EFFECTS OF DIOXINS EXPOSURE ON SOCIAL EMOTIONAL BEHAVIOR OFCHILDREN LIVING IN A HOT SPOT AREA, VIETNAM

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Introduction

In Vietnam, there are some areas around former US military airbases which were storages of the herbicides sprayed during the Vietnam War, and called "hot spot" of dioxin contamination. Previous studies shown that the levels of dioxins, especially 2,3,7,8-tetrachlorodibenzo-p-dioxin (TetraCDD), were dramatically elevated in "hot spot". The residents around "hot spot" are highly risky to exposure of 2,3,7,8-TetraCDD, because of not only previous exposure but also resent exposure due to contaminated water from air base. Thanh Khe district in Danang city surround Danang airbase which is one of hot spot, and residents are suggested to be at health risk by recent exposure. The dioxin levels in breast milk of the mothers in the hot spots were reported to be approximately 4-fold higher than those of mothers in unsprayed areas[1]. Thus, Vietnamese infants living in hot spots are also exposed to dioxin during pregnancy through the placenta and postnatally through breastfeeding.

In a hot spot in Danang, Vietnam, we have reported that infants whose maternal breast milk contained higher dioxins showed lower neurodevelopmental scores of 4-month-old and 12-month-old infants. Especially, at 12 months of age, several dioxin congeners exhibited significant inverse associations with communication skill scores including expressive language and social emotional scales tested by Bayley scales, suggesting that dioxin exposure may influence on social interactions and increase social communication deficits such as autism spectrum disorders (ASD).

Therefore, we try to investigate the effects of dioxin exposure on social interactions of children aged at 3 year old living in a hot spot of dioxin contamination by using autism spectrum rating scale (ASRS).

Materials and methods

1. Study subjects and health survey for 3 year-old children

Survey of newborns in Thanh Khe district hospital was started on July, 2008, and 159 babies was enrolled to the survey until January, 2009. When the infants became 1 month old, nurses of commune health center visited them, and followed up 147 infants (93%). In this 1 month survey, breast milk samples were collected and transferred to Japan for pretreatment and measurement of dioxin concentration of 17 isomers of polychlorinated dibenzodioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) in Kanazawa Medical University.

In November, 2011, when our infant cohort became 3 years old, a health follow-up survey was conducted to clarify their neurodevelopment including social–emotional behavior. To evaluate their social–emotional behavior and autistic symptoms, ASRS was performed for 122 participants (77%) in the survey. Job, salary, educational years, smoking and drinking habit of parents were also obtained by face to face interview.

2. Breast milk sample analysis

About 10 g breast milk was used to extract fat content. A series of purification operations consisting of alkali digestion, hexane extraction and chromatography were carried out. The established method of analysis was described in details elsewhere[2]. The final extract were concentrated to 20 µl and analyzed by gas chromatography coupled to high-resolution mass spectrometry (HR-GC/MS, MStation-JMS700, JEOL, Japan)

Toxic equivalent of PCDDs (PCDDs TEQ), PCDFs (PCDFs TEQ) and PCDDs/PCDFs TEQ (total TEQ) were calculated by adding up the multiplying each congener concentration with its toxic equivalent factor (TEF) referred from the WHO 2005-TEF[3].

Results and discussion

Table 1 lists characteristics of the parents and children, including mean values for characteristics of the subjects such as age at the survey, socio-economic factors of parents, infant factors at birth, infant gender (rate of boys) and rate of the first child, body size of children. None of the mothers were smokers, but 77.9 % of the fathers were smoking every day. Fathers who drink alcohol every day was 10%.

Means of age was 37 months old and almost children were born at full term and not low birth weight. Means of age adjusted Z scores of body size parameters calculated by WHO infant growth standard were lower than 0, suggesting their body size was generally smaller than WHO standards. For ASRS scores, their means of the present subjects were generally higher than standard population, especially means of UB (unusual behavior), ST(stereotypy), BR (behavioral rigidity) and SS (sensory sensitivity) scores were more than 60 (Mean of standard population is 50).

Although fathers' smoking status didn't show any relations with SMRS scores, but scores of SC (social communication), DSM (DSM-IV-TR scale), PS (peer socialization), AS (adult socialization) and TOT (total score) of children whose fathers drink alcohol every day were significantly higher than those of children whose fathers don't drink every day. Maternal height showed significant correlations with SC, DSM, AS and TOT. Gestational weeks and birth weight of children were also significantly correlated with ST score. Differences between genders in UB, DSM and AL (atypical language) scores were found. Moreover, there were significant relations between fathers' salary and SC, SER (social emotional reciprocity) and BR, between fathers' age and SER, and between fathers' educational years and SC, DSM, AS and SER. Therefore, we analyzed the relationships between ASRS scores and dioxins in breast milk after adjustment for multi confounding factors such as fathers drinking habit (everyday or not), maternal height, children's gender, gestational weeks, birth weight, salary, age and educational years of fathers, as well as children's age at the survey.

