PERPUSTAKAAN KAMPUS KESIHATAN
UNIVERSITI SAINS MALAYSIA

Neurobehavioural Effects of Long-Term Exposure to Organophosphates in Tobacco-Growing Farmers in Kelantan

Professor Rusli Bin Nordin, MBBS, MPH, PhD

Principal Researcher

USM Short Term Research Grant

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UNIVERSITI SAINS MALAYSIA
DITERIMA
27 OCT 2001
Bahagian R & D
Pusat Pengajian Sains Perubatan

LAPORAN AKHIR PROJEK PENYELIDIKAN
R & D JANGKA PENDEK

A. MAKLUMAT AM

Tajuk Projek: Kesan Neurotingkahlaku Kronik Akibat Keracunan Insektisid Organofosfat Di Kalangan Penanam Tembakau

Tajuk Program: .....

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Tarikh Mula: 01 MEI 2001

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(berserta No. K/P) (550508105791)

Nama Penyelidik Lain: DR. RAZLAN MUSA
(berserta No. K/P) DR. DAW WIN KYI
DR. HASANAH CHE ISMAIL

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B. PENCAPAIAN PROJEK:

(Sila tandakan / pada kotak yang bersesuaian dan terangkan secara ringkas di dalam ruang di bawah ini. Sekiranya perlu, sila gunakan kertas yang berasingan).

[V] Penemuan asli/peningkatan pengetahuan
(Abstract) (1)

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Pengerusi
Jawatankuasa Penyelidikan
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Universiti Sains Malaysia
16150 Kelantan.
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C. PEMINDAHAN TEKNOLOGI

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D. KOMERSIALISASI

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C. PEMINDAHAN TEKNOLOGI

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E. PERKHIDMATAN PERUNDINGAN BERBANGKIT DARIPADA PROJEK (*Klien dan jenis perundingan*)

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F. PATEN/SIJIL INOVASI UTILITI
(*Nyatakan nombor dan tarikh pendaftaran paten. Sekiranya paten/sijil inovasi utiliti telah dipohon tetapi masih belum didaftarkan, sila berikan nombor dan tarikh fail paten*).

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G. PENERBITAN HASIL DARIPADA PROJEK

(i) LAPORAN/KERTAS PERSIDANGAN ATAU SEMINAR

(1) Kertaskerja yang telah diterima untuk pembentangan oral di Kelantan Health Conference 2001 pada 4-5 November 2001 anjuran bersama Jabatan Kesihatan Kelantan dan Jabatan Pembatan Masyarakat, PPSP, USM di New Pan Pacific Hotel, Kota Bharu (Abstract) (2)

(2) Abstrak yang telah dibentangkan di 2nd ASEAN Conference on Primary Health Care, anjuran FPUPAM, Perak Medical Practitioners' Society & Perak Medical College, 16-18 Mac 2001, Ayuen Hotel, Ipoh, Perak (Abstract) (3)

(ii) PENERBITAN SAINTIFIK

(1) Rusli Bin Nordin et al.

Neurobehavioural Effects of Long-Term Exposure to Organophosphates in Tobacco-Growing Farmers

~~(2)~~ (Submitted to INDUSTRIAL HEALTH on 30 August 2001)

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H. HUBUNGAN DENGAN PENYELIDIK LAIN

(Sama ada dengan institusi tempatan ataupun di luar negara)

(1) Department of Public Health & Occupational Medicine, Faculty of Medicine, Graduate School of Medicine, The University of Tokyo, Japan

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(2) ~~(3)~~ National Institute of Industrial Health 6-21-1 Nagao, Tama-ku, Kawasaki 214-8585, Japan

~~(4)~~ (Dr. Shunichi Araki, Director-General)

I. SUMBANGAN KEWANGAN DARI PIHAK LUAR
(Nyatakan nama ajensi dan nilai atau peralatan yang telah diberi).

(1) –

(2) –

(3) –

J. PELAJAR IJAZAH LANJUTAN
(Nyatakan jumlah yang telah dilatih di dalam bidang berkaitan dan sama ada di peringkat sarjana atau Ph.D).

