

暴露於神經毒物的台灣老年人其記憶缺失 及記憶抱怨的評估

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摘要

神經毒物例如多氯聯苯 (Polychlorinated biphenyls-PCBs) 或多慮呋喃 (polychlorinated dibenzofurans-PCDFs)，主要影響神經系統功能運作。近年來研究發現暴露於上述毒物的成年人會有記憶及學習障礙，但很少研究這些人是否會有記憶障礙、主觀記憶抱怨及自主生理狀況不良的情形。本研究希望了解神經毒物，對於易感族群的老年人，是否會影響其記憶功能、主觀記憶抱怨，或生理身體狀況不良的情形。

本回溯性研究為 1979 年台灣“油症”暴露患者，其中年齡≥60 歲之老年人為收案對象，並重新訪談及測試。我們使用結構性且信效度良好的問卷，及中文版魏氏智力測驗第三版(WAIS-R-III)，還有魏氏記憶評估修訂版(WMS-R)作為主要工具。記憶功能含符號特徵(Digit Span)，視覺記憶 (Visual Memory Span)，注意力及數字廣度(Attention and Digit Span)，語言記憶測試(Verbal Memory Recalls)，學習能力 (learning ability)，30 分鐘回憶測試(30-minute delayed recall)，及主觀記憶抱怨等(subjective memory complaints)評估。從 328 樣本數中，166 人為暴露者，及 162 人為非暴露者。暴露組比起非暴露組有較多的身體生理狀況抱怨，諸如指甲變型、貧血、氣喘、高血壓、及皮質角化，呈顯著性差異。此外記憶功能如 ADS，VMS，學習能力，語言記憶的第 4,5 次測試，及 30 分鐘回憶測試等，兩者亦呈顯著性差異($p < 0.05$)。而主觀記憶抱怨和 VMR ($p = 0.04$)及 ADS ($p = 0.03$) 亦呈正相關性。本世代追蹤中研究中，暴露於神經毒物如 PCBs/PCDFs 的老年人，其主觀身體生理功能抱怨、記憶功能評估及主觀記憶抱怨，皆比未暴露者來得多。結論顯示過去暴露於神經毒物的患者，容易導致身體上的、精神上的負擔，以及記憶功能之缺失。研究說明環境污染應該預防勝於治療。

關鍵詞：神經毒物、記憶功能、主觀記憶抱怨、身體生理狀況、老年人

Memory Impairments and Memory Complaints in the Elderly Exposed to Neurotoxin in Taiwan

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Abstract

Received: Feb. 19, 2012; accepted: April, 2012.

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Neurotoxins, such as Polychlorinated biphenyls (PCBs) and polychlorinated dibenzofurans (PCDFs), affect central nervous system functioning. Recent studies have shown that elderly individuals exposed to these toxic compounds have reported memory and learning deficits. Little is known about the reported health status, memory function and memory complaints of these elderly individuals. This study aimed to evaluate memory-related issues and health conditions in elderly individuals exposed to neurotoxin of PCBs and/or PCDFs.

We conducted a retrospective cohort study of the Yu-Cheng population in Taiwan. Registered subjects and matched controls (age \geq 60 years) were recruited. We utilized self-reported health questionnaires and neuropsychological tests of the Wechsler Adult Intelligence Scale-Revised version in Chinese (WAIS-R-III) and the Wechsler Memory Scale-Revised (WMS-R). Memory modalities such as digit symbol (DS), visual memory span (VMS), attention and digit span (ADS), 5-trial verbal memory recalls (VMR), learning ability, 30-min delayed recall, and subjective memory complaints (SMCs) were evaluated. We analyzed a total of 328 subjects; 166 subjects were PCB/PCDF-exposed subjects and 162 were non-exposed subjects. The exposed elderly subjects were more likely to report health conditions such as nail deformity, anemia, asthma, hypertension, and hyperkeratosis. In addition, memory tests revealed a decline in ADS, VMS, learning ability, trial 4 and trial 5 of the VMR, and 30-min delayed recall test results in exposed subjects ($p < 0.05$). The SMCs correlated significantly with memory decline in the VMR ($p = 0.04$) and ADS ($p = 0.03$) tests. In the Taiwanese cohort, the elderly subjects exposed to PCBs/PCDFs reported more health problems, memory decline, and memory complaints. Our results provided evidence that exposure to neurotoxins may lead to physical and psychological burdens as well as memory complaints in future follow-ups. The results also demonstrated preventive strategies in environmental protection are more important than treatment after toxic exposure.