Partial correlations between ASRS scores and concentrations of 17 dioxin congeners and TEQs of PCDDs, PCDFs and PCDDs/Fs in maternal breast milk were analyzed after controlling for age or multi confounding factors, and shown in Table 2. SC and SER scores showed significant relationships with 1,2,3,7,8-PentaCDF after adjustment for age or multi factors. SER score also showed significant relationship with OctaCDF. Positive relationship between ASR score and 1,2,3,4,7,8,9-HeptaCDF was found, but inverse relationship between AL score and 2,3,7,8-TetraCDF was also observed in the present study.

These results may suggest that dioxins, especially some furan isomers associated with increased some ASRS scores related to social-emotional behavior and attention. Lee et al. (2007) also reported association between some dioxin isomers' concentration in serum and learning disability (LD) and attention deficit hyperactive disorder (ADHD) in Korean school aged children. Larger scale and longer follow-up study in Vietnamese infants exposed to dioxin during pre and post natal period is necessary to clarify the relationships between dioxins and social emotional development during childhood leading to ASD and/or ADHD.

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Table 1 Characteristics of the subjects and scores of Autism Spectrum Rating Scale

		Mean / %	SD	Min.	Max
Mothers					
Age	years	28.6	6.1	18	42
Weight	kg	56.9	7.1	42	71
Height	cm	154.2	4.9	141	176
Education	years	8.3	3.5	0	14
Salary per month	$x10^3$ Dong	2201	1514	0	10000
Fathers					
Age	years	34.8	6.2	23	54
Education	years	9.6	2.6	0	12
Salary per month	$x10^3$ Dong	3399	2040	0	10000
Smoking habit	%	77.9			
Drinking everyday	%	10.5			
Children					
Age	months	37.0	1.8	33	40
Gestational weeks at birth		39.5	0.8	37	41
Birthweight	g	3239.8	380.1	2324	4616
Rate of boys	%	50.8			
Rate of the first child	%	28.7			
Weight (actual value)	kg	13.7	1.9	9.5	19.9
Weight (Z-score)		-0.38	1.1	-3.45	2.58
Height (actual value)	cm	92.6	3.7	80	100
Height (Z-score)		-0.85	0.9	-3.72	1.46
BMI		15.9	1.6	12.6	22.5
Head circumference (actual value)	cm	48.5	1.4	45	52
Head circumference (Z-score)		-0.35	0.9	-2.61	1.83
Head/Height		0.52	0.02	0.48	0.60
Abdominal circumference	cm	48.4	3.5	40	62
Autism Spectrum Rating Scale (ASRS)					
SC: Social Communication	T-score	50.5	8.9	26	80
UB: Unusual Behavior	T-score	60.7	5.5	44	81
DSM: DSM-IV-TR scale	T-score	56.5	6.9	45	85
PS: Peer Socialization	T-score	52.0	11.2	25	85
AS: Adult Socialization	T-score	57.3	10.2	36	84
SER: Social/Emotional Reciprocity	T-score	51.2	9.9	26	78
AL: Atypical Language	T-score	40.6	9.2	31	82
ST: Stereotypy	T-score	62.0	6.5	41	74
BR: Behavioral Rigidity	T-score	61.0	7.7	40	80
SS: Sensory Sensitivity	T-score	61.5	7.4	39	79
ASR: Attention/Self-Regulation	T-score	47.8	7.8	29	64
TOT: Total Score	T-score	56.3	6.2	44	83

Note: T-scores have a mean of 50 and a standarddized deviation of 10.