	Nama Pelajar
Sarjana	DR. ARIZA BINTI ABDUL RAHMAN (MC
	DR. KAMARUL IMRAN BIN MUSA (MC
Ph.D	

K. MAKLUMAT LAIN YANG BERKAITAN

WHO Neurobehavioural Core Test Battery (WHO NCTB) can be used to identify subclinical neurobehavioural impairment in patients/workers exposed to neurotoxic chemicals in the workplace.

18.10.2001
Tarikh

Tandatangan

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16/7/93

ABSTRACT

In order to investigate the neurobehavioural effects in workers chronically exposed to organophosphate pesticides in Malaysia using the WHO neurobehavioural core test battery (NCTB), a cross-sectional study of 45 organophosphate-exposed tobacco-growing farmers and 45 controls was conducted. Seven tests of the NCTB — profile of mood states, simple reaction time, digit symbol, digit span, Santa Ana manual dexterity, Benton visual retention, and pursuit aiming tests — were administered to the subjects. The mean serum cholinesterase activity in organophosphate-exposed farmers (8924.7 IU/l) was significantly different from controls (116421.4 IU/l) but within normal range (5300 to 12900 IU/l). The results of analysis of covariance, in which age, length of education, and duration of employment, (covariates) were controlled in 45 exposed farmers and 45 controls, showed that the mean scores on the Profile of mood states-vigour (POMS-vigour), digit symbol correct, digit span forward and digit span backward, Santa Ana non-preferred hand, Benton visual retention test and pursuit aiming tests were significantly lower in the exposed farmers than controls. The results of stepwise multiple regression analysis revealed that none of the neurobehavioural tests' score for 45 organophosphates-exposed farmers were significantly related to serum cholinesterase (Pearson's product-moment correlation [$p > 0.05$]). However, scores on the digit symbol correct, digit span backward and pursuit aiming tests were significantly related to length of education. **We therefore conclude that chronic effects on the nervous system have occurred in this group of farmers and that these effects are likely to be associated with long-term repeated exposure to organophosphate pesticides.**

Key words: organophosphate pesticides, long-term exposure, neurobehavioural effects, WHO neurobehavioural core test battery (WHO NCTB), tobacco-growing farmers

ABSTRACT (2)

Neurobehavioural Effects of Long-Term Exposure to Organophosphates in Tobacco-Growing Farmers

Rusli Bin Nordin, Ariza Binti Abdul Rahman, Lin Naing, Razlan Bin Musa and Kamarul Imran Bin Musa

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Running title: NEUROBEHAVIOURAL EFFECTS OF LONG-TERM EXPOSURE TO ORGANOPHOSPHATES IN TOBACCO-GROWING FARMERS

ABSTRACT

In order to investigate the neurobehavioural effects in workers chronically exposed to organophosphate pesticides in Malaysia using the WHO neurobehavioural core test battery (NCTB), a cross-sectional study of 45 organophosphate-exposed tobacco-growing farmers and 45 controls was conducted. Seven tests of the NCTB — profile of mood states, simple reaction time, digit symbol, digit span, Santa Ana manual dexterity, Benton visual retention, and pursuit aiming tests — were administered to the subjects. The mean serum cholinesterase activity in organophosphate-exposed farmers (8924.7 IU/l) was significantly different from controls (116421.4 IU/l) but within normal range (5300 to 12900 IU/l). The results of analysis of covariance, in which age, length of education, and duration of employment, (covariates) were controlled in 45 exposed farmers and 45 controls, showed that the mean scores on the Profile of mood states-vigour (POMS-vigour), digit symbol correct, digit span forward and digit span backward, Santa Ana non-preferred hand, Benton visual retention test and pursuit aiming tests were significantly lower in the exposed farmers than controls. The results of stepwise multiple regression analysis revealed that none of the neurobehavioural tests' score for 45 organophosphates-exposed farmers were significantly related to serum cholinesterase (Pearson's product-moment correlation [$p > 0.05$]). However, scores on the digit symbol correct, digit span backward and pursuit aiming tests were significantly related to length of education. We therefore conclude that chronic effects on the nervous system have occurred in this group of farmers and that these effects are likely to be associated with long-term repeated exposure to organophosphate pesticides.