Keywords: Neurotoxin, Memory Tests, Subjective Memory Complaints, Reported Health Consequences, Elderly

I. Introduction

Polychlorinated biphenyls (PCBs) and the derivatives of polychlorinated dibenzofurans (PCDFs) are neurotoxin chemicals [1-2], and their use has been discontinued in Taiwan [3]. The most serious public health event in Taiwan's history was the outbreak caused by PCB contamination (Yu-Cheng episode) in 1979 [4-6]. People who consumed PCB-contaminated rice oil suffered from skin chloracne, arthritis, neuropathy, headache, and general malaise [7]. A follow-up study revealed adverse consequences, including metabolic abnormality, reproductive disorders, developmental retardation, and memory deficits in adolescents and the elderly [6, 8-11]. Although PCDFs had become important recently, the toxic mechanisms to human body are far less known to PCBs.

Polychlorinated biphenyls can affect the central nervous system because they are lipophilic and can accumulate in fat. The impact on cognitive functions may relate to the results of disruptions of thyroid hormones, neurotransmitters or other mechanisms [8, 12]. Animals fed a diet containing chloride compounds showed learning disabilities, behavioral retardation, and difficulties in complex task performance [13-16]. In human studies, expectant mothers exposed to PCBs delivered babies with low intelligence quotients (IQs). In addition, these babies were underdeveloped, motor-delayed, and poorly nourished [17-20]. This prolonged and persistent effect on the young adult and elderly nervous system has been observed in Michigan, Taiwan, Mohawk and other cohorts [11,21-23].However, there was lack of studies on the perceived physical and psychological complaints of



elderly subjects exposed to these compounds. This study aimed to assess the relationships between self-reported health conditions, memory function, and subjective memory complaints (SMCs) after previous exposure to PCBs/PCDFs.