Table 2 Partial correlation coefficients between scores of autism spectrum rating scale and dioxins in breast milk after controlling for age or multi factors

		Autism Spectrum Rating Scale (ASRS)						
	control	SC	PS	AS	SER	AL	SS	ASR
2,3,7,8-TetraCDD	age	0.002	-0.011	-0.057	0.023	-0.001	0.080	0.139
	multi	0.012	-0.031	-0.078	0.037	-0.035	0.051	0.181
1,2,3,7,8-PentaCDD	age	-0.017	0.001	-0.069	0.013	-0.110	0.189 *	0.049
	multi	-0.056	-0.079	-0.089	-0.136	-0.136	0.101	0.054
1,2,3,4,7,8-HexaCDD	age	-0.009	-0.052	-0.081	0.050	-0.148	0.157	0.084
	multi	-0.050	-0.147	-0.101	-0.143	-0.143	0.091	0.096
1,2,3,6,7,8-HexaCDD	age	-0.062	-0.089	-0.093	-0.020	-0.156	0.157	0.067
	multi	-0.092	-0.176	-0.107	-0.175	-0.175	0.083	0.084
1,2,3,7,8,9-HexaCDD	age	0.054	0.006	-0.043	0.109	-0.097	0.188 *	0.130
	multi	0.050	-0.067	-0.023	-0.077	-0.077	0.128	0.169
1,2,3,4,6,7,8-HeptaCD	age	0.026	-0.029	-0.127	0.093	-0.117	0.162	0.065
	multi	0.049	-0.059	-0.102	-0.080	-0.080	0.118	0.094
OctaCDD	age	-0.007	-0.022	-0.130	0.057	-0.109	0.188 *	-0.040
	multi	-0.045	-0.063	-0.146	0.040	-0.114	0.120	-0.085
2,3,7,8-TetraCDF	age	0.038	-0.005	-0.103	0.115	-0.266 **	-0.045	0.045
	multi	0.045	-0.026	-0.073	0.115	-0.314 **	-0.056	0.072
1,2,3,7,8-PentaCDF	age	0.187 *	0.122	0.005	0.219 *	-0.009	-0.145	0.152
	multi	0.239 *	0.147	0.019	0.266 **	-0.005	-0.144	0.146
2,3,4,7,8-PentaCDF	age	-0.026	-0.036	-0.094	0.011	-0.140	0.125	0.079
	multi	-0.068	-0.124	-0.117	-0.022	-0.172	0.053	0.107
1,2,3,4,7,8-HexaCDF	age	0.040	-0.001	-0.051	0.083	-0.134	0.114	0.130
	multi	-0.003	-0.098	-0.098	0.057	-0.147	0.066	0.139
1,2,3,6,7,8-HexaCDF	age	0.041	0.004	-0.045	0.089	-0.163	0.106	0.115
	multi	-0.010	-0.100	-0.095	0.057	-0.184	0.058	0.115
1,2,3,7,8,9-HexaCDF	age	0.126	0.080	-0.017	0.165	0.008	0.034	0.043
	multi	0.132	0.046	0.048	0.151	0.042	0.023	0.041
2,3,4,6,7,8-HexaCDF	age	0.126	0.072	-0.060	0.147	-0.076	0.055	0.166
	multi	0.145	0.022	-0.092	0.165	-0.026	-0.012	0.209 *
1,2,3,4,6,7,8-HeptaCD	age	0.144	0.076	-0.046	0.199 *	-0.086	0.010	0.178
	multi	0.128	0.003	-0.103	0.192	-0.062	-0.039	0.177
1,2,3,4,7,8,9-HeptaCD	age	0.174	0.085	-0.021	0.168	0.001	-0.028	0.288 **
	multi	0.198	0.065	-0.065	0.190	0.022	-0.086	0.291 **
OctaCDF	age	0.154	0.114	0.119	0.212 *	0.057	-0.155	0.037
	multi	0.154	0.110	0.125	0.206 *	0.087	-0.151	0.004
TEQ PCDDs	age	-0.007	-0.007	-0.070	0.025	-0.080	0.174	0.096
	multi	-0.034	-0.076	-0.073	0.015	-0.102	0.099	0.107
TEQ PCDFs	age	0.023	-0.009	-0.071	0.067	-0.148	0.112	0.113
	multi	-0.020	-0.105	-0.106	0.037	-0.166	0.050	0.131
TEQ PCDDs/Fs	age	0.005	-0.008	-0.073	0.043	-0.112	0.155	0.104
	multi	-0.031	-0.091	-0.088	0.022	-0.132	0.084	0.131

SC: Social Communication, PS: Peer Socialization, AS: Adult Socialization, SER: Social/Emotional Reciprocity, AL: Atypical Language, SS: Sensory Sensitivity, ASR: Attention/Self-Regulation

*: P<0.05, **: P<0.01

age: controlling for child's age at the test, multi: controlling for child's age at the test, gender, gestational weeks at b birthweight, mother's weight, monthly salary (Vetnam Dong), alcohol drinking (every day), education years of fathe