Key words: organophosphate pesticides, long-term exposure, neurobehavioural effects, WHO neurobehavioural core test battery (WHO NCTB), tobacco-growing farmers

Paper to be presented at the Kelantan Medical Sciences Conference 2001 organised by Kelantan State Health Department and Department of Community Medicine, School of Medical Sciences, Health Campus Kubang Kerian, USM, 4-5 November 2001 in New Pan Pacific Hotel, Kota Bharu.

ABSTRACT (3)

Neurobehavioural Effects of Long-Term Exposure to Organophosphates in Tobacco-Growing Farmers

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Key words: organophosphate pesticides, long-term exposure, neurobehavioural effects, WHO neurobehavioural core test battery (WHO NCTB), tobacco-growing farmers

Paper Presented at the 2nd ASEAN Conference on Primary Health Care, Theme: Priorities in Primary Health Care in ASEAN, Organized by FPMPAM, Perak Medical Practitioners' Society, and Perak Medical College, 16-18 March 2001, Syuen Hotel, Ipoh, Perak

Original Article

Neurobehavioural Effects of Long-Term Exposure to Organophosphates in Tobacco-Growing Farmers

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Running title: NEUROBEHAVIQURAL EFFECTS OF LONG-TERM EXPOSURE TO ORGANOPHOSPHATES IN TOBACCO-GROWING FARMERS

Original Article

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Key words: organophosphate pesticides, long-term exposure, neurobehavioural effects,

WHO neurobehavioural core test battery (WHO NCTB), tobacco-growing farmers

INTRODUCTION

Human research increasingly supports the development of chronic neurological sequelae following acute exposures to organophosphates (OP) (Aiuto et al., 1993; Ames et al., 1995; Bazylewicz-Walczak et al., 1999; McConnell et al., 1994; Rosenstock et al., 1990; Rosenstock et al., 1991; Savage et al, 1988; Steenland et al., 1994). Aiuto et al. (1993) provided clinical documentation of delayed polyneuropathy in a child after accidental chlorpyrifos ingestion whilst McConnell et al. (1994) showed evidence of methamidaphos-induced peripheral neuropathy among Nicaraguan agricultural workers. Significant correlation between high OP exposures and neurologic sequelae (Ames et al., 1995) as well as neurobehavioural performances (Bazylewicz-Walczak et al., 1999) has also been observed. Studies by Savage et al. (1988), Rosenstock et al. (1990; 1991), and Steenland et al. (1994) suggest strongly that people who have developed clinically observable symptoms following a single, high concentration OP exposure have deficits in attention, memory, and coordination that persist for many years. However, the possibility that a background of previous lower-level exposures to other pesticides contributing to the chronic neurological sequelae, cannot be entirely discounted (Rom, 1998).

Concerns have been expressed that repeated low-level exposure over months or

years might result in chronic damage to the nervous system (Davies, 1990; Mearns et al., 1994; Savage, 1992; Stephens et al., 1995; Wagner et al., 1994). Subjects affected by these kinds of exposures were reported to have poor mental health and problems with memory and concentration. Animal studies have also shown that subtle neurobehavioural impairments may persist long after normalization of acetyl cholinesterase activity following prolonged exposure to OP (Gralewicz and Socko, 1997; Socko, 1999). However, many reports on workers chronically exposed to low levels of OP were unable to provide conclusive evidence of neuropsychological impairment in those workers (Beach et al. 1996; Daniell et al., 1992; Duffy et al., 1979; Duffy and Burchfiel, 1980; Jager et al., 1970; Kaplan et al., 1993; Korsak and Sato, 1977; London et al., 1997; Steenland, 1996; Stephens et al., 1995; Wagner, 1994).

In the present study, the authors assessed neurobehavioural effects of long-term, low-level exposure to OP on tobacco-growing farmers in Kelantan, Malaysia.

