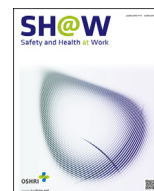




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Original Article

Carpal Tunnel Syndrome Among Male French Farmers and Agricultural Workers: Is It Only Associated With Physical Exposure?

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ABSTRACT

Background: Exploratory study to investigate whether co-exposure to physical wrist stressors and chemicals is associated with carpal tunnel syndrome (CTS) in French male farmers and agricultural workers.**Methods:** Cross-sectional study of 711 men aged 30–65 years and working as either farmers or agricultural workers in 2009–2010 within a cohort covered by the French Agricultural Workers' and Farmers' Mutual Benefit Fund. CTS and exposure to physical wrist stressors and chemicals were assessed using a self-administered questionnaire. Associations between CTS and personal/medical factors, exposure to physical wrist stressors, exposure to chemicals, and co-exposure to physical wrist stressors and chemicals were studied using multivariate logistic regression models.**Results:** Forty-four men [5.6% [95% confidence interval (CI) 4.0–7.7]] reported that they had suffered from unilateral/bilateral CTS during the last 12 months. CTS was associated with age, current smoking [odds ratio (OR) = 2.1 (1.0–4.5)], and exposure to physical wrist stressors [OR = 2.6 (1.1–5.9)]. An association was found between CTS and co-exposure to physical wrist stressors and chemicals [OR = 3.3 (0.8–14.3), $p = 0.044$] in comparison with the no-exposure group.**Conclusions:** This exploratory study shows an association of CTS with exposure to biomechanical wrist stressors in male farmers and agricultural workers and suggests an association of CTS with co-exposure to physical wrist stressors and chemicals. Owing to the limitations of the study, this result must be confirmed by a prospective study with objective assessments of the outcome and exposure before drawing conclusions on the possible synergistic effects of mechanical stressors and chemicals on the impairment of the median nerve.© 2019 Occupational Safety and Health Research Institute, Published by Elsevier Korea LLC. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Carpal tunnel syndrome (CTS) is a common entrapment neuropathy responsible for paresthesia of the hand and impaired fine motor control for digit force production and dexterity [1]. CTS represents a leading cause of compensation claims of workers worldwide, with workers in the agriculture, manufacturing and construction sectors being particularly affected [2,3].

Certain personal characteristics (e.g., age, sex, wrist shape, and genetics) [4–7], medical conditions (e.g., obesity, diabetes mellitus, and arthritis) and habits (e.g., smoking) [8–11] are known to increase the risk of CTS. Working conditions exposing workers to biomechanical stressors have also been identified as risk factors for CTS, namely forceful manual exertion, repetitive movements, and hand-arm transmitted vibrations [2,12–16].

High prevalence of CTS has been reported in farmers and agricultural workers in areas such as viticulture, specialized crops, and

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gardening [17–21]. Most farmers and agricultural workers are exposed to multiple physical wrist stressors (e.g., manual handling of loads, repetitive movements and awkward wrist postures) in their working environment, leading to increased pressures in the carpal tunnel [20] and median nerve dysfunction [22].

Many agricultural workers are also exposed to multiple chemical agents such as pesticides, either through directly handling pesticides or through working in recently treated fields, as well as mixtures of organic solvents (OSs) and paints during the maintenance and repair of machinery [23–27]. Information on the possible impact of such chemical exposure on the risk of CTS is still scant, despite the potential neurotoxic effects of some chemicals (e.g., pesticides) [28]. In addition, workers may be exposed to environmental stressors (e.g., cold and hot environments) and psychosocial stressors, thus justifying an integrative approach of the occupational exposures [27,29].

Many studies have investigated the effects of exposure to physical stressors on the risk of CTS [2,12–16]. However, few studies have shown concern for the potential effects of exposure to chemicals on the risk of CTS or the effects of co-exposure to neurotoxic chemicals and physical stressors [30,31]. Agricultural workers are particularly exposed to biomechanical stressors and chemicals during agricultural tasks and maintenance and repair activities; this raises the question of potential synergistic effects of mechanical stressors and chemicals on the risk of CTS. As suggested for diabetic polyneuropathy, exposure to chemicals may generate diffuse subtle nerve damage rendering the median nerve more prone to entrapment at the carpal tunnel (“double-crush hypothesis revisited”) [32] and potentiating the effect of mechanical stress during tasks exposing workers to physical wrist stressors and chemicals [31,33]. Beside impairments of the peripheral nervous system, subclinical change of the central nervous system (CNS) may occur in agricultural workers exposed to chemicals [26,34–36]. Such CNS impairments may decrease the sensorimotor control of finger force production and dexterity generating higher mechanical stress of the median nerve in case of co-exposure to chemical and physical wrist stressors [1].

