行政院國家科學委員會專題研究計畫　成果報告

環境職業生殖危害（四）—鉛暴露工人受孕所需時間及其下一代出生異常與神經行為障礙之研究

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Environmental and occupational reproductive hazards (4) - Time-to-pregnancy study, and adverse birth outcomes and neurobehavioral deficits among the offspring of lead exposed workers

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一、中文摘要

環境與職業中的鉛暴露造成的健康效應在過去幾十年中已廣泛地被探討，鉛可能會對神經系統產生有害效應，並對認知、記憶力、智力等方面產生影響；但對於鉛暴露工人的下一代的健康效應則鮮少研究。本研究是回溯性世代研究，選定 34 位其父親在受孕期間或是母親在懷孕期間受到鉛暴露且年齡為六至八歲的小孩，個別進行問卷訪視以及神經行為的測量；此外，依照暴露來源分類：父親受暴露、母親受暴露以及雙親皆受到暴露，其血鉛平均值分別是 23.3、14.0 及 25.5 μg/dl。依據研究結果，連續性操作當中的按錯次數在不同暴露來源分組中會呈現出生前鉛暴露劑量越高，錯誤次數也有顯著地增加。第二部份為選一非工業區鄉鎮，並選定一間國民小學之一至三年級小朋友視為參考族群，進行相同的問卷以及神經行為測量。再依性別、年齡以 1 比 4 配對出 136 位小朋友作為本研究之非暴露組，比較兩組在控制其它變項後出生前鉛暴露與神經行為表現之相關性。有許多測驗項目包括手指敲擊、連續性操作、視覺數字反應以及圖像記憶等，在比較有無暴露兩組神經行為結果上有達到統計上顯著差異。本研究的結果指出出生前的鉛暴露對於後來的神經行為發展的影響在處理干擾因子後可能因為樣本數不足而無法看出效應。此外，本研究首次以電腦化「神經行為表現測驗」測量出生前鉛暴露對學齡時期孩童的神經行為發展情形，可能因為該工具對此劑量造成之效應敏感度不足所致。本研究限制主要是樣本數不足以及未取得出生後環境鉛暴露之直接生物指標。

關鍵詞：兒童、鉛、神經行為測驗、出生前暴露後來效應

Abstract

Environmental and occupational lead exposure induced health effect has been widely explored in several decades. Lead might produce adverse effect to nervous system and influence cognition, memory and intelligence. However, few studies have yet investigated its effect on reproduction and potential effect on offspring. The present study was a retrospective cohort study. We selected 34 valid children whose ages were between six and eight years and one or both of their parents worked at lead battery factories before their deliveries. We individually interviewed their parents to complete questionnaire and conducted a neurobehavioral test using Chinese version neurobehavioral performance system (NES2). We used annual examination of blood lead and divided into three groups, namely, paternal, maternal and parental exposure whose mean blood lead were 23.3, 14.0 and 25.5μg/dl, respectively. The results showed error counts of continuous performance test would significantly increase with an elevation of prenatal lead exposure dose. Moreover, we selected the children of an elementary school in non-industrial area as a reference population. We used a 1:4 ratio of exposure to non-exposure subjects with same gender and age. These 136 children subgroup were considered as a non-exposure group. After controlling potential confounders there were significantly differences between exposure and non-exposure group in several test items such as finger tapping and continuous performance test. The study was the first time to measure neurobehavioral effect of prenatal lead exposure in school age. The results demonstrated prenatal lead exposure might induce minimal effect of

lately neurobehavioral development. Our limited evidence may come from small sample size, lack of lead exposure data after delivery, and insensitive neurobehavioral measure for the lead effects.

Keywords: children, lead, neurobehavioral test, prenatal exposure delayed effects

二、緣由與目的

.Lead was an ancient mental and been extensively used in industrial and medical field. In Taiwan the major sources of lead were industrial pollution and exhaust gas from motor vehicles. Leaded gasoline was totally phase out in Taiwan but environmental and contamination has been deposited. In addition to environmental pollution, industrial lead was still a serious and potential problem. The major routes of environmental lead pollution would be absorbed by human were ingestion and inhalation. Blood lead value was generally an index of acute exposure and reflected shorten period exposure level. But lead toxicity appeared to be cumulative and irreversible and long-term lead would be stored in bone or tooth.