SUBJECTS AND METHODS

Subjects

Forty-five male tobacco-growing farmers residing in Bachok District, Kelantan, who were occupationally exposed to OP, participated in the research after adequate explanation by one of the authors and the study was conducted with their informed consents during August, and September of 2000. Criteria for inclusion were (1) male; (2) aged between 18 to 59 years; and (3) at least 2 years experience as farmers. Potential participants were excluded if their medical histories revealed (1) pesticide poisoning within 3 months prior to the study (which could be associated with subacute, irreversible sequelae; (2) diseases or injuries to the central nervous system (including trauma with period of unconsciousness totalling more than 15 minutes; (3) a history of learning disability or congenital defects of the central nervous system; and (4) a history of alcohol, narcotic, or other drug abuse. Each case was individually matched to a control subject from the School of Medical Sciences, University Science Malaysia, Kelantan, who has never been exposed to OP for age (within 1 to 3 years). Persons younger than 15 year were excluded from the study because the adult neuropsychological test battery was not appropriate for them, and person older than 70 were excluded because more extreme "normal ageing" effects on neuropsychological performance would be expected for such subjects. They consumed neither drugs nor

alcohol on the day of the testing, and none of them abused substances. Age, length of education, duration of employment, and serum cholinesterase activity (ChE) in cases and controls are shown in Table 1. Except for age, highly significant differences were found between the cases and controls regarding length of education, duration of employment, and ChE ($p < 0.001$).

Methods

Neurobehavioural tests. Seven tests from the WHO Neurobehavioural Core Test Battery (NCTB) were performed by the OP-exposed cases and controls at the worksite and the Occupational and Environmental Laboratory, Department of Community Medicine, School of Medical Sciences, University of Science Malaysia, respectively, according to the operational guide of WHO (1986). Profile of mood states (POMS) was used to asses affect in the domain of tension-anxiety, depression, anger-hostility, vigour, fatigue and confusion. Simple reaction time (SRT) was used to estimate attention and response speed, digit symbol (DSy) for the perceptual-motor speed test, digit span (DSp) [forward (DSpf) and backward (DSpb)] for the auditory attention and memory test, Santa Ana manual dexterity [preferred hand (SAph), non-preferred hand (SAnph)] to estimate manual dexterity, Benton visual retention

(BVR) for the visual perception and memory test, and pursuit aiming (PA) for assessing motor steadiness. A brief description of the tests, with functional domains within parentheses, is listed below.

1. *Profile of mood states (affect).* The profile of mood states questionnaire is on which the subject rates himself on a scale from zero to four about feeling experienced during the previous seven days. These include 65 items and provide a six-point mood profile: tension, depression, anger, vigour, fatigue and confusion. The profile of mood states was a sensitive indicator of neurotoxicity in a previous study of workers exposed to inorganic lead (Maizlish et al.,1995).

2. *Simple reaction time (psychomotor performance).* The subject's task was to give fast motor responses to repetitive visual stimuli presented at randomly varied intervals of 1.0 to 10.0 seconds by a standard reaction time tester (Software Science, USA). The subject was presented with 64 stimuli to which he must respond within 6 minutes. Only stimulus-to-reaction time in milliseconds of up to 3 seconds were considered successful for each trial and used in the calculation of average reaction time.

3. *Digit symbol (psychomotor performance).* The digit symbol (Dsy) worksheet contains a list of numbers that are associated with certain simple symbols and a list of random digits from one through nine with blank squares below each digit. The subject's task was to fill the blank squares with the symbols paired to their corresponding digits and to do so as quickly as he could for 90 seconds. The scoring was based on the number of

symbols correctly filled in.

4. *Digit span (attention and memory).* The digit span test is comprised of two different parts, digits forward (DSpf) and digits backward (DSpb), each consisting of seven pairs of progressively longer sequences of random numbers. The task of the subject was to repeat the sequences, which the examiner read aloud, in the same order as they were given in the digits forward test and in the reverse order in the digits backward test. Two points were given for correctly repeating both sequences, 1 point for one correct sequence, and 0 for no correct sequence. Each of the tests awarded a maximum of 14 points.