This is an exploratory study aiming to investigate the association of co-exposure to physical wrist stressors and chemicals with CTS in a French population of male farmers and agricultural workers. The hypothesis of the study was a higher risk of CTS in workers co-exposed to both physical wrist stressors and chemicals when compared with workers exposed only to physical wrist stressors or chemicals during manual agricultural work.

2. Method

2.1. Study population

Within the framework of the Cohort for Epidemiological Surveillance in Connection with Occupation (COSET) programme (COSET-MSA study), a pilot study was carried out in 2010 in five French administrative areas among workers in agriculture and related occupations covered by the Mutualité Sociale Agricole (MSA, French Agricultural Workers’ and Farmers’ Mutual Benefit Fund). This surveillance programme aims to study health characteristics and morbidity trends in relation to occupational factors [37].

Workers included were nonsalaried (e.g., farmers and stud farm managers) and salaried workers (e.g., agricultural workers) aged between 18 and 65 years who had worked at least 90 days in a workplace affiliated to the MSA in one of the five French administrative areas concerned. In each area, 2,000 individuals were randomly selected from the MSA database after stratification for gender, age and employment status (salaried vs. nonsalaried

workers). Among the 10,000 selected workers, 9,477 had a valid postal address, and 2,363 responded to a self-administered postal questionnaire (participation rate: 24.9%) (Fig. 1). Salaried workers, workers in service companies, or those who had held their job for longer than 6 months were more likely to respond [38].

Analyses were carried out only on the data of the cross-sectional pilot study implemented in 2010 and restricted to individuals aged over 30 (there was no CTS in individuals under 30 in the data set), who were active in farming when filling in the questionnaire and who had been working for at least 12 months. Only men’s data ($n = 711$) were analyzed because of the low number of women in this sector ($n = 332$).

2.2. Data collection

Information on personal characteristics (age, height, and weight), health status, habits (alcohol and tobacco consumption), and exposure to work-related stressors was collected using the postal questionnaire.

2.3. Outcomes

The presence of CTS in the preceding 12 months was assessed by answering the question: “Do you suffer, or have you suffered, from CTS in the last 12 months (whether CTS required sick leave and/or treatment or not)?”.

2.4. Personal and medical risk factors

Body mass index was calculated, and obesity was defined as a body mass index of 30 kg/m² or greater. Information on diabetes mellitus, rheumatoid arthritis, and thyroid diseases (whether requiring prescription drugs or not) was collected. Current tobacco consumption and alcohol use disorders (Alcohol Use Disorders Identification Test) [39] were self-assessed.

2.5. Work-related psychosocial stressors

Effort–reward imbalance (ERI) was assessed for the current professional situation using a validated French version of Siegrist’s questionnaire [40].

2.6. Work-related physical stressors

Physical exposure in the preceding 12-month period was assessed by questionnaire for a typical workday using definitions from the European criteria document for the relatedness of MSDs (Appendix I) [41,42].

“Physical wrist exposure” was defined as exposure to at least one of the following five factors:

1. *High physical perceived exertion* [score over 15 on the Borg rating of Perceived Exertion scale, graduated from 6 (“very, very light”) to 20 (“maximum exertion”)],
2. *Repetitive hand movements* (performing more than two actions per minute for more than 4 hours/day),
3. *Hand-transmitted vibrations* (using a vibrating hand-tool for more than 2 hours/day),
4. *Awkward wrist postures* (repetitive or sustained wrist bending for more than 2 hours/day),
5. *Repetitive pinching* (holding tools/objects in a pinch grip for more than 4 hours/day).