Environmental lead exposure was proven that lead caused health hazard in general population and lead workers. Previous studies revealed lead induced disorder in hematopoietic system, nervous system, reproductive system kidney and psychology.[1-3] Lead has long been considered a neurotoxicant. The question of low-level lead exposure has been studied widely over the past several decades. As mentioned in a previous study, children residing near a battery factory had lower intelligence than control group.[1-4] In most studies to be associated with diminished cognitive and perceptual function in children and young adults.[5-9] As above many epidemiological studies have demonstrated inverse associations between blood lead concentrations and children's IQ at successively lower lead concentrations.[10,11]

Neurobehavioral was a part of neuropsychology and its definition was behavioral alteration due to cranial nerve damaged or neurology deficit. Neuropsychological dysfunction caused by occupational exposure to lead,[12-14] methylmercury,[15] arsenic,[16] and organic solvent[17,18] have been documented in many studies. But it was a controversial issue whether the offspring of lead workers would be affected or not. In addition, lead exposure caused latterly adverse effect on intelligence development, sensor-motor skill, sustained attention and achievement performance during school age.[19-23] DNA-protein cross-links (DPCs), sister chromatid exchanges (SCEs) and high-SCE frequency cells (HFCs) were reliable biomakers for monitoring workers exposure to lead.[24] We suggested prenatal lead exposure induced genetic level effect might influence the development of offspring of the lead workers.

Likely above described recent long-term effect of lead was widely respected topic of research.[25] Blood lead was generallyconsidered currently exposure level. The half-life of lead in blood was 36±5 days. Thus presently accumulative lead level was estimated tibia bone or shed deciduous tooth instead of blood.26 Many studies used X-ray fluorescence (XRF) to estimate skeletal concentrations of lead to explore the association between long-term lead exposed from environmental or occupational and neurobehavioral effect.[26,27] But considered measurement sensitivity and practicability, it was a feasible way to collect shed deciduous tooth to represent the children's accumulative lead exposed. Deciduous dentine may be shown to be particularly useful biomarker in the reconstruction of records of in-utero exposures to Pb.[28,29] Several studies clarified tooth lead level related to lately IQ and neurobehavioral development.[30,31]

Furthermore several studies on rats and other rodents indicated that lead exposure were associated with reproductive effect, especially in male workers, including impairment of spermatogenesis and chromosomal alteration.[32-34] Adverse effects of lead on sperm concentration and susceptibility to acid induced denaturation of sperm chromatin are unlikely at blood lead concentrations below 45 μg/dl.[32]

Although several evidences proposed that lead would induce neurobehavioral performance including motor skill and cognitive ability, health effect from prenatal lead exposure was still controversial. Thus the study explored difference between three prenatal lead sources, maternal, paternal and parental, and neurobehavioral effect. On the other hand we compared neurobehavioral performance and a few of characteristics and developmental condition of exposure and non-exposure group to know efficiency of prenatal lead level.

三、材料與方法

3.1 The pilot study

This pilot study was to identify appropriate NES subtests and to estimate test time for each subtest. We selected three classes from 1st-, 2nd-, and 3rd- grades in an elementary school where resided in Taipei city. Two assistants introduced the NES test to the children first. We tested all students of one class at an information classroom in the same time. Based on this pilot study, we found most of children could not understand backward span of Visual Digit Span and some of children would talk and attempt to help each other. Thus, test time of Continuous Performance test (CPT) was 5 minutes originally which may be too long to children and we shortened the test time of CPT in 3 minutes in the main study. Secondly, we increase manpower support in the main study.