5. *Santa Ana manual dexterity (manual dexterity).* The Santa Ana equipment consists of a base plate with 48 square depressions and equal number of fitted pegs having a cylindrical upper part and square base. The subject's task was to turn each peg 180 degrees, as fast as possible. Separate measurements were taken for the preferred hand (SAph), and the non-preferred hand (SAnph). Two trials were given for each hand and each trial lasted 30 seconds. The sum of correctly turned pegs in the two trials constituted the score for each hand.

6. *Benton visual retention (perception and memory).* The Benton visual retention (BVR) test (recognition form) consists of 20 cards presented as 10 pairs of two. The first of

symbols correctly filled in.

4. *Digit span (attention and memory)*. The digit span test is comprised of two different parts, digits forward (DSpf) and digits backward (DSpb), each consisting of seven pairs of progressively longer sequences of random numbers. The task of the subject was to repeat the sequences, which the examiner read aloud, in the same order as they were given in the digits forward test and in the reverse order in the digits backward test. Two points were given for correctly repeating both sequences, 1 point for one correct sequence, and 0 for no correct sequence. Each of the tests awarded a maximum of 14 points.

5. *Santa Ana manual dexterity (manual dexterity)*. The Santa Ana equipment consists of a base plate with 48 square depressions and equal number of fitted pegs having a cylindrical upper part and square base. The subject's task was to turn each peg 180 degrees, as fast as possible. Separate measurements were taken for the preferred hand (SAph), and the non-preferred hand (SAnph). Two trials were given for each hand and each trial lasted 30 seconds. The sum of correctly turned pegs in the two trials constituted the score for each hand.

6. *Benton visual retention (perception and memory)*. The Benton visual retention (BVR) test (recognition form) consists of 20 cards presented as 10 pairs of two. The first of

each pair contains the pattern to be memorized and the second contains four patterns, one of which is identical to the pattern presented previously. After looking at each card presented for ten seconds, the subject must recognize the right patterns among the confounders in the next card presented immediately after. The score was given for the number of patterns correctly recognized.

7. *Pursuit aiming (motor steadiness).* The subject's task was to place one dot inside each circle following the pattern given on the test sheet. This task was to be performed as quickly as possible. Two trials, each lasting 60 seconds, were to be accomplished and the number of correctly placed dots in both trials constituted the score.

Serum cholinesterase activity (ChE). Five ml of venous blood, drawn from each subject, was placed in a plain test tube and centrifuged over 4000 rpm for 5 min. The ChE was read from a Hitachi 912 automated machine (Knedel and Bottger, 1967). Reference values for men (all ages), according to den Blaauwen et al. (1983), was 5300 to 12900 IU/l.

Statistical Analysis. Student's *t* test was used to analyse differences in the variables listed in Table 1 between the OP-exposed cases and controls. The level of

statistical significance for the difference between cases and controls was set at 0.05. The relationship between the results of neurobehavioural tests and the level of exposure was examined by the analysis of covariance (ANCOVA); factor is group (cases or controls) and covariates are age, length of education, and duration of employment. The relationship between the neurobehavioural performances and age, length of education, duration of employment, alcohol consumption, and ChE in 45 OP-exposed cases was analysed with Pearson's product moment correlation and with stepwise multiple linear regression analysis. ChE together with one of the four remaining variables (i.e., age, length of education, and duration of employment) were entered and removed at $p < 0.05$. These analyses were carried out using SPSS© version 9.0 in the Unit of Biostatistics and Research Methodology, School of Medical Sciences, Universiti Sains Malaysia, Health Campus Kubang Kerian, Kelantan, Malaysia.

RESULTS

Results of the analysis of covariance for neurobehavioural tests in 45 OP-exposed cases and 45 controls are shown in Table 2. The mean scores on the POMS-vigour, digit symbol correct, digit span forward and digit span backward, Santa Ana non-preferred hand, Benton visual retention test and pursuit aiming tests were

significantly lower in the cases than controls (Table 2)

In the stepwise multiple regression analysis, none of the neurobehavioural tests' scores for 45 OP-exposed cases was significantly related to ChE (Pearson's product-moment correlation or Spearman's rank correlation [$p > 0.05$]). However, score on the digit symbol correct, digit span backward and pursuit aiming (PA) test, were significantly related to the length of education (Table 3).