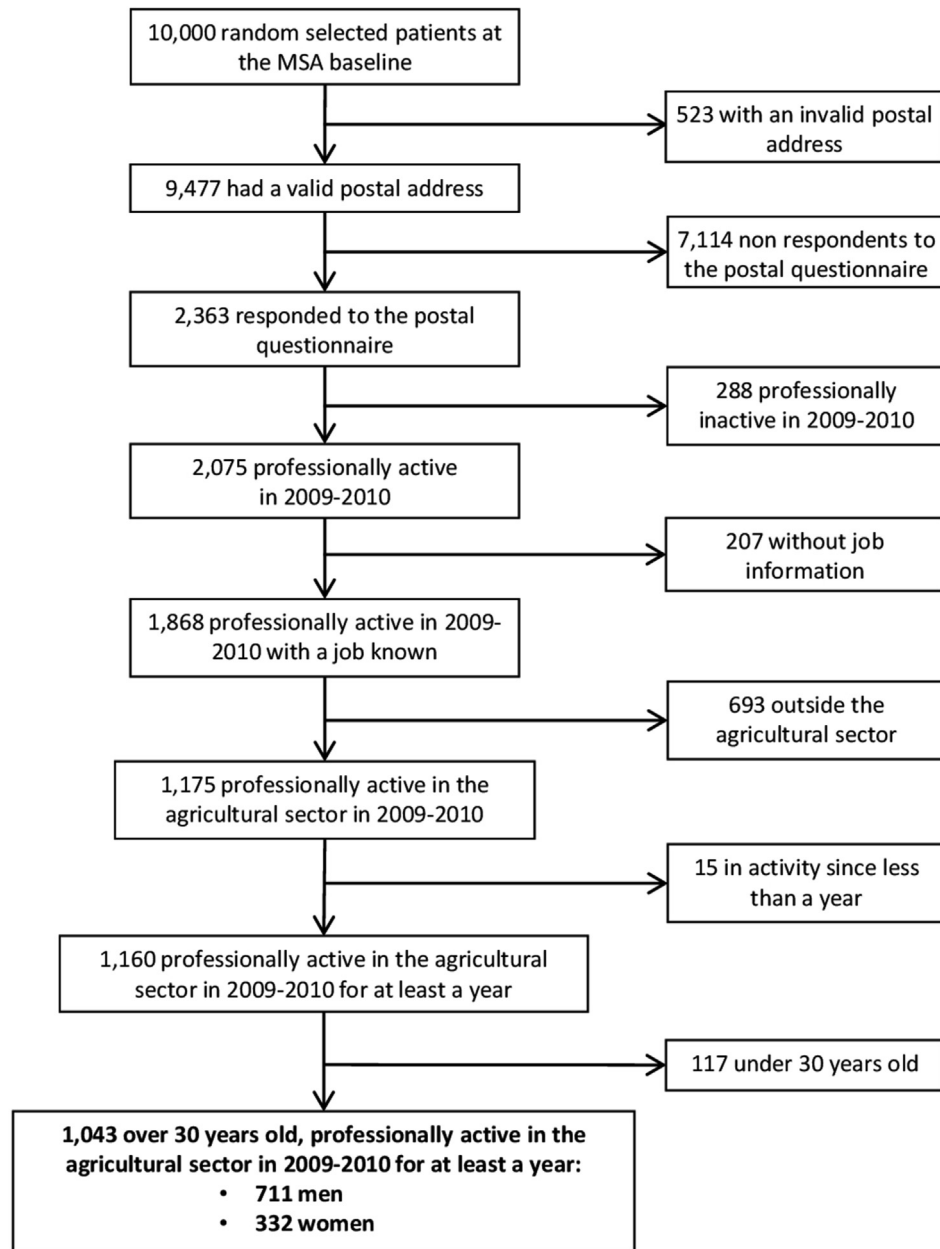


Fig. 1. Flow chart of the study population. (MSA, Mutualité Sociale Agricole).

2.7. Work-related chemicals

Chemical exposure to at least one of the six chemical products (generic names) was assessed for their entire occupational life: trichlorethylene, white spirit (mineral spirit), cellulosic diluents, paints and varnishes, inks and dyes, and pesticides (weed killers, insecticides, and fungicides) for the treatment of plants, seeds, and cultivated soils (Appendix I).

2.8. Co-exposure to work-related physical stressors and chemicals

A “co-exposure” variable to physical wrist stressors and chemicals was created according the following four categories:

1. *No-exposure group*: no exposure to any of the five physical wrist stressors and no exposure to any of the six chemicals,
2. *Physical exposure group*: only exposure to at least one of the five physical wrist stressors,
3. *Chemical exposure group*: only exposure to at least one of the six chemicals,
4. *Co-exposure group*: exposure to both (at least one of the five) physical wrist stressors and (at least one of the six) chemicals.