3.2 Study Population

Exposure group

This was a retrospective cohort study to evaluate neurobehavioral development of lead-exposure workers' offspring. The workers' information was collected from the Bureau of Labor Insurance (BLI) including identification number (ID), date of birth, gender, dates of employment and discharge, and job title. As each factory, which employs more than 5 workers, is compulsory to join the national labor insurance by law. There were 11,608 workers in the lead battery industries in Taiwan. We linked the data with 1978-2001 Taiwan birth database and a total of 14,803 children were born in the period. Considering shedding age of deciduous teeth (age 6-8 and born in 1994-1996), the availability of their parents' blood lead measurements, and the exposue windows including preconceptional and prenatal stages for each child, there were 461 children in total. However, we choose only 70 children whose parents worked in lead-battery factories of Tainan County in this study.

Non-exposure group

We also selected an elementary school in non-industrial area whose has the same developmental level with the town of lead-battery factories. A total of 938 students of 1st, 2nd and 3rd grades completed the same questionnaire and nurobehavioral evaluation system test. We matched children's age and gender and their parents' education level in a 1:4 basis of exposure to non-exposure subjects and, then, 136 children were randomly selected as a non-exposure group.

3.3 Lead Exposure Measures

Preconceptional and prenatal lead of children was obtained from parents' occupational blood lead, which was measured before or during pregnancy. The blood lead data was from a notification database since July 1993, called Program to Reduce Exposure by Surveillance System-Blood Lead Levels (PRESS-BLLs).[35] Data was divided into three groups of maternal only, paternal only, and parental exposure. Figure 1 shows average blood lead values of these lead exposures.

3.4 Neurobehavioral Test

Considering the practicable and suitable to children who were 6-8 years old, we used the Chinese version of Neurobehavioral Evaluation System-2 (CNES-2),[36,] which included attention, learning, memory, visual-span, motor, and verbal skill functional categories. According to previous literature and the pilot study, we selected five subtests including finger tapping (FT), continuous performance test (CPT), visual digit span (VDS), pattern memory (PM), and pattern comparison (PC) in this study.

Finger Tapping

Children were required to press a specified button on keyboard with the preferred and non-preferred hand in turn. Then completed with alternative hands and it was using two buttons. There was one trial in every subtest and individually spent 15-s. This test evaluated motor response speed of children.

Continuous Performance Test

Five kinds of geometric shapes were randomly displayed on the screen and the children were instructed to tap the keyboard as soon as possible after a triangle was displayed on the screen. Three positive stimuli were given randomly and stimuli. Reaction time, omission, and errors were recorded. This test measured sustained visual attention, contrast sensitivity and response latency.

Visual Digit Span

Children were instructed to reproduce longer series of digits (forward span) that were displayed individually for 600 ms with an inter-stimulus interval of 1000 ms. Initial forward and backward span lengths were three and two digits respectively. Longer spans are increasingly presented until the child makes two errors in a span length. The measures included the lengths of the longest span answered correctly forward and backward. This test was a test for measuring short-term memory and visual memory function.

Pattern Memory

There was an array within dark and light blocks showing on the screen. Then three patterns displayed on the screen and the children had to select an array the same as former. There were 15 trials in the item and modified the difficult level to suit the ability of children.

Pattern Comparison

Three stimulus arrays (each 10*10 elements) were presented simultaneously on the screen. Individual squares within each array were either dark or light. Two of the arrays were identical. The children had to select the different array as rapid as possible. Response time and number of errors were recorded.

Both of exposure and non-exposure group were using notebook to test. Nevertheless, exposure group all test in face to face at home and introduced by a measurer. In contrast to non-exposure group were test in a classroom and was applied on a class as the basic unit.

3.5 Potential Confounders

The questionnaire obtained the information on demography characteristics and disease history of children, occupation and education level of parents, and their general life style such as smoking and drinking habits during the pregnancy period. Detail items were showed on Appendix A. Family income in the questionnaire was considered a proxy of social economical status, which was partially correlated to home rearing.

