Letter to the Editor

Association between Organophosphate Exposure and Mental Health among Rural Residents from Two Towns in China*

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Organophosphate (OP) pesticides are a class of chemicals that are typically derived from phosphoric, phosphonic, and phosphinic acids, and are commonly used in agriculture[1]. China is the largest producer of pesticides and one of the most intensive pesticide users in crop production in the world. Pesticide poisoning has been shown to be an important public health problem among Chinese farm workers[2]. Multiple routes of exposure to OP pesticides occur through food contamination, environmental and household pollution, proximity to agricultural fields, and agricultural work[3].

OP insecticide poisoning accounts for 74.03% of all pesticide poisonings reported by the National Institute of Occupational Health and Poison Control at the Chinese Center for Disease Control and Prevention[4]. The health effects of acute and chronic poisoning by OP pesticides are irreversible damage to physical and mental health[5]. The mechanisms underlying injury to the human nervous system can be irreversible, thus causing disruption in nerve conduction[5]. The long-term consequences caused by acute exposure to OPs are neurologic and psychiatric disorders, such as psychotic episodes, depressed mood, as well as deficits in sustained attention, memory, and sequencing[1]. Similarly, neurological and psychiatric abnormalities are also associated with chronic exposure to OPs, including motor dysfunction (extrapyramidal symptoms), anxiety, depression, psychotic symptoms, deficits in attention, information processing, and learning[1,3]. A prospective birth cohort study showed that the concentration of some OP metabolites measured in maternal urine during pregnancy was positively associated with adverse behaviors, including withdrawal, attention problems, depression, hyperactivity, and aggression[6].

The toxicity of OPs has been studied extensively; however, the studies regarding the effects of chronic OP exposure on mental health, especially on depression, impulsivity, aggression, and anxiety, are limited[1-6]. Thus, the present study was designed to determine the association between OP exposure and mental health in rural residents using questionnaires, with the goal of protecting people who have the potential to be exposed to OPs, especially the population who are in proximity to agricultural fields and agricultural work. Our objective was to provide a scientific foundation for recommending protective measures to reduce occupational exposure to OP pesticides.

This cross-sectional study was approved by the Institutional Review Board of Colorado State University and Jilin University (102236H). In this study, two towns from 426 towns in Jilin Province were randomly selected. After we obtained demographic information on the two towns, we used a random number table to conduct a simple sampling. Regarding the estimation of sample size, we utilized the tool for sample size calculation at the website of Creative Research System (α = 0.05, confidence interval was set ± 5 standard deviation).

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Through calculation, the maximum sample size was 384. In practice, we selected 302 participants. Inclusion criteria were as follows: registered as a permanent resident in 2013 in one of the two selected towns in Jilin Province China; > 18 years of age; and providing informed consent to participate in the survey. Pregnant women were excluded from the study and subjects who had attempted suicide by ingesting pesticides, who were taking drugs that affect neurological function and those with a family history of neurological diseases were also excluded.

Exposure was defined as having handled pesticides by purchasing, spraying, mixing, diluting and transporting them within 2 years prior to the start of the study.

Trained investigators conducted face-to-face interviews with the participants between January 2012 and November 2013. The questionnaire included demographic information, exposure to OPs, the revised Chinese version of the Center for Epidemiological Studies-Depression Scale (CES-D), the Barratt Impulsivity Scale (BIS), the Buss-Perry Aggression Questionnaire (BPAQ), and the State-Trait Anxiety Inventory (STAI). The CES-D, BIS, BPAQ, and STAI were used to assess the mental status of the participants.

Demographic information included name, age, home address, contact details, gender, ethnicity, income, marital status, education and occupation.

The information about exposure to pesticides included a history of chronic or acute exposure to OPs, and if so, the duration of exposure and symptoms occurring immediately after exposure to OPs.

The reliability and validity of the CES-D, BIS, BPAQ, and STAI-Y to measure depression, impulsivity, aggression, and depression have been well-documented[7,8]. Regarding quality control measures in this study, the investigators were professionally trained. Data collection in the two towns was completed by the same group of investigators to assure consistency in data collection.

The data collected were used to create a database using Epidata 3.1 through double entry as a cross-check for accurate data entry. SPSS 21.0 was used to perform statistical analyses. Cronbach's alpha was used to calculate the internal consistency of each of the measures used in the study. Normally-distributed variables were summarized using the mean ± SD, with comparisons between groups performed using a *t*-test. Non-normally distributed variables were summarized with medians (P25, P75); the comparison among groups was performed using a rank test. To determine whether the results are of practical significance, we also calculated the effect size and the correlation coefficient (r). Categorical variables are described as percentages. Comparisons between groups was performed using a x^2 test. All the statistical tests were two-sided with a test level $\alpha = 0.05$ and a significant difference $P < 0.05$.