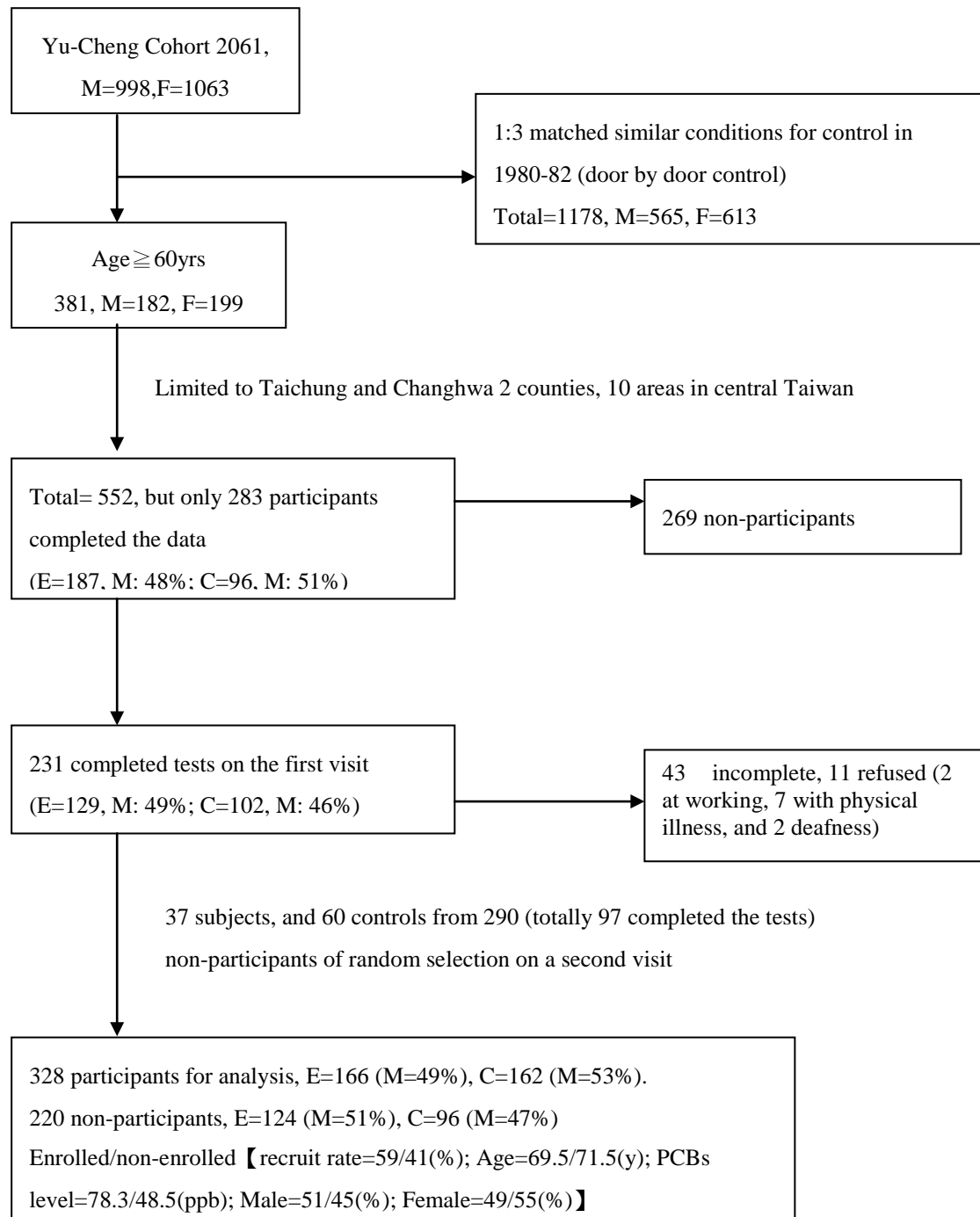


Figure 1 A flow chart of eligibilities in Yu-Cheng cohort in Taiwan
(E) Exposed and (C) control subjects with male and female distribution.



II. Materials and methods

We conducted a retrospective cohort study with prospective measurements from an existing cohort of the 1979 exposure in mid-central Taiwan (the Yu-Cheng cohort). This study was approved by the Committee for Human Research at Cheng-Kung University Medical College. The details of this cohort and the matched unexposed subjects have been previously described [7]. All subjects had ceased the rice-oil exposure since 1980 following the notification of the Yu-Cheng event. For the study examining neurocognitive function, only Yu-Cheng and unexposed subjects aged 60 years or older by July 1st, 2002 were recruited. Among 381 Yu-Cheng subjects aged 60 years or older, 290 were alive and resided in one of the 10 townships in central Taiwan that were involved with the study; these subjects were selected as candidates for this study. For each Yu-Cheng subject, approximately 3 gender- and age-matched (within 3 years) unexposed individuals were identified from their neighborhood [7]. Among these 3 potential reference subjects, only one of the subjects was randomly selected to be the comparison subject (262 fulfilled the criteria). Of the 552 (290 subjects, 262 controls) eligible subjects, 231 subjects (129 subjects and 102 controls) (42%) provided complete and useful information for data analysis. We added another 290 subjects from a second random selection to increase the study power. Among them, 97 (37 subjects and 60 controls) completed the tests. We excluded those who have moved out this area, have suffered from head injury or stroke recently, have psychiatric disorders or have taken sleeping pills before the tests. The data are shown in Figure 1. During home visits, subjects received a structured questionnaire, including demographic information, memory-domain tests, geriatric depression scale-short form (GDS-S) and SMCs. These tests were arranged in the following sequence: a verbal memory recall (VMR), digit symbol (DS), attention and digit span (ADS), learning ability, 30-min delayed recall, and visual memory span (VMS) tests. These tests were followed by SMCs and SF-36 to avoid as much interference as possible. Finally, 166 exposed subjects and 162 controls completed the memory tests, and 148 of the 166 exposed subjects and 65 of the 162 controls completed the entire questionnaire.