3.6 Statistical Analysis

Independent Student's t test was used to compare the NES results between the exposure and non-exposure groups. One-way ANOVA test was employed in comparing the neurobehavioral effect among the three lead exposure groups, namely paternal only, maternal only, and parental. Furthermore, we explored the association between lead exposure and neurobehavioral performance after controlling potential confounders using multiple linear regression models. Confounders or covariates were selected on the basis of previous literature. There were 17 independent variables in final models, namely gender, age, height, body mass index (BMI), birth weight, parity, paternal and maternal education, distances from children's house to petrol station and street, postnatal wage years of parental, computerized game familiarity, income, and five questions before test: do you wear glasses now, how long did you sleep last night, do you feel right now, did you intake any caffeine in 24 hours ago, did you take any drug that affected your attention. Two-tailed probability of p=0.05 was chosen for significance testing in statistic.

四、結果與討論

Table 1 presented characteristics of exposure group. Dividing into three subgroups, maternal, paternal and parental groups, and average blood lead levels were showed in Figure 1 and Table 2. Parental exposure during pregnancy has the highest level (PbB=25.5 μg/dl) and paternal exposure has moderate lead level (PbB=23.3 μg/dl) and finally maternal exposure group has suffered with the lowest lead (PbB=14.0 μg/dl). Height and weight displayed relationship in trend with average lead values, likely with a previous study.[45] Except factors showed on Table 1, other factors in questionnaire such as disease and intake drug in pregnancy, Mother smoking or drinking, computerize game familiarity, distance from gasoline station were mostly consistent in every subjects.

Table 3 described characteristics of exposure and non-exposure. Only parity and height were significant in independent T test and exposure group was comparable with non-exposure group.

Table1 Characteristics of exposure group. (N=34)

	Parental	Paternal	Maternal	Subtotal
N	6	11	17	34
Age	7.0	7.2	7.1	7.1
Gender				
Boy	1	4	9	14
Girl	5	7	8	20
Parity				
1	4	10	15	29
2	2	1	2	5
Birth weight(g)				
Mean				
SD	2958.3 (267.2)	3280.5 (664.6)	3147.1 (365.6)	3158.4 (470.9)
Gestation weeks				
Mean	39.0	39.6	39.5	39.4
SD	(1.8)	(1.8)	(1.1)	(1.4)
Height(cm)				
Mean	112.8	121.3	120.7	119.4
SD	(6.7)	(8.3)	(11.9)	(10.1)
Weight(kg)				
Mean	23.0	23.7	25.3	24.3
SD	(3.6)	(5.2)	(7.1)	(5.9)
Body Mass Index				
Mean	19.3	16.2	16.7	16.9
SD	(4.6)	(2.4)	(2.7)	(2.9)
Paternal education	0	2	2	4
Above senior	6	9	15	30
Below junior				
Maternal education	0	1	1	2
Above senior	6	10	16	32
Below junior				
Father Smoke				
Yes	5	5	8	18
No	1	6	9	16
Father drinking				
Yes	2	4	4	10
No	4	7	13	24
Father change working clothes	2	5	-	7
Mother change working clothes	2	-	5	7
Road distance(m)				
<10	0	0	1	1
10-50	0	4	3	7
50-100	2	1	4	7
>100	3	5	8	16
Missing	1	1	1	3
Current family income(NT/month)	0	0	1	1
<10000	0	0	2	2
10000-30000	4	4	2	10
30000-50000	2	7	10	19
>50000	0	0	2	2
Missing				
Breast feeding				
Yes	2	5	2	9
No	4	6	15	25

Table 2. Blood lead of maternal, paternal and parental exposure group.

	N	PbB(μg/dl) Mean ± SD
Parental	6	25.5± 11.7
Paternal	11	23.3± 13.5
Maternal	17	14.0± 11.3

Figure1 Blood lead distribution of subgroups.