The response rate with completed questionnaires was 88%. Of the 266 participants, 113 were male and 153 were female. The age of the participants was between 26 and 83 years; the mean age was 55.85 ± 10.35 years. The dominant ethnic group was Han and the minority group accounted for 15.9% (most were Man and Chao). The majority of the participants were farmers and responsible for doing farm work. Most of the participants (80.5%) had medical insurance.

The participants were classified into exposure or non-exposure groups based on a history of using organophosphates; 87 participants were exposed and 179 were non-exposed. There were significant differences in the percentage comparing exposed to non-exposed participants based on gender (P = 0.008), family income (P = 0.031), marital status (P = 0.021), percentage of participants responsible for farm work (P = 0.002), and consuming alcohol (P = 0.006). There were more females among the nonexposed. Compared with the non-exposed, the exposed had a higher percentage of family income > 10,000 yuan (approximately 1,563 dollars), working on the farm, alcohol consumption, and being married. There were no significant differences in age, ethnic group, occupation, education, or health insurance ($P > 0.05$). The demographic information is shown in Table 1.

Prevalence of OP-related Symptoms Of those in the OP-exposed group, 77.0% reported eye irritation, 84.8% reported nausea or vomiting, 73.6% reported chest distress, 78.1% reported dyspnea and 72.5% reported sweating.

Scale Consistency Testing Cronbach's alpha showed the internal consistency of the measures to range from acceptable-to-excellent (CES-D = 0.775, BIS = 0.769, BPAQ = 0.918, and STAI = 0.880).

Status of Study Population Mental Health The comparison of CES-D, BIS, BPAQ, and STAI between the exposure and non-exposure groups is shown in Table 2.

CES-D The somatic activity and retarded activity scores (P = 0.002, $r_{s\&r}$ = 0.188), and interpersonal relationships (P = 0.018, r_i = 0.145) between the exposed and non-exposed were significantly different, unlike depressive (P = 0.113, r_d = 0.097)

and positive moods (P = 0.958, r_p = 0.003).

BIS There was no significant difference in overall impulsivity scores or in the three dimensions of impulsivity among the participants in the exposed and non-exposed groups (P > 0.05).

BPAQ The exposed participants had higher scores for aggression than the non-exposed (mean, 38.53 *vs*. 33.98, P = 0.025). Specifically, the significant difference involved the hostility dimension (median, 13.00 *vs*. 10.00, P = 0.002); however, there was no significant difference in scores between the exposed and non-exposed in the three dimensions (physical aggression, verbal aggression, and anger; P > 0.05).

STAI There was no significant difference in the STAI scores between the exposed and non-exposed (P > 0.05).

In addition, we also analyzed the effects of covariates, such as sex, income, and marital status on the CES-D, BIS, BPAQ, and STAI scores. The results showed a significant difference in STAI scores between males and females (P = 0.002), but no significant difference in CES-D, BIS, and BPAQ scores between males and females (P > 0.05). We found a significant difference in BPAQ between different income groups (P = 0.005), but not for the CES-D, BIS, and STAI scores between different income

Table 1. General characteristics of the study population

Variables	Total	Non-exposure	Exposure	t/χ^2	P
N	266	179	87		
Age (Mean ± SD)	55.85 ± 10.35	55.6 ± 11.63	56.16 ± 7.08		0.740
Gender, *n* (%)				7.05	**0.008**
Male	113 (42.5)	66 (36.9)	47 (54.0)		
Female	153 (57.5)	113 (63.1)	40 (46.0)		
Ethnicity, *n* (%)				0.43	0.510
Han	222 (84.1)	147 (83.1)	75 (86.2)		
Others	42 (15.9)	30 (16.9)	12 (13.8)		
Occupation, *n* (%)				*	1.000
Farmers	257 (97.3)	172 (97.2)	85 (97.7)		
Others	7 (2.7)	5 (2.8)	2 (2.3)		
Education, *n* (%)				0.69	0.405
Primary and below	176 (66.7)	115 (65.0)	61 (70.1)		
Others	88 (33.3)	62 (35.0)	26 (29.9)		
Average family income, *n* (%)				4.67	**0.031**
≥ 10,000 Yuan (1,563 US dollars)	169 (64.5)	105 (60.0)	64 (73.6)		
< 10,000 Yuan (1,563 US dollars)	93 (35.5)	70 (40.0)	23 (26.4)		
Marital status, *n* (%)				5.31	**0.021**
Married	241 (92.3)	156 (89.7)	85 (97.7)		
Others	20 (7.7)	18 (10.3)	2 (2.3)		
Medical insurance, *n* (%)				2.72	0.099
Self support	52 (19.5)	40 (22.4)	12 (13.8)		
Others	214 (80.5)	139 (77.6)	75 (86.2)		
Responsible for major labor, *n* (%)				9.96	**0.002**
Self	183 (70.1)	111 (63.8)	72 (82.8)		
Others	78 (29.9)	63 (36.2)	15 (17.2)		
Drinking, *n* (%)				7.69	**0.006**
Yes	202 (75.9)	57 (65.5)	145 (81.0)		
No	64 (24.1)	30 (34.5)	34 (19.0)		