2.9. Statistical analyses

The data have been weighted to provide estimates that were representative of the working population covered by the MSA in

the five French administrative areas, aged between 18 and 65 years, who had worked at least 90 days. Nonresponse to the survey was corrected from the data available for all randomly selected subjects (respondents and nonrespondents): sociodemographic data (sex, age, geographical area, and salaried/nonsalaried status), socio-professional data from the MSA (last entry, compensated accident at work/occupational diseases), and health data from the French Health Insurance Information System database (reimbursement of care, absenteeism for health reasons, and hospitalization). The final weights were then calculated using the following calibration variables available in the source population: sex, age, salaried/nonsalaried status, and geographical area [43].

Twenty percent (20.4%) of workers had missing values for at least one of the variables studied. Consequently, a multiple imputation method was performed. We assumed that the missing data were missing at random. Variables included in the imputation models were CTS, personal and medical factors, work-related physical stressors, work-related chemicals, weight, and five auxiliary variables not present in the logistic models (occupational category and type of culture: corn, vine, arboriculture, and straw cereals). Ten imputed data sets were created using a fully conditional approach [44].

Weighted univariate logistic regression analyses were run to test associations between the occurrence of CTS and each variable in men 45. Five weighted multivariate logistic regressions were then performed:

- *Model 1*: Including personal and medical risk factors. Rheumatoid arthritis and thyroid diseases were not included because of the low number of cases thereof ($n = 3$ and $n = 6$, respectively); all other personal and medical factors were forced into the models because of their association with CTS in the literature (e.g., age, obesity, diabetes mellitus, current tobacco, and alcohol consumption);
- *Model 2*: Physical wrist exposure added to model 1;
- *Model 3*: Chemical exposure added to model 1;
- *Model 4*: Physical wrist exposure and chemical exposure added to model 1;
- *Model 5*: Co-exposure to physical wrist exposure and chemical exposure added to model 1.

High effort-reward imbalance (ERI ratio > 1) was retained in the models if it was significantly associated with CTS ($p < 0.05$) in the univariate analysis. A sensitivity analysis was conducted on complete case workers (complete case analysis), and all models were rerun.

All analyses were performed using SAS 9.4 software. Descriptive analyses were calculated using the *surveyfreq* and the *surveymeans* procedures. The logistic models were executed with the *surveylogistic* procedure. The *mi* procedure was used to impute the missing data, and the *mianalyze* procedure was used to combine the results of the descriptive analyses and to obtain the estimated parameters and the associated covariance matrix of logistic regression [46]. Odds ratios with 95% confidence intervals [OR (95% CI)] are presented for each model.

3. Results

3.1. Population

A small majority of the 711 male workers under analysis were farmers (53.6%). Almost a third were blue-collar workers and laborers (32.1%) [agricultural and forestry blue-collar workers and

laborers (25.7%), gardeners (4.2%)], and a smaller group was comprised of agricultural technicians (7.4%).

Job seniority in the last job was high [median 17.8 years (IQR 8.9–25.8)], and most workers had kept the same job (60.8%) or had had only had two jobs (30.4%) since the beginning of their career.

The main activity sectors were pastoral farming (28.1% including raising cattle, poultry, and pigs), arable farming (20.9% including growing vegetables and cereals), viticulture (7.8%), fruit-growing (6.9%), mixed farming (pastoral and arable) (7.6%), and agricultural services (10.7%) (Table 1).

3.2. Outcomes

Forty-four men [5.6% (95% CI 4.0–7.7)] suffered from unilateral/bilateral CTS during the last 12 months, whether CTS required sick leave and/or treatment or not.

3.3. Personal and medical risk factors

The prevalence of obesity was relatively low in this male population (10.7%); 4.2% of workers suffered from diabetes mellitus, and very few suffered from rheumatoid arthritis (0.5%) or thyroid diseases (1.1%). Alcohol use disorders concerned only 5.0% of the workers, and 27.1% were current smokers (Table 1).

3.4. Work-related physical stressors (in the preceding 12-month period)

Exposure to physical wrist stressors was common since almost half of these farmers and agricultural workers (49.3%) were exposed to at least one of the five physical wrist stressors under study. The main physical factors were high perceived physical exertion (25.1%), frequent awkward wrist postures (24.3%), and repetitive hand movements (21.4%), followed by hand-transmitted vibrations (12.7%) and repetitive/forceful pinch grips (4.7%) (Table 1).