DISCUSSION

The mean scores on the POMS-vigour, digit symbol correct, digit span forward and digit span backward, Santa Ana non-preferred hand, Benton visual retention test, and pursuit aiming tests were decreased significantly in the OP-exposed cases on the day when testing was done (Table 2 and 3). We therefore suggest that chronic effects on psychomotor performance (i.e. sustained attention, response speed, motor steadiness and auditory memory), as measured by the POMS-vigour, digit symbol correct, digit span forward and digit span backward, Santa Ana non-preferred hand, Benton visual retention test and pursuit aiming tests are caused directly by OP exposure. However, we could not verify whether these chronic effects were associated with the duration (acute

or chronic) or intensity (high-level or low-level) of exposure to OP. Future studies should be designed to clarify the relation between chronic neurobehavioural effects of OP and duration, and also intensity, of exposure to OP.

None of the neurobehavioural tests, i.e. the Santa Ana non-preferred hand was significantly associated with ChE in 45 OP-exposed cases in the present study. Perhaps ChE is not a good predictor of the chronic effects of OP on neurobehavioural performances.

Of the three potential predictors (i.e., age, length of education, and duration of employment), only length of education appeared to be important confounders in the present study.

The present study, however, had several limitations. A prospective study would be a more appropriate design to investigate the relation between level of exposure and chronic effects of OP. Serum cholinesterase activity (ChE) has not been established to be an effective predictor of neurobehavioral performances in many studies; instead, urinary dialkylphosphates has been shown to be significantly related with neuropsychological performances. Drevenker et al. 1991 have confirmed that dialkylphosphorus metabolites in the urine are a more sensitive index of absorption than cholinesterase inhibition in the serum. Other studies have used red blood cell

cholinesterase as a more suitable predictor than ChE. Finally, sample size of cases and controls must be increased and appropriate matching of cases and controls for other biologically plausible confounders is necessary in order to increase the statistical power of the tests.

ACKNOWLEDGEMENTS

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Table 1. Differences in age, length of education, duration of employment, alcohol consumption, and serum cholinesterase activity (ChE) between 45 OP-exposed cases and 45 controls*

Variable	Cases	Controls	Differences† *p* value
Age (yr)	44.4(9.6)	42.4(8.5)	>0.05
Length of education (yr)	7.0(3.5)	10.5(3.0)	< 0.001
Duration of employment (yr)	19.7(9.9)	12.9(7.4)	< 0.001
ChE (IU/l)	8924.7(1754.0)	11421.4(1855.4)	< 0.001

*Mean values with standard deviations in parentheses are shown.

†Student's *t* test

Table 2. Differences in neurobehavioural tests between 45 OP-exposed cases and 45 controls: analysis of covariance*

Test†	Cases		Controls		Differences
	Mean	SD	Mean	SD	*F* value
Profile of mood states					
tension anxiety	5.64	3.3	7.00	4.0	0.903
depression	5.53	6.5	6.70	6.9	0.822
anger hostility	5.42	4.4	7.77	5.6	1.667
vigour	14.20	5.0	18.75	4.1	5.789
Fatigue	5.69	5.2	4.48	3.6	0.481
confusion	4.62	2.8	5.18	3.2	0.296
Simple reaction time [X 10^{-2}]	26.82	4.8	26.07	4.1	0.665
Digit symbol (DSy)	26.10	12.2	46.40	12.5	36.685§
Digit span (DSp)					
Forward (DSpf)	7.87	2.4	8.29	2.6	3.180‡
Backward (DSpb)	3.93	1.6	4.11	1.8	6.690§
Santa Ana manual dexterity					
Preferred hand (SAph)	42.24	10.48	44.53	7.7	1.727
Non-preferred hand (SAnph)	39.20	10.7	42.84	5.4	2.718‡
Benton visual retention (BVR)	5.93	1.9	7.71	5.1	3.036‡
Pursuit aiming (PA)	71.4	20.6	99.16	26.6	8.430§

*Factor is group (cases or controls) and covariates are age, length of education, duration of employment, and alcohol consumption.

