 , Xianchen Liu 2 , Leon Yue-Liang Guo 3 , Nai-Wen Guo 4 , Mei-Lin Yu 5, Chen-Chin Hsu 6 and Walter J. Rogan 2

Dept. of Psychiatry, Chung Shan Medical and Dental College, Taichung, Taiwan[1]; Epidemiology Branch, National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA[2]; Depts. of Occupational and Environmental Medicine[3] and Public Health[4], National Cheng Kung University Medical Center, Tainan, Taiwan; Dept. of Psychology, Kaohsiung Medical University, Kaohsiung, Taiwan[5]; Dept. of Psychiatry, En Chu Kong Hospital, San-shia, Taipei, Taiwan[6]

Introduction

In children, the most severe effects from exposure to PCBs and related compounds occurred among the offspring of women poisoned by complex mixtures of heat-degraded PCBs. In Taiwan in 1979, in the *Yucheng* incident, over 2,000 people became ill after they consumed cooking oil contaminated with heat-degraded PCBs. In the 3 years after the outbreak, 8/39 children born to exposed women died[1]. In 1985, we studied 117 of the 123 surviving children. They had ectodermal defects, developmental delay, more behavioral problems and higher activity levels[2]. Between 1985 and 1992, the exposed children's cognitive test scores were not improving relative to controls as they got older, nor was the effect smaller in children who were born up to 6 years after the exposure had taken place[3]. A similar pattern was seen on tests for behavior problems and increased activity[4]. We present here data from follow-up behavioral and cognitive testing of the same children through 1995.

Methods

In 1984 we located the 123 living *Yucheng* children, who had been born to 74 exposed women between June 1978 and March 1985 [2]; 117 of them attended a physical examination in April 1985, and 118 children participated in the cognitive and behavioral follow-up study. For each *Yucheng* child, a control matched on age (within 15 days for those under one year, and within one month for those older), sex, neighborhood, maternal age (within 3 years), and socioeconomic status was selected for the follow-up study. The exposed families were aware that they were participating in a follow-up study of the *Yucheng* children. The control families were told that they were participating in a general study of child development and behavior. We have followed the children using several different psychological instruments, because the children have different abilities at different ages. Here we report data from 1992 to 1995 for two psychological domains. For behavioral problems, we used the Child Behavior Checklist (CBCL) [5] to obtain standardized parents' reports on children's behavioral and emotional problems. For cognitive ability, we used the Chinese Version of Wechsler Intelligence Scales for Children-Revised (WISC-R), which yield an IQ. We compared the differences in IQ and

CBCL scale scores at each follow-up between exposed and controls using paired T tests. We also fit linear regression models to control for sex, year of birth and year of assessment and to address the possible mediating effect of elapsed time between exposure and birth on differences found between exposed children and their controls. To examine whether children born longer after the exposure are less affected, the children were separated by year of birth. Partial correlations were performed to examine relationships among age, IQ and CBCL scales after controlling for sex and year of assessment.

Results and Discussion

Of the original 118 matched pairs, 115 completed follow-up until 1991, 112 pairs in 1992, 100 in 1993, 105 in 1994, and 96 in 1995. For the CBCL, we looked for cohort effects by examining age-specific results for each birth year. We hypothesized that, at any given age, children born later after the exposure occurred should be less affected, that is, the difference between them and their controls should be smaller. However, we saw no evidence of that, which allowed us to test the hypothesis that the exposed children's behavior was recovering relative to controls as they get older by looking at the age-specific differences between exposed and control children, collapsing over the year in which the child was born. The total score from the CBCL in Yucheng children declined from 11 years of age on, while scores for their controls did not show this tendency (Table 1).

Table 1: Mean Scores (SD) of CBCL in Yucheng Children and Controls by Age

Age	Yucheng		Control		
(years)	n	M(SD)	n	M(SD)	Δ
7	18	54.1(13.6)	19	48.8(9.9)	5.5
8	34	52.8(12.6)	34	47.5(8.3)	5.3*
9	45	53.9(12.1)	48	50.0(9.2)	3.9
10	66	53.2(11.9)	67	48.8(8.0)	4.4**
11	59	51.8(9.9)	53	49.0(9.7)	3.3
12	78	51.7(11.1)	77	47.7(7.9)	4.1**
13	63	51.2(11.7)	62	47.9(9.2)	3.4
14	62	51.2(11.4)	60	48.5(8.3)	2.7
15	41	49.7(9.2)	43	48.2(7.1)	1.4
16	33	48.1(7.8)	47	47.0(7.1)	1.4

CBCL: Child Behavior Checklist

Δ represents mean of (Yucheng score – control score) after controlling for sex, year of birth and year of assessment, using linear regression models.