3.5. Work-related chemicals (for the entire occupational life)

Most workers were exposed to at least one of the six chemical products under study (77.3%) for their entire working life (Table 1). Almost three-quarters (73.8%) were exposed to pesticides for the treatment of plants, seeds, and cultivated soils, 19.4% to at least one OS and 15.4% to paints and varnishes. Other exposure to chemicals was less common (see Table 1 for more details). The median duration of exposure was high for pesticides [20.5 years (IQR 12.9–28.7)] and OSs [white spirit (mineral spirit): 18.6 years (IQR 13.0–25.0)].

3.6. Co-exposure to work-related physical stressors and chemicals

Almost four out of 10 workers (38.5%) were co-exposed to chemical agents and physical wrist stressors (co-exposure group) (Table 1). Roughly, the same proportion (38.8%) was only exposed to chemicals (chemical exposure group). Only 10.8% were exposed only to physical wrist stressors (physical exposure group) and 11.9% were unexposed (no-exposure group). The four groups did not differ according to personal risk factors for CTS (age, obesity, and alcohol use disorders), except for a higher prevalence of current smoking ($p < 0.001$) in the physical exposure only group (46.4%) compared with the no-exposure (27.1%), chemical exposure only (22.6%), and co-exposure (24.4%) groups. Exposure to each physical wrist stressor did not differ between the physical exposure only

Table 1

Occupational category, industry sectors, personal/medical factors and exposure to work-related physical stressors and chemicals in male farmers and agricultural workers (N = 711) suffering or not of self-declared CTS

Variable	CTS (N=44)		No CTS (N=667)		P	Total (N=711)	
	N (crude obs)	% (weighted imp)	N (crude obs)	% (weighted imp)		N (crude obs)	% (weighted imp)
Occupational category (Nmiss: 0)							
Farmers	22	50.2	378	53.8	na	400	53.6
Small sized farms	7	19.6	66	9.0		73	9.6
Middle sized farms	0	0.0	48	8.0		48	7.6
Large sized farms	14	28.1	258	36.0		272	35.6
Craftsmen, salesmen and managers	3	4.5	17	3.7		20	3.8
Professionals	1	0.6	12	1.6		13	1.5
Technicians and associate professionals ^β	3	6.0	59	7.5		62	7.4
Technicians	1	2.2	23	3.1		24	3.0
Foremen	2	3.9	23	2.7		25	2.8
Low grade white collar workers	0	0.0	9	1.7		9	1.6
Blue collar workers and laborers ^γ	15	38.7	192	31.7		207	32.1
Gardeners	3	6.5	19	4.0		22	4.2
Agricultural laborers	12	32.2	153	25.3		165	25.7
Industry sector (Nmiss: 0)							
Crop growing	5	12.8	137	21.4	0.062	142	20.9
Fruit growing	6	15.7	42	6.4		48	6.9
Viticulture	11	18.8	60	7.2		71	7.8
Farm animal breeding (cattle, poultry, pork farming)	7	20.0	198	28.5		205	28.1
Mixed farming and breeding (animal and crop farming)	4	7.3	55	7.6		59	7.6
Services for agriculture	8	16.3	59	10.4		67	10.7
Other agricultural industry sectors	3	9.1	116	18.5		119	18.0
Personal/medical factors							
Age (years) (Nmiss: 0)					0.022		
30-39	3	10.4	155	25.3		158	24.4
40-49	15	33.1	253	39.0		268	38.7
50 or more	26	56.5	259	35.7		285	36.9
Obesity (BMI ≥ 30 kg/m ²) (Nmiss: 4)	4	12.6	75	10.6	0.775	79	10.7
Diabetes mellitus (Nmiss: 14)	3	8.3	24	3.9	0.420	27	4.2
Rheumatoid arthritis (Nmiss: 0)	1	4.8	2	0.2	0.336	3	0.5
Thyroid disease (Nmiss: 0)	1	2.7	5	1.0	0.529	6	1.1
Current smoking (Nmiss: 35)	13	38.5	149	26.4	0.200	162	27.1
Alcohol use disorders (Nmiss: 35)	4	10.0	30	4.7	0.344	34	5.0
Work-related physical stressors							
1.High physical perceived exertion (Nmiss: 9)	16	36.1	165	24.5	0.180	181	25.1
2.Repetitive hand movements (Nmiss: 26)	14	28.5	124	20.9	0.323	138	21.4
3.Hand-transmitted vibrations (Nmiss: 22)	11	22.9	71	12.1	0.120	82	12.7
4.Awkward wrist posture (Nmiss: 18)	15	31.1	139	23.8	0.364	154	24.3
5.Repetitive pinching (Nmiss: 17)	4	14.2	23	4.1	0.159	27	4.7
Physical wrist exposure (1-5) (Nmiss: 27)	32	71.1	304	48.0	0.010	336	49.3
Work-related chemical exposure							
1.Trichloethylene (Nmiss: 58)	8	15.0	33	6.5	0.120	41	6.9
2.White spirit (mineral spirit) (Nmiss: 53)	9	18.5	92	15.9	0.750	101	16.1
3.Cellulosic diluent (Nmiss: 57)	3	10.7	16	2.4	0.189	19	2.8
4.Paints and varnishes (Nmiss: 43)	12	26.1	90	14.8	0.135	102	15.4
5.Ink and dyes (Nmiss: 45)	2	4.3	18	2.9	0.865	20	3.0
6.Pesticides (Nmiss: 34)	34	81.1	475	73.3	0.291	509	73.8
Organic solvents (1-3) (Nmiss: 55)	12	26.5	105	18.9	0.381	117	19.4
Chemical exposure (1-6) (Nmiss: 36)	36	87.5	497	76.7	0.096	533	77.3
Physical-chemical co-exposure (Nmiss: 23)							
No exposure group	3	6.3	73	12.3	0.008	76	11.9
Physical exposure group	5	6.3	74	11.1		79	10.8
Chemical exposure group	9	22.7	267	39.7		276	38.8
Co-exposure group	27	64.8	230	36.9		257	38.5