†Results were expressed as standard scores according to the operational guide of WHO (1986).

‡$p < 0.05$.

§$p < 0.001$.

Table 3. Regressions of neurobehavioural tests on age, length of education, duration of employment, and serum cholinesterase activity (ChE) in 45 OP-exposed cases: stepwise multiple regression analysis*

Criterion variable	R†	Set of independent variables selected‡
Digit symbol (Dsy)	0.640	Education (0.640//)
Digit span backward (DSpb)	0.512	Education (0.512#)
Pursuit aiming (PA)	0.534	Education (0.534#)

*Serum cholinesterase activity (ChE) together with one of the remaining variables were entered and removed at a significance level of $p < 0.05$.

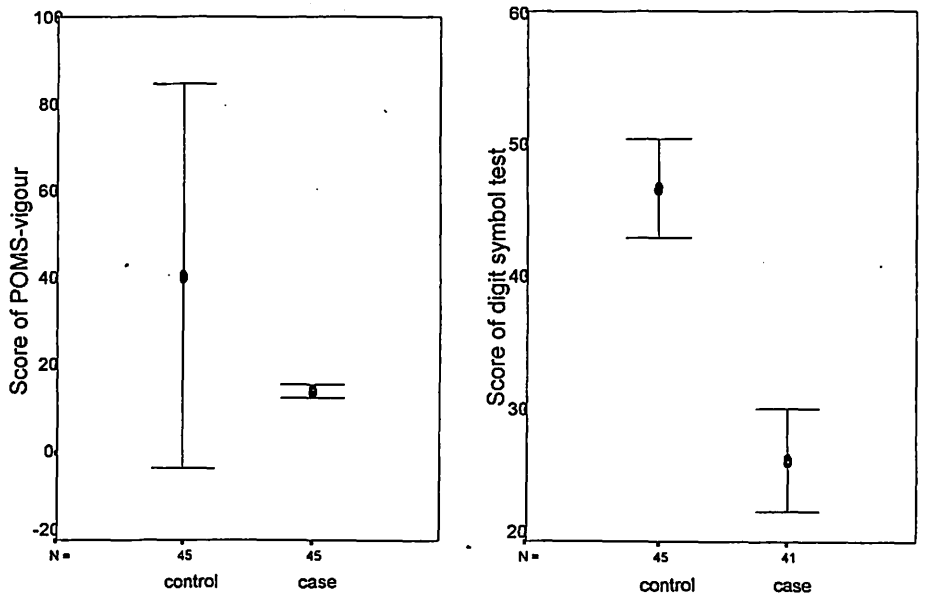
†Multiple regression coefficient.

‡Standardized partial regression coefficients in parentheses.

#$p < 0.05$.

//$p < 0.01$.

Fig. 1. Differences in POMS-vigour, digit symbol correct, digit span forward, and digit span backward, Santa Ana non-preferred hand, Benton visual retention test and pursuit aiming tests between 45 organophosphate-exposed cases and 45 unexposed controls (analysis of covariance controlling for age, length of education, and duration of employment).