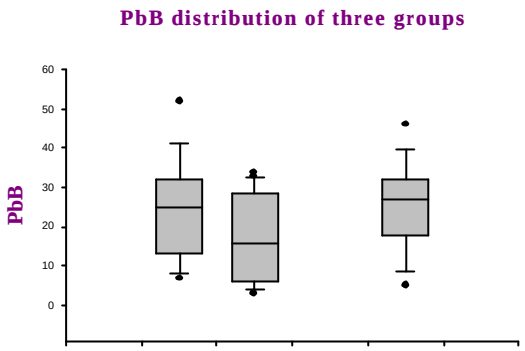

Table 3. Factors in exposure and non exposure

	Exposure N=34	Non-exposure N=136
Children age		
Mean±SD	7.7± 0.6	7.7± 0.6
Gender		
Boy	14	69
Girl	20	101
Maternal age in pregnancy		
Mean±SD	27.6± 3.8	28.1± 5.0
Birth weight (g)		
Mean±SD	3158.4± 470.7	3160.0± 475.2
Gestation weeks		
Mean±SD	39.4± 1.4	39.0± 1.6
Parity*		
1	29	64
2	5	51
3		14
4		5
5		2
Height (cm)*	119.7± 10.3	123.1± 7.0
Weight (kg)	24.5± 6.1	25.5± 5.1
Body Mass Index (BMI)	16.8± 3.1	16.8± 2.3
Paternal education		
Above senior high school	4	31
Below junior high school	30	104
Missing	0	1
Maternal education		
Above senior high school	2	13
Below junior high school	32	122
Missing	0	1
Distance from petrol station (m)		1
<10		4
10-50		10
50-100	32	116
>100	2	5
Missing		
Distance from road (m)		
<10	1	20
10-50	7	22
50-100	7	20
>100	16	66
Missing	3	8
Computer game familiarity		
Yes	5	41
No	28	92
Missing	1	3
Current family income (NT/month)		
<10000	1	3
10000-30000	2	13
30000-50000	10	50
>50000	19	60
missing	2	10

*p<0.05 in independent T test

4.1 Neurobehavioral performances test

Table 4 indicates eleven test outcomes in three subgroups in exposure group. Only comission of CPT test is significantly differ among three subgroups. In addiction there are four outcomes, FT, CPT (non-response), VDS (backward) and PM (incorrect count), showed that the poorest performance group is parental exposure. One the other hand, Table 5 shows neurobehavioral performance in exposure and non-exposure group. Preliminarily analysis in independent T test mention that FT, CPT (false positive and latency), VDS (forward), PM (correct and error latency) are different between two groups.

4.2 NES between exposure and non-exposure groups

Due to without biological postnatal exposure index instead of parental work seniority which was recorded in Bureau of Labor Insurance (BLI). Because most of parents of exposure group were not change working clothes before went home, we suggest parental work seniority is an indirect index of mainly postnatal environmental exposure.

Table 4 indicates that the relationship between different prenatal exposure sources. Furthermore, table 5 provided association between neurobehavioral performance and exposure or not. As table6, considering risk factor effect, birth weight has significant or borderline effect to finger tapping (preferred hand) and continuous performance test (non-response). Family income is a proxy of social economical status and is concerned with home education and it is borderline effect to finger tapping (preferred hand). Height is a developmental index and it is a significant influence finger tapping (non-preferred hand) and visual digit span (forward). Owing to NES is a computerize test thus children's familiarity in using computers is an important factors should be considered. As the tables show, playing computer game is a significant or borderline factor to continuous performance test (latency) and finger tapping (alternative hand). Attention would influence neurobehavioral test outcomes. Before NES test there were several questions to assure mental and spirit condition. One of the questions is 'how long were you slept last night' and the factor was significant to visual digit span (forward). Prenatal lead exposure is a main

target in the study and as tables mention that prenatal lead exposure is a significant factor in continuous performance test latency. Postnatal environmental lead exposure is expecting considered a major confounder. Work seniority is a borderline effect to continuous performance test latency. Likewise, distance from house to nearly gasoline station is a significant factor in average responsive time of error pattern memory.

This study evaluated the neurobehavioral development of offspring among the lead exposure workers. Considering subclinical symptoms were undetected in several clinical diagnose batteries. We included the children who between six to eight years old and one of or both of their parents who worked in a battery industry during pregnancy to be exposure group. In order to identify risk factors in CNES-2 test in measuring children, we selected a non-exposure group but we excluded children who did not complete questionnaire or CNES-2. The procedure may produce selection bias.