CTS, carpal tunnel syndrome; na, not applicable; BMI, body mass index; obs, observed data set; imp, imputed dataset; Nmiss, number of missing data.

In bold, P < 0.05.

α: Chi-square test cannot be computed because at least one table cell has 0 frequency. β: Technicians and associate professionals perform mostly technical and related tasks and teach at certain educational levels. Most occupations in this group require skills at the third ISCO level (education which begins at the age of 17 or 18 years and leads to an award not equivalent to a first university degree). γ: The blue collar worker' category includes skilled agricultural, forestry and fishery workers (ISCO-08 group 6) and agricultural, forestry, and fishery laborers (ISCO-08 group 9, elementary occupations).

and co-exposure groups, except for repetitive hand movements, with results showing a lower prevalence in the co-exposure than in only physical exposure group (40.2% vs. 53.5%, $p = 0.087$). Exposure to chemicals did not differ between the chemical exposure only and

co-exposure groups, except for trichlorethylene and white spirit, (mineral spirit) for which there was a higher prevalence in the co-exposure group than in the chemical exposure only group [13.2% vs. 6.0% ($p = 0.031$) and 25.8% vs. 16.7% ($p = 0.037$) respectively].

Table 2

Univariate and multivariate analyses for CTS in male farmers and agricultural workers (N = 711)

Variable	Univariate regression		Model 1		Model 2		Model 3		Model 4		Model 5	
	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P
Personal/medical factors												
Age (years)		0.054		0.016		0.015		0.019		0.017		0.015
30–39	1		1		1		1		1		1	
40–49	2.1 [0.6–7.6]		2.2 [0.6–8.3]		2.3 [0.6–9.1]		2.2 [0.6–8.3]		2.3 [0.6–9.0]		2.2 [0.6–8.7]	
50 or more	3.8 [1.1–13.5]		4.5 [1.3–15.9]		4.7 [1.3–17.2]		4.4 [1.2–15.7]		4.6 [1.3–16.9]		4.7 [1.3–17.0]	
Obesity (BMI \geq 30 kg/m ²)		0.735		0.968		0.965		0.964		0.983		1.000
No	1		1		1		1		1		1	
Yes	1.2 [0.4–3.6]		1.0 [0.3–3.2]		1.0 [0.3–3.5]		1.0 [0.3–3.3]		1.0 [0.3–3.6]		1.0 [0.3–3.5]	
Diabetes mellitus		0.278		0.474		0.592		0.468		0.621		0.670
No	1		1		1		1		1		1	
Yes	2.2 [0.5–9.2]		1.8 [0.4–8.1]		1.5 [0.3–7.2]		1.8 [0.4–8.2]		1.5 [0.3–7.1]		1.4 [0.3–6.8]	
Current smoking		0.155		0.037		0.047		0.025		0.032		0.031
No	1		1		1		1		1		1	
Yes	1.7 [0.8–3.7]		2.2 [1.1–4.5]		2.1 [1.0–4.5]		2.3 [1.1–4.8]		2.3 [1.1–4.9]		2.3 [1.1–5.0]	
Alcohol use disorders		0.204		0.251		0.315		0.331		0.404		0.408
No	1		1		1		1		1		1	
Yes	2.2 [0.6–7.8]		2.1 [0.6–7.4]		1.9 [0.5–7.2]		1.9 [0.5–7.5]		1.8 [0.5–7.2]		1.8 [0.5–6.9]	
Physical wrist exposure		0.018				0.023				0.026		
No	1				1				1			
Yes	2.7 [1.2–6.0]				2.6 [1.1–5.9]				2.6 [1.1–5.9]			
Chemical exposure		0.153					0.172		0.188			
No	1					1		1				
Yes	2.2 [0.7–6.2]					2.2 [0.7–6.6]		2.1 [0.7–6.7]				
Physical-chemical co-exposure		0.032										0.044
No exposure group	1										1	
Physical exposure group	1.1 [0.1–7.6]										1.0 [0.1–7.1]	
Chemical exposure group	1.1 [0.2–5.4]										1.1 [0.2–5.4]	
Co-exposure group	3.4 [0.8–14.2]										3.3 [0.8–14.3]	