In 1980–1982, serum PCB levels were analyzed in approximately 80% of Yucheng individuals using packed column, electroncapture gas chromatography and the Webb–McCall method adapted to a computerized data system; a Japanese PCB mixture (Kanechlor 500) was used as a reference standard [24].

III. Memory tests

We used a modified neurobehavioral battery consisting of six tests to assess a wide range of memory functions, including learning capacity, working memory, and long-term memory performance [25-27]. We used the Chinese version of the Wechsler Adult Intelligence Scale-Revised (WAIS-R), and used the ADS to measure immediate learning and short-term memory. The ADS comprised 2 subtests, forward and backward, which involved different cognitive processes. The DS assessed mental flexibility, executive function, and visual-scanning memory. The DS contained a list of numbers corresponding to certain symbols and a list of random digits (from 1 through 7) with a blank square below each digit. The VMR test was used to assess ten clustering items that were recalled 5 cycles after verbal repetition. After finishing these 5 trials, a delayed recall test was conducted 30 minutes later without prior notification. The learning ability was calculated as the last trial minus the first trial. The VMS of the Wechsler Memory Scale-Revised (WMS-R) was used for visual attention and visual memory. In addition, SMCs were obtained by answering “yes” or “no” to questions that were relevant to memory deficits, which had been proven to be reliable in previous publications [28-29]. The following list includes some examples of the modified questions that we asked the subjects: “did you feel like that you are



forgetting something?”, “did you forget things that you just said?”, “is it more difficult to remember things than it used to be?”, and “did you forget an appointment with someone days or weeks ago?” A score of 6–12 was estimated, and higher scores indicated a greater level of agreement to the questions. The correlation between the memory tests and the self-rated SMCs were evaluated by simple linear regression. All of above preliminary queries were validated in a pilot survey.

IV. Statistical analysis

The study records of outlier values on the memory measures were reviewed to check for poor performance or recording errors. We applied linear regression models to assess the effects of covariates. The influences of other factors on the subjects' perceived health condition, such as smoking and alcohol consumption, were also treated as potential confounders. Along with age and education, these confounding variables were used to adjust the test results. The Student's *t*-test was used for comparison between continuous variables in smoking, drinking, height, weight, and BMI. The chi-square tests were used for nominal variables including both exposed and non-exposed comparison in memory tests. ANOVA was used for simple linear regression adjusted by age, sex and education. All statistical analysis was two-sided.

Table 1 Demographic data of the PCB-exposed and non-exposed group

	Male			Female		
	Exposed (n = 82)	Non-exposed (n = 87)	<i>p</i>	Exposed (n = 84)	Non-exposed (n = 75)	<i>p</i>
Education			0.06*			0.16
0–3 y, n (%)	22 (26.8)	18 (20.7)		50 (59.5)	35 (46.7)	
4–6 y, n (%)	40 (48.8)	59 (67.8)		29 (34.5)	37 (49.3)	
7–9 y, n (%)	8 (9.8)	5 (5.8)		3 (3.6)	3 (4)	
>9 y, n (%)	12 (14.6)	5 (5.8)		2 (2.4)	0 (0)	
Age			0.31			0.32
60–64 y, n (%)	23 (28)	21 (24.1)		29 (34.5)	15 (20)	
65–69 y, n (%)	23 (28)	23 (26.4)		23 (27.4)	26 (34.7)	
0–74 y, n (%)	17 (20.7)	23 (26.4)		17 (20.2)	20 (26.7)	
>75 y, n (%)	19 (23.2)	20 (23)		15 (17.9)	14 (18.7)	
Smoking, n (%)	48 (58.5)	28 (32.2)	0.47	20 (23.8)	18 (24)	0.44
Drinking, n (%)	15 (18.3)	17(19.5)	0.22	12 (14.3)	12 (16)	0.37
Height (cm), mean (SD)	164.2 (6.25)	163.2 (7.28)	0.29	155.3 (5.70)	156.9 (5.88)	0.07
Weight (kg), mean (SD)	64.6 (8.60)	64.1 (8.77)	0.74	56.4 (7.70)	56.8 (10.35)	0.89
BMI, mean (SD)	23.9 (2.90)	23.9 (2.89)	0.88	23.6 (3.08)	23.1 (3.82)	0.31
PCB (ng/g), mean (SD)	68.1 (65.83)	--		88.2 (109.57)	--	