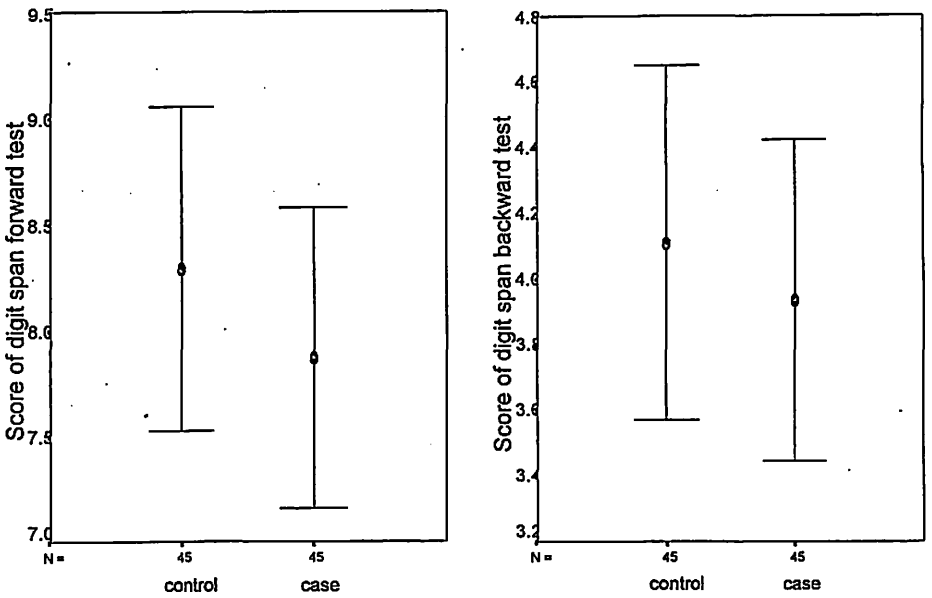
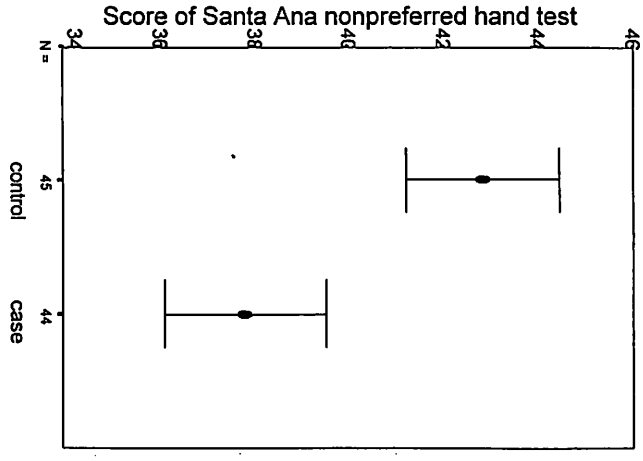
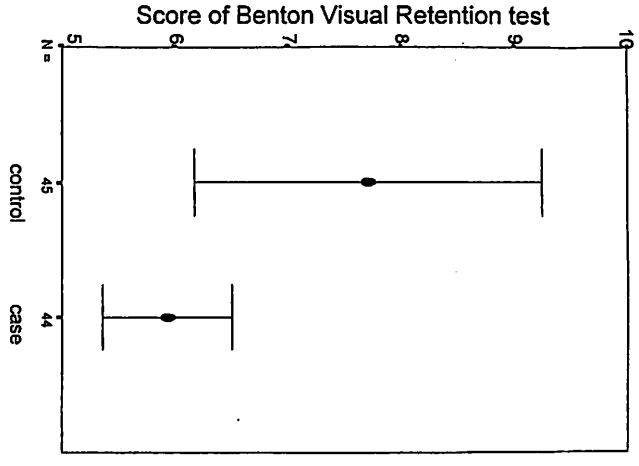
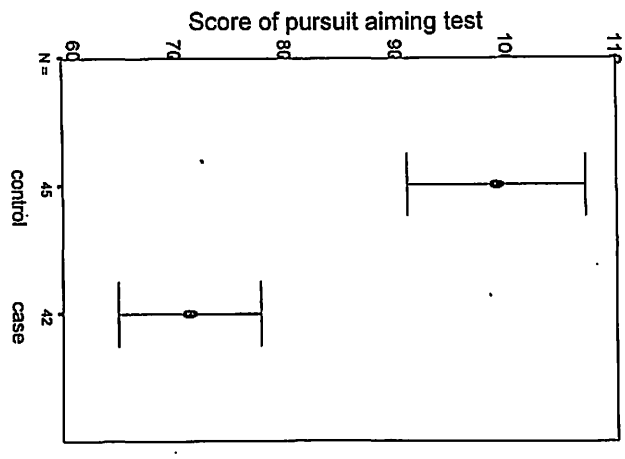


Fig. 1, continued.


Score of Santa Ana nonpreferred hand test
34
36
38
40
42
44
46
N =
control
45
case
44


Score of Benton Visual Retention test
5
6
7
8
9
10
N =
control
45
case
44


Score of pursuit aiming test
60
70
80
90
100
110
N =
45
42
control
case