OR: odds-ratio; 95% CI: 95% confidence interval; BMI: body mass index.

In bold, $P < 0.05$.

Model 1: Including personal and medical risk factors.

Model 2: Physical wrist exposure added to model 1.

Model 3: Chemical exposure added to model 1.

Model 4: Physical wrist exposure and chemical exposure added to model 1.

Model 5: Co-exposure to physical wrist stressors and chemical exposure added to model 1.

3.7. CTS risk models

Table 2 shows the multivariate models for CTS which are adjusted for personal and medical factors (model 1), exposure to physical wrist stressors (model 2), chemicals (model 3), physical wrist stressors and chemicals (model 4), and co-exposure to physical wrist stressors and chemicals (model 5). High effort–reward imbalance was not associated with CTS (ERI ratio > 1) (crude OR 1.3 [0.5–3.5], $p = 0.58$), and therefore, it was not included in the multivariate models.

As for personal/medical factors, age was associated with an increased risk of CTS, with similar odds ratios for all models: ~2.2 for men aged 40–49 years and 4.5 for men over 50, both compared with 30–39 years. No association was found with obesity and diabetes mellitus, regardless of the model. Contrary to alcohol use disorders, current smoking was associated with CTS in all models.

Concerning physical work-related stressors, CTS was associated with exposure to at least one physical wrist stressor after adjustment for personal/medical factors [model 2, OR = 2.6 (1.1–5.9)] but also after adjustment for personal and medical factors and exposure to chemicals [model 4, OR = 2.6 (1.1–5.9)].

As regards chemical exposure, an association with CTS was observed in workers exposed to chemicals after adjustment for personal/medical factors [model 3, OR = 2.2 (0.7–6.6)] without reaching the level of statistical significance. The OR value did not vary after adjustment for personal/medical factors and physical wrist stressors [model 4, OR = 2.2 (0.7–6.7)]. As shown in model 5,

an association was found between CTS and co-exposure to physical wrist stressors and chemicals ($p = 0.044$), with a higher OR in the co-exposure group [OR = 3.3 (0.8–14.3)]. Complete-case and multiple imputation analyses gave similar results.

4. Discussion

This exploratory study of a large sample group of French male farmers and agricultural workers suggests an association of CTS with co-exposure to physical wrist stressors and chemicals during agricultural tasks and maintenance and repair activities.