Table 2 Memory tests between PCBs-exposed and non-exposed groups in aged people

	Exposed	Non-exposed	Aged-	Fully-
	(n = 166)	(n = 162)	adjusted	adjusted
	Mean ± SD	Mean ± SD	<i>p</i>	<i>p</i>
<i>Verbal Memory of Recalls</i>				
<i>Total</i>	26.89 ± 7.60	28.48 ± 7.89	0.11	0.06
<i>Trial 1</i>	3.39 ± 1.67	3.41 ± 1.65	0.92	0.90
<i>Trial 2</i>	5.11 ± 1.93	5.17 ± 1.78	0.78	0.76
<i>Trial 3</i>	5.08 ± 2.19	5.82 ± 2.04	0.27	0.19
<i>Trial 4</i>	6.16 ± 2.45	6.70 ± 2.29	0.04*	0.02*
<i>Trial 5</i>	6.39 ± 2.71	7.03 ± 2.55	0.03*	0.02*
<i>Learning ability</i>	2.97 ± 2.71	3.65 ± 2.80	0.04*	0.03*
<i>Delay recall in 30 min</i>	5.01 ± 2.83	5.60 ± 2.93	0.10	0.06
<i>DS</i>	22.39 ± 1.47	24.94 ± 11.71	0.14	0.09
<i>ADS</i>				
<i>Total</i>	15.20 ± 3.61	16.55 ± 3.82	0.002*	0.001*
<i>Forward</i>	11.10 ± 2.32	12.13 ± 2.42	< 0.001*	< 0.001*
<i>Backward</i>	4.09 ± 2.06	4.24 ± 2.04	0.14	0.12
<i>VMS</i>				
<i>Total</i>	11.11 ± 2.83	11.76 ± 2.93	0.05*	0.04*
<i>Forward</i>	6.70 ± 1.55	6.97 ± 1.65	0.15	0.13
<i>Backward</i>	4.43 ± 1.67	4.80 ± 1.78	0.06*	0.05*
<i>GDS-S</i>	6.82 ± 0.21	6.85 ± 0.24	0.97	0.89

1. DS = digit symbol, ADS = attention and digit span, VMS = visual memory span, GDS-S= geriatric depression score-short form
2. ANOVA, fully-adjusted for age, sex, and education, significant $p < 0.05$

V. Results

A total of 328 subjects were included in the analysis. They consisted of 57% (166/290) of the exposed subjects and 61% (162/262) of the control subjects. The mean age was 69.9 ± 5.9 years (range: 60.0–84.3 years) in males and 69.2 ± 6.1 years (range: 60.0–91.7 years) in females. The exposed females had a lower level of education than the exposed men. The eye and ear problems which were inspected and diagnosed by Drs, might affect the accuracy of visual and auditory memory tests. The problems were not significantly different in our patients and control groups. The demographic data are shown in Table 1.

Gender, age, and education were potential confounders in memory tests. Exposed subjects exhibited a greater decline in memory tests than controls (Table 2). Significant differences were observed in learning ability ($p = 0.03$), ADS-forward and ADS-total ($p < 0.01$), VMS-total ($p = 0.04$), VMS-backward ($p = 0.05$), trial 4 and trial 5 of VMR ($p = 0.02$), total trials of VMR ($p = 0.06$), and the 30-min delayed recall ($p = 0.06$) test results. These results demonstrated that memory modalities were impaired in PCBs/PCDFs exposed elderly subjects. The effects of serum PCBs on memory performance were tested using linear or multivariate regression modeling. The influence of PCBs by years was predicted to be linear decay by extrapolation [30-31]. After the elimination of the confounders, there were no associations between continuous or logarithmic concentrations of PCBs and memory tests. We observed a dose-response effect in ADS-forward ($p < 0.01$) at medium and high levels of



