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ORIGINAL ARTICLE

Pesticide Use and its Effects on Daily Functioning among Elderly Farmers

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ABSTRACT

Background: Poor pesticide handling practices are recorded on a regular basis in Greece, where the average farmer is elderly. This raises concerns regarding their compliance with pesticide regulations and the associated health implications. Our purpose in undertaking the present study was to examine elderly farmers' attitudes regarding pesticide handling and safety issues, as well as, the potential link between pesticide exposure and daily functioning capacity.

Methods: Participants were 1443 elderly individuals, 276 of whom reported long-term, direct exposure to pesticides (spraying in gardens, open fields, and/or a greenhouse). Several aspects of pesticide handling were gleaned via a self-report questionnaire. Ability to perform everyday tasks was assessed with the Blessed Dementia Rating Scale.

Results: On average, participants were not consistent with respect to safety practices. Half could not recall the specific brand names of the pesticides they used and 47.5% reported using chemical cocktails, often exceeding the maximum recommended frequency of applications per year. In many cases, they reported application of banned pesticides, such as DDT, and more than half reported applying pesticides without protective equipment. Analyses showed that exposure to pesticides was associated with impaired everyday functioning (OR = 1.16; 95%, CI = 1.04-1.28) and specifically, with an inability to interpret surroundings and recall recent events, a tendency to dwell on the past and changes in bladder-sphincter control.

Conclusion: We found poor awareness and adherence to safety practices regarding pesticide use among elderly farmers, as well as an association between pesticide use and everyday functioning. Relevant health and environmental implications are discussed.

ABBREVIATIONS

BDR–S: Blessed Dementia Rating Scale; BS: Broad Spectrum; C: Contact; CDR: Clinical Dementia Rating; DDT: Dichlorodiphenyltrichloroethane; EPA: US Environmental Protection Agency; EU: European Union; IARC: International Agency for Research on Cancer; LD: Lethal Dose; MaND: Major Neurocognitive Disorder; MiND: Minor Neurocognitive Disorder; MRL: Maximum Residue Levels; OR: Odds Ratio; S: Systemic; SA: Selective Action; SD: Standard Deviation

INTRODUCTION

The proper and sustainable use of pesticides in the European Union is subject to strict regulations (see http://ec.europa.eu/ for a detailed list). Yet, noncompliance

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issues are recorded on a regular basis with multi-faceted implications for public health. Data have shown that Greece, among other countries, is facing a constantly rising health issue with respect to pesticide mishandling and imports of illegal substances [1,2]. According to a study by the European Food Safety Authority [3], Greece ranked first among all European countries in terms of exceeding MRLs[1] in tomato samples. Recent studies further confirmed the hazardous consequences of poor pesticide handling practices, with river water samples found to exceed maximum allowable concentrations of pesticide residues [4]. Additionally, a study of 87 Greek mothers found high concentrations of pesticide compounds in breast milk, exceeding tolerable daily intake for infants [5].

The impact of acute long-term pesticide exposure on humans has been recorded since 1950 [6]. There is, now, sufficient evidence that imprudent pesticide use is linked to neurological syndromes [7,8], extrapyramidal symptoms [9] and other health problems [10]. Regarding the elderly population, numerous studies have shown that long-term exposure to pesticides is linked to cognitive decline, the development of Alzheimer's disease and neuropsychological impairment [11-15]. The pathway that these pesticide-born cognitive impairment affects functional domains in everyday life is still unclear.

It is imperative to examine pesticide exposure and its link to decline in particular domains of everyday functioning, in order to implement targeted interventions and raise public awareness. This need is even greater in Greece, where, according to the most recent, 2011 National Greek Census [16] the average Greek farmer is of young old age[2] and rural areas have larger proportions of elderly inhabitants than urban centers; a fact, also, supported by a study conducted by Eurostat in 2018 [17]. In addition, in terms of pesticide handling, older adults constitute a high-risk group, as they generally have a lower level of (or no) education than younger adults, and, thus, may potentially have difficulties following the instructions pertaining to proper pesticide use, as indicated by a recent study [18].

Our goal in undertaking the present study was to thoroughly explore elderly farmers' attitudes towards pesticide use and present the safety issues associated with them, as well as, investigate the ways this exposure can affect their everyday life functioning.

MATERIALS AND METHODS

Participants and demographics

Data for the present study were collected as part of a large, longitudinal, population-based epidemiological study conducted in Larissa, Thessaly, Greece [19]. The total cohort included 1943 individuals over 64 years of age [(59.3% were female; total sample mean age = 73.0 (SD = 5.7) years]. Participants were recruited from municipal rolls and were contacted by phone to voluntarily participate in the study. All participants had survived World War II and the subsequent Greek civil war; thus, most had had limited educational opportunities. Their mean education was 7.73 years (SD = 4.8, range = 0-20) and 5.8% of them were illiterate. Of the total sample, two hundred and seventy-six participants [77.2% men; sample mean age = 73.87 years (SD = 4.9); mean years of education = 6.68 (SD = 4.19)] had reported repeated direct exposure to pesticides while spraying their garden and/or professionally spraying fields and/or having a greenhouse and personally using pesticides in it. Those participants constituted the group exposed to pesticides. According to the number of areas they reported pesticide application to, these participants were sub