4.1. Limitations of the study

The COSET-MSA study suffered from several limitations, namely a rather low participation rate (24.9%). Weightings were calculated, using data available for both respondents and nonrespondents (sociodemographic, medical, and occupational data) to take into account nonresponse to the questionnaire [38]. Moreover, a multiple imputation method was performed to take into account the partial nonresponse representing 20.4% of the sample; the analysis of sensitivity on observed data sets confirms the results obtained on imputed data sets (Appendix II). The study suffers from a lack of statistical power, and its cross-sectional design precluded any causal conclusion between co-exposure to physical wrist stressors and chemicals and CTS. Because CTS and exposure were self-reported, workers suffering from CTS may have overestimated

their exposure. We cannot exclude an inverse causality bias leading the workers most exposed to physical wrist stressors and chemicals to declare more CTS. Moreover, exposure to chemicals might also be a marker for greater hand force being used at work. The definition of CTS lacked specificity [47], leading to possible misclassification bias as farmers suffering from mild CTS may have failed to declare it when answering the questionnaire. All models were adjusted for age, obesity, diabetes mellitus, current tobacco, and alcohol consumption to consider the main potential personal and medical risk factors for CTS and/or peripheral neuropathy. However, we cannot exclude recall bias for mild disorders because the factors were self-reported.

The diverse nature and the seasonal variability of the tasks and activities performed create substantial challenges for exposure assessment of agricultural workers [23]. In this study, exposure to pesticides for the treatment of plants, seeds, and cultivated soils was self-reported and globally assessed for the entire working life without precise information concerning the chemical properties of the pesticides used and the possible presence of neurotoxic agents. Few OSs were assessed, and we cannot exclude exposure to other neurotoxic OSs which may lead to a possible misclassification of exposure. Because exposure information was self-reported, error (misclassification) in exposure estimation may have occurred because of poor recall. Although the validity of self-reported estimates of solvent exposure is not known, several studies have shown that recall of pesticide use among farmers does correlate with both expert judgment and biological sampling [26]. Thus, there is reason to believe that members of this study population were able to provide valid estimates of past occupational exposures. Nevertheless, the type of exposure (processing, agricultural spreading, or cleaning equipment) and use of personal protective equipment to limit dermal, oral, or respiratory exposure were not assessed in the present study.

4.2. Results

The prevalence of CTS in this population was higher than in the French general working population [48]. The increased risk of CTS in older workers and current smokers correlates with previous findings in the general population [4,5,8,49]. According to other studies, the COSET-MSA study suggests a high exposure of farmers and agricultural workers to repetitive hand movements and hand-transmitted vibrations [19,20,50,51] and a higher prevalence of CTS in workers who are the most exposed [18,21,50]. Such exposure during agricultural work can trigger the hypothetical pathophysiological pathways of CTS involving ischemic effects of the median nerve because of increased pressure in the carpal tunnel at the wrist, mechanical injury due to traction and contact stress on the nerve and the effect of vibration on the median nerve [22,52–54]. No association was found with effort-reward imbalance, but the relationship between CTS and psychosocial factors at work remains unclear in the literature [12,14,15,55]. The study was restricted to male farmers and workers because of the low number of women in this sector, but we cannot exclude the existence of potential sex/gender differences among co-exposed workers because male workers are generally more exposed to chemicals and strenuous work than women [19,20,27].

To the best of our knowledge, the impact of chemical exposure on the risk of CTS has rarely been studied despite the potential neurotoxicity of some chemicals [28,33,56,57]. Ophir et al. [31] reported an increased risk of CTS-like symptoms following sub-clinical sensory polyneuropathy (affecting mainly the median and sural nerves) in workers exposed to prolonged low-level organophosphate exposure in rural communities in Israel. However, a case-control study of CTS conducted in the general population of

Wisconsin failed to report an association between CTS and chemical exposure after adjustment for the main personal, medical, and physical factors [30]. Our results suggest that the majority of these French farmers and agricultural workers are exposed to multiple chemical agents, namely pesticides and mixtures of OSs [23–26]. The study suggests an association of CTS with co-exposure to physical wrist stressors and chemicals, but not for those solely exposed to chemicals and uniquely exposed to physical wrist stressors. However, owing to the lack of statistical power, objective outcome, and exposure assessments of the study, the hypothesis of a higher risk of CTS in workers co-exposed to both physical wrist stressors and chemicals when compared with workers exposed only to physical wrist stressors or chemicals during manual agricultural work should be confirmed by larger and prospective studies before drawing any general conclusions.

In conclusion, this exploratory study suggests an association of CTS with co-exposure to physical wrist stressors and chemicals in male farmers and agricultural workers. Owing to the limitations of the study, this result must be confirmed prospectively and in other working populations before drawing conclusions on the possible synergic effects of mechanical intracarpal stress and chemical impairment of the median nerve.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Ethics

The study protocol was approved by the French Data Protection Authority (CNIL) and the French Institutional Review Committee (CNIL number 909091 and DR-2010-321).

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.shaw.2019.12.003>.

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