Several batteries were used to evaluate the neurobehavioral development such as WHO - Neurobehavioral Core Test Battery (WHO-NCTB), Pediatric Environmental Neurobehavioral Test Battery (PENTB)[38-,40] and neurobehavioral evaluation system (NES).[41,42] Initially, NES was used to investigate the effect of potential toxic substance on CNS function of adult.[43] Modified the test items in NES to appropriate children to operate.[44] Furthermore, NES was modified to the Chinese version of Neurobehavioral Evaluation System-2, CNES-2).[36,37] The CNES-2 was a computer-assisted test and it could be extensive processed simultaneously.

Table 4. NES results of subgroups of exposure groups.

Test	Measurement	All(N=34)		Parental(n3=6)		Paternal(n2=11)		Maternal(n1=17)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Finger Tapping	Preferred hand	62.2	13.7	51.7	14.4	65.0	9.3	64.2	14.8
	Nonpreferred hand	56.6	11.1	52.5	12.2	59.4	9.4	56.3	11.8
	Alternating hand	30.6	12.7	25.2	12.2	34.6	13.3	29.9	12.4
Continuous	Omission	1.6	2.2	2.7	2.1	0.6	1.5	1.9	2.4
Performance Test	Comission*	1.9	1.5	1.5	1.1	1.1	0.9	2.6	1.7
	Latency	607.1	87.2	612.6	100.0	596.8	76.0	611.9	94.1
Visual Digit Span	Forward span	3.6	2.4	2.3	2.7	4.0	2.8	3.8	2.0
	Backward span	2.8	1.5	2.3	0.5	3.1	1.5	2.7	1.8
Patten Memory	Incorrect count	1.0	1.2	1.7	1.6	0.6	0.7	1.0	1.2
	Correct latency	3304.4	2173.0	1983.0	905.0	4369.6	2446.3	3081.5	2062.7
	(ms)	5040.0	3826.4	2507.7	1184.7	9247.8	3324.0	3827.6	3076.1
	Error latency (ms)*								
Pattern	Incorrect count	1.1	2.1	1.3	2.3	0.3	0.7	1.5	2.6
Comparison	Correct latency	5404.5	1274.3	4760.5	517.0	5706.9	953.4	5436.2	1574.2
	(ms)	5641.3	1633.4	5028.7	483.0	5682.0	1346.3	5860.8	2007.8
	Error latency (ms)								

Table 5. Results of NES between exposure and non-exposure groups.

Test	Measurement	Exposure		Non-exposure		P
		Mean	SD	Mean	SD	
Finger Tapping	Preferred hand	62.2	13.7	74.9	12.5	.000
	Nonpreferred hand	56.6	11.1	68.2	11.9	.000
	Alternating hand	30.6	12.7	45.5	19.5	.000
Continuous	Nonresponse	1.6	2.2	1.6	2.3	.853
Performance Test	False positives	1.9	1.5	3.4	2.4	.000
	latency	607.1	87.2	551.3	80.0	.000
Visual Digit Span	Forward span	3.6	2.4	5.0	2.1	.002
	Backward span	2.8	1.5	2.8	2.0	.984
Patten Memory	Incorrected count	1.0	1.2	0.9	1.0	.589
	Correct Latency (ms)	3304.4	2173.0	6068.4	1791.6	.000
	Error Latency (ms)	5039.9	3826.4	8064.4	3694.2	.003
Pattern Comparison	Incorrected count	1.1	2.1	1.3	2.8	.675
	Correct Latency (ms)	5404.5	1274.3	6087.4	2058.9	.067
	Error Latency (ms)	5641.3	1633.4	6891.8	5121.3	.390

Table 6. Multiple linear regresstion of exp. and non-exp. group.