For cognitive function, we also hypothesized that, at any given age, cognition in children born later after the exposure occurred should be less affected, that is, the difference between them and their controls should be smaller. However, as with the CBCL scores, there is no consistent tendency for the paired difference in the cognitive scores to be smaller among the children born later. The absence of such a cohort effect allows us to examine whether the children are less affected as they get older by comparing the differences in the age-specific means, collapsing over year of birth. In contrast to behavioral problems, differences of IQ between exposed children and their controls did not to decline

with advancing age.

(Table 2).

TABLE 2. Mean IQ (SD) in Yucheng Children and Controls by Age

	Yucheng		Control		
Age (years)	n	M(SD)	n	M(SD)	Δ
7	19	99.8(13.4)	19	99.6(14.0)	0.3
8	34	97.5(14.7)	35	102.3(13.8)	-4.8
9	45	100.2(13.9)	47	104.2(11.6)	-3.9
10	66	100.6(15.9)	67	104.3(11.6)	-3.8
11	59	99.8(15.9)	56	106.2(9.9)	-6.4*
12	66	103.8(15.2)	66	107.7(10.7)	-3.9
13	55	101.9(14.3)	55	104.8(12.4)	-3.0
14	36	104.2(13.4)	37	105.8(13.2)	-1.6
15	24	97.0(15.5)	28	103.5(9.3)	-4.6

Δ represents mean of (Yucheng score – control score) after controlling for sex, year of birth and year of assessment, using linear regression models.
*P<0.01; (Student t test)

We find that children born to PCB-poisoned mothers continue to have mild effects on their behavior when tested in 1992 to 1995. We find that the youngest children show the greatest effect, no matter how long after the exposure they were born, but the older children are recovering. For cognitive function, however, the differences between the exposed and control children still show no decline as the children get older. Together with our previous observations [3], these data suggest that *Yucheng* children had persistent cognitive deficit up to 16 years of age. Behavioral alterations appear in animals exposed perinatally to PCBs. The most consistent finding is hyperactivity among animals exposed to PCBs *in utero*, and it was observed in mice, male rats, and rhesus monkeys [6]. One group of rhesus monkeys that had been exposed to PCBs perinatally was hyperactive at six and twelve months of age but was hypoactive at 44 months test [7].
The continued mild behavioral disorder and cognitive deficits in these children is likely due to the persistence of the chemicals in their mothers resulting in *in-utero* exposure long after the exposure to the mother ceased. Even though the levels in the mothers were declining, there appeared to be sufficient agent to be toxic for at least six years after the exposure. The biological mechanism by which these PCBs, which are contaminated with polychlorinated dibenzofurans and other compounds, cause behavioral and cognitive toxicity is unclear, and is an area of ongoing laboratory investigation.

References

1. Hsu ST, Ma CI, Hsu SK, Wu SS, Hsu NH, Yeh C, Wu SB (1985). Environ Health Perspect.59, 5-10.

2. Rogan WJ, Gladen BC, Hung KL, Koong SL, Shih LY, Taylor JS, Wu YC, Yang D, Ragan NB, Hsu CC (1988). Science. 241, 334-336.

3. Chen YCJ, Guo YL, Hsu CC, Rogan WJ (1992) JAMA. 268, 3213-3218.

4. Chen Y-CJ, Yu M-LM, Rogan WJ, Gladen BC, Hsu CC (1994). Am J Public Health. 84, 415-421.

5. Achenbach TM. *Manual for the Child Behavior Checklist/4-18 and 1991 profile.* Burlington, VT: University of Vermont Department of Psychiatry; 1991:-288.

6. Tilson HA, Jacobson JL, Rogan WJ (1990). Neurotoxicol Teratol.12, 239-248.

7. Bowman RE, Heironimus MP (1981). Neurobehav Toxicol Teratol.3, 15-18.