groups ($P > 0.05$). Marital status showed no effect on the CES-D, BIS, BPAQ, or STAI scores ($P > 0.05$).

Our study suggested that exposure to organophosphates increases depression and aggression in exposed participants with the demonstration of depression in somatic activity, retarded activity, aggression, and hostility. These findings are in agreement with Malekirad's study[9], long-term, chronic exposure to organophosphates increases social dysfunction in an exposed population and the proportion of anxiety, insomnia, and severe depression was significantly higher than the control group.

A previous study showed that farm workers exposed to OPs showed more negative moods, such as anger, hostility, depression and nervousness than controls[10]. There was no difference in BIS scores and STAI scores between exposure and controls groups. It may be that exposure status did not reach the toxicity threshold required to produce effects on impulsivity and anxiety[10].

In our study, through the analysis of covariates, we found that covariates could affect the scores of CES-D, BIS, BPAQ, or STAI. There was no significant difference in STAI between exposure and nonexposure groups, which may be associated with the different distribution of sex between these two groups. However, there was a significant difference in BPAQ scores between exposed and nonexposed groups, which may be associated with the different income levels between these two groups; those with high income were less likely to be exposed to pesticides. These results should be further explored.

The study had some limitations. First, the study was cross-sectional, so it could not establish associations between exposure and effect, due to both being measured at the same time. Cohort studies should be conducted if possible. In addition, it was not possible to fully understand the relationship between OP exposure and mental state by only investigating the exposure history of the study subjects through questionnaire rather than determining pesticide exposure by detecting the concentration of metabolites of OP in biological materials. More studies are needed to explore the effects of OPs on human mental health using a longitudinal study design with biomarkers of exposure.

Table 2. The status of mental health among subjects with and without OPs exposure

Item	Total Median (P25, P75) /Mean ± SD	Non-exposure Median (P25, P75) /Mean ± SD	Exposure Median (P25, P75) /Mean ± SD	*t/Z*	*P*
CES-D	20.00 (13.00, 26.00)	18.00 (12.00, 25.00)	22.00 (16.00, 27.00)	2.582	**0.010***
Depressed affect	6.00 (2.00, 9.00)	5.00 (1.00, 9.00)	6.00 (3.00, 9.00)	1.584	0.113*
Positive affect	9.00 (6.00, 10.00)	9.00 (6.00, 10.00)	9.00 (7.00, 10.00)	0.053	0.958*
Somatic and retarded activity	4.00 (2.00, 7.00)	3.00 (1.00, 7.00)	6.00 (3.00, 8.00)	3.061	**0.002***
Interpersonal	0.00 (0.00, 1.25)	0.00 (0.00, 1.00)	1.00 (0.00, 2.00)	2.365	**0.018***
BIS	64.18 ± 8.64	64.04 ± 8.53	64.46 ± 8.91	0.372	0.710
Attentional Impulsiveness	17.00 (15.00, 19.00)	17.00 (15.00, 19.00)	17.00 (15.00, 19.00)	1.373	0.170*
Motor Impulsivenes	20.72 ± 4.10	20.58 ± 4.01	21.00 ± 4.28	0.782	0.435
Non planning Impulsiveness	26.75 ± 4.45	26.91 ± 4.35	26.43 ± 4.66	0.825	0.410
BPAQ	35.47 ± 16.77	33.98 ± 17.76	38.53 ± 14.14	2.259	**0.025**
Physical Aggression	10.42 ± 5.82	9.96 ± 5.92	11.37 ± 5.52	1.866	0.063
Verbal Aggression	5.89 ± 3.25	5.88 ± 3.42	5.91 ± 2.89	0.073	0.942
Angry	8.91 ± 4.78	8.60 ± 4.90	9.54 ± 4.49	1.513	0.132
Hostility	11.00 (6.00, 14.00)	10.00 (5.00, 13.00)	13.00 (7.00, 16.00)	3.154	**0.002***
T-AI	35.95 ± 8.30	35.97 ± 8.34	35.92 ± 8.26	0.048	0.962

Note. *Rank sum test.

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Conflicts of Interest The authors declare that there are no conflicts of interest.

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