Test	Measurement	Unstandardized Coefficients β	Std. Error	t	Sig.
Finger Tapping	Preferred hand	-5.106	6.020	-.848	.399
	Nonpreferred hand	-8.192	6.081	-1.347	.181
	Alternating hand	-5.426	9.955	-.545	.587
Continuous	Nonresponse	-1.548	1.317	-1.175	.243
Performance Test	False positives	-1.710	1.185	-1.443	.152
	Latency*	128.296	38.699	3.315	.001
Visual Digit Span	Forward span	-.434	1.149	-.377	.707
	Backward span	9.932E-02	1.027	-.097	.923
Patten Memory	Incorrected count	-.161	.589	-.273	.786
	Correct Latency (ms)	-1697.3975	1078.107	-1.575	.119
	Error Latency (ms)	4047.318	2432.435	1.664	.101
Pattern Comparison	Incorrected count	-1.722	1.415	-1.217	.227
	Correct Latency (ms)	-803.109	1096.398	-.732	.466
	Error Latency (ms)	3050.449	2417.020	1.262	.210

Model after controlling factors including, postnatal exposure years, gender, children age, height, weight, BMI, parity, BW, paternal and maternal education, distance from gasoline station and road, computerized familiarity, family income, and five pretest questions.

Limitation of age rang from six to eight because the present information of Program to Reduce Exposure by Surveillance System-Blood Lead Levels (PRESS-BLLs) was 1993-1998. And school age children could test in a school classroom.

Results revealed prenatal parental exposure group would be lower birth weight than other two groups. As well as birth weight, height was a growth developmental index and shown similar outcome, which was consistent with previous studies.[45,46] As shown in Table 4, CPT (comission) and PM (error latency) were different between maternal, paternal and parental exposure in ANOVA test. According to blood lead level, parental exposure has the highest lead exposure dose and maternal exposure group suffered the lowest dose. Most NES outcomes such as finger tapping, continuous performance test (non-response), visual digit span and pattern memory (incorrect count.) were observed that the children of parental exposure group were performed poorer neurobehavioral performance. However paternal exposure effect was not significantly observed. It might be the sample size was not large enough and the dose was too low to detect.

Comparison of exposure versus non-exposure group, there was only continuous performance test would be significantly influenced by lead exposure. Lead-relatived disruption of serial reaction performance has tentatively been interpreted in terms of impulsiveness or reduced inhibitory control.[47] After controlling for possible confounding factors of age, gender, education level of parental, birth outcome and possible postnatal exposure level, the study showed that continuous performance test, used to measure sustain visual attention, was a significant effect of two group even exposure level was below 30μg/dl. A negative association between tapping and lead exposure in children has been demonstrated.[48] But the association was not obvious in the study, it might be owing to sample size was insufficient or test setting were different.

In spite of we used wage years of parents to be postnatal exposure level, it was great that if we could directly measure postnatal cumulative lead level. As far as non-exposure group we did not obtain long term exposure data such as tibia bone or shed deciduous tooth lead. On the other hand, due to PRESS-BLLs was recorded blood lead value per year thus we could not distinguish what pregnancy phase that measured. However, the HOME scale, which was taken into account in many recent prospective lead studies, was not available here. Thus, causative role of prenatal lead in affecting lately neurobehavioral remain equivocal.

The objective of this study was to know whether prenatal lead exposure would induce genetic level effect and influenced neurobehavioral of offspring of the lead workers. Nevertheless, sample size was not large enough to interpret causal association and after control confounding factors we still could not observe significant effect. The Chinese version neurobehavioral performance test (CNES) was never used in testing children's neurobehavioral before; neither was applied on a class as the basic unit. The study was the first to measure neurobehavioral effect of prenatal lead exposure at school age. The results demonstrated prenatal lead exposure might induce minimal effect of lately neurobehavioral development.

In addition to factors considered in the study, children neuropsychology problem such as attention deficit and hyperactivity disorder (ADHD) was an important factor. Although we ask related questions in

questionnaire, obtain clinical data would be better.

Prenatal lead was induced minimal neurobehavioral effect in children. Parental effect was still controversial. In present study, limited evidence may come from small sample size, lack of lead exposure data after delivery, and insensitive neurobehavioral measure for minimal lead effects. We suggest that further studies can enlarge sample size and measure accurate postnatal lead exposure level to assure causal association.

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