PCBs (data not shown) when we stratified PCBs into high (≥ 90 ppb), medium (30 -89 ppb), and low (< 30 ppb) levels. (Table 3)

Table 3 Cognitive tests and stratified PCBs level by adjusted covariates of education, age and sex

Variable	Control (N=162)		PCB $\geq 0, < 30$ ppb (N=42)		PCB $\geq 30, \leq 90$ ppb (N=63)		PCB > 90 ppb (N=43)		<i>p</i> value
	Mean	(\pm SE)	Mean	(\pm SE)	Mean	(\pm SE)	Mean	(\pm SE)	
VMR (Total)	28.4	(± 0.7)	27.5	(± 1.3)	26.6	(± 1.0)	27.1	(± 1.3)	0.49
Trial 4	6.7	(± 0.2)	6.1	(± 0.4)	6.0	(± 0.3)	6.5	(± 0.4)	0.17
Trial 5	7.0	(± 0.2)	6.5	(± 0.4)	6.2	(± 0.3)	6.6	(± 0.4)	0.15
Learn ability	3.6	(± 0.2)	2.7	(± 0.5)	2.7	(± 0.4)	3.5	(± 0.4)	0.06
Delay recall 30 min	5.6	(± 0.2)	5.4	(± 0.5)	5.2	(± 0.4)	4.4	(± 0.5)	0.15
DS	25.1	(± 1.3)	24.3	(± 2.2)	23.3	(± 2.1)	21.9	(± 2.0)	0.67
ADS-Forward	12.1*	(± 0.2)	11.8	(± 0.4)	11.1*	(± 0.3)	11.0*	(± 0.4)	0.002*
ADS-Backward	4.5	(± 0.2)	4.4	(± 0.4)	4.3	(± 0.3)	3.7	(± 0.3)	0.25
VMS-Forward	7.0	(± 0.1)	7.1	(± 0.3)	6.8	(± 0.3)	6.4	(± 0.3)	0.20
VMS-backward	4.8	(± 0.2)	4.5	(± 0.3)	4.7	(± 0.3)	4.1	(± 0.3)	0.19

1. Post-hoc Tukey HSD for dosing significance (* $p < 0.05$) in ADS-forward with medium and high PCBs level.
2. Totally 18 exposed subjects had no PCBs concentration, and the dose effects might be under-estimated.

Table 4

Self-reported health status and the physician's diagnosis in the PCBs-exposed and non-exposed subjects

	Male			Female		
	Exposed (n = 82)	Non-exposed (n = 87)	<i>p</i>	Exposed (n = 84)	Non-exposed (n = 75)	<i>p</i>
Cataract, n (%)	17 (20.7)	4 (4.6)	0.11	22 (26.2)	6 (8)	0.53
Hearing impairment, n (%)	14 (17.1)	5 (5.7)	0.43	12 (14.3)	4 (5.3)	0.94
Asthma, n (%)	11 (13.4)	1 (1.1)	0.05*	11 (13.1)	2 (2.7)	0.36
Nail deformity, n (%)	23 (28)	1 (1.1)	$< 0.001^*$	28 (33.3)	0 (0)	$< 0.001^*$
Chloracne, n (%)	29 (34.5)	1 (1.1)	$< 0.001^*$	24 (28.6)	0 (0)	$< 0.001^*$
Hyperkeratosis, n (%)	13 (15.9)	2 (2.3)	0.07	9 (10.7)	0 (0)	0.06*
Gout, n (%)	19 (23.2)	15 (17.2)	0.15	13 (15.5)	2 (2.7)	0.23
Anemia, n (%)	20 (24.4)	3 (3.4)	0.02*	30 (35.7)	6 (8)	0.12
Hypertension, n (%)	37 (45.1)	20 (23)	0.84	35 (41.7)	6 (8)	0.03*
Disc herniation, n (%)	15 (18.3)	7 (7.5)	0.79	19 (22.6)	6 (8)	0.81
Hepatitis, n (%)	6 (7.3)	1 (8)	0.25	3 (3.6)	0 (0)	0.30
Nephritis, n (%)	8 (9.8)	4 (4.6)	0.95	8 (9.5)	1 (1.3)	0.29
Bronchitis, n (%)	28 (34.1)	8 (9.2)	0.07	15 (17.9)	5 (6.7)	0.93
Headache, n (%)	2 (2.4)	2 (2.3)	0.50	6 (7.1)	2 (2.7)	0.96
Neuritis, n (%)	1 (1.2)	1 (1.1)	0.63	0 (0.0)	0 (0.0)	0.00
Diabetics, n (%)	12 (14.6)	9 (10.3)	0.36	18 (21.4)	3 (4)	0.17
Hyperthyroidism, n (%)	1 (1.2)	0 (0)	0.47	3 (3.6)	0 (0)	0.30
Hypothyroidism, n (%)	0 (0)	0 (0)	--	0 (0)	0 (0)	--

Chi-square and Fisher exact if cell < 5 , significant $p < 0.05$



Table5 Physical symptoms, PCB concentration, memory complaints (SMCs) by the landmark of chloracne (+, -) in the PCB-exposed group

Chloracne	Male (n = 82)			Female (n = 84)		
	(+) (n = 29)	(-) (n = 53)	<i>p</i>	(+) (n = 24)	(-) (n = 60)	<i>p</i>
Physical symptoms						
Nail deformity, n (%)	15 (51.7)	8 (15.1)	<0.01*	15 (62.5)	13 (27.1)	<0.01*
Hyperkeratosis, n (%)	3 (10.3)	10 (18.9)	0.23	6 (25)	3 (5)	0.02*
Anemia, n (%)	11 (37.9)	9 (17.0)	0.06*	10 (41.7)	20 (33.3)	1.00
Asthma, n (%)	6 (20.7)	5 (9.4)	0.31	5 (20.8)	6 (10)	0.49
Hypertension, n (%)	10 (34.5)	27 (50.9)	0.09	17 (70.8)	18 (30)	0.01*
Gout, n (%)	6 (20.7)	13 (24.5)	0.59	5 (20.8)	8 (13.3)	0.75
PCBs, n (mean ng)	27 (74)	42 (65)	0.57	21 (122)	75 (75)	0.11
SMCs, n (mean score)	29 (8.2)	48 (7.5)	0.07*	23 (9)	48 (7.6)	<0.01*

1. Chi-square and Fisher exact.
2. Subjects with higher SMC indicate worse memory complaints..

The perceived health status was assessed through a physician's diagnosis of illness. The exposed subjects had more chloracne and nail deformity than the controls. We also noted a higher prevalence of anemia and asthma in exposed males and a higher prevalence of hypertension in exposed females (Table 4). Similar to a previous study examining affected subjects greater than 30 years of age, there were no statistical differences in arthritis, diabetes, neuritis, or headache [7]. Because chloracne has been shown to be a sensitive physical sign of PCB concentration and exposure severity [7,32], it was used as a biomarker for the comparison between SMCs, SF-36 score, and the exposure state in the exposed and control groups. In our study, in the exposed group, both male and female subjects with chloracne had higher PCB levels. However, exposed females with chloracne complained of more memory problems than exposed females without chloracne, and this difference was statistically significant ($p < 0.01$). The SMCs in exposed males were less apparent, as shown in Table 5 Using a linear regression model to correlate with SMCs and memory tests by sex, a significant association was noted among exposed male in VMR ($p= 0.04$), and among exposed female in ADS ($p= 0.03$).

VI. Discussion

Our study provided evidence that memory decline, particularly learning and attention, was associated with exposure to PCBs in the elderly [11, 33]. This is the first study in Yu-Cheng population of PCBs/PCDFs-exposed elderly subjects that had reported increased health problems, poor memory test results, and memory complaints. In our results, the decline in ADS, VMR, VMS, and the 30-min delayed recall test results might reflect the interruption of hippocampal-circuit processing related to memory function [13,34]. Our PCB-cohort, as well as previous studies of persistent organic pollutant (POP) exposure, showed that the ADS is the most sensitive test to toxic evaluation [35]. The exposed subjects had lower scores in most test modalities. These lower scores were attributed to the accumulation of lipid-soluble toxin in fat tissues and then the toxin may interrupt hormone and neurotransmitter related mechanisms, causing cognitive deficits [4, 12]. Similar to the outcome of the Michigan cohort, we clearly showed that memory and attention were impaired in the exposed elderly subjects but not the motor dexterity. Although some verbal learning deficits were reported in some



studies [9, 21] differed from our results, we cannot rule out the potential additive toxins such as lead, mercury, and other toxicants, in addition to PCBs exposure.

After adjusting for age and education, the exposed females exhibited greater memory decline than the exposed males. The etiology is not clear, but we hypothesized that hormones might play a role in these menopausal women. A change in the androgen status has been reported in animals that were perinatally exposed to PCBs, and the exposed female offspring had more spatial discrimination [4, 10, 15]. Several studies, however, have shown that boys had lower dexterity skills, and girls had better spatial abilities [17-18]. This association, however, is still inconclusive in adolescents [36]. A mechanism in animal study was proposed that the estrogen-nourishing receptors in hippocampus were prone to be sensitized to estrogen-like substance such as PCBs or PCDFs exposure [33]. This hypothesis deserves further investigation in menopausal women.

The effects of PCB concentrations and cognitive performance in ADS were significantly correlated (ADS-forward, $p=0.004$). When we eliminated the effects of the covariates, there were no statistically significant differences between the continuous PCB levels and the memory tests. When we stratified PCBs into high, medium, and low levels, we found significant differences in ADS-forward at medium and high doses. This association highlighted that PCBs/PCDFs exposure 30 years ago had effects on current attention and learning ability. The high PCB concentrations in the Taiwanese cohort, which were different from the slow accumulation of lower dose exposure in the Michigan population, showed a similar effect on learning and attention, suggesting that the hippocampus is susceptible to the effects of PCBs [23, 33]. Although not all tests show memory decline, certain memory deficits in PCB-exposed elderly subjects stressed the importance of choosing appropriate or standardized parameters to demonstrate the significance of subtle changes. Indeed, a random selection of neuropsychological tests in the toxic evaluation may not result in accurate measures.

Finally, children born to mothers exposed to PCBs/PCDFs in the Yu-Cheng cohort showed cognitive decline similar to the decline observed by Jacobson [12, 19]. According to an ongoing study by Guo's team [37, 38], the neuropsychological impairments seemed to occur in the 3rd generation of descendants. This observation suggested that, once the PCB-toxicant interfered with human endocrine integrity, it had a persistent trans-generational influence on abnormal dexterity including central nervous system functioning. This hypothesis was also supported by a recent study [10]. All these researches highlighted countering environmental pollutants through prevention rather than trying to remove these pollutants after exposure.

This study has some limitations. First, although the association of memory complaints with impaired cognitive performance is relevant, it is not the causal relationship by a cross-sectional design, and SMCs were not associated with all memory modality declined. Second, the replies which were collected from the patients but not from family members might have some information or recall bias. Third, only six queries seemed too short to reflect detail self-reported memory complaints. A full-length structured questionnaire of SMCs or a prospective study design is needed to ascertain the good linkage between SMCs and memory tests in toxic exposure research in the future.

VII. Conclusion

In summary, the PCB/PCDF-exposed elderly in the Yu-Cheng cohort had memory and learning deficits. Exposed men had more verbal recall complaints and women had more short-term memory complaints, as shown by memory deficits in neuropsychological tests. We found that Taiwanese elderly subjects exposed to PCBs/PCDFs had more frequent medical problems and more memory complaints that are consistent with their memory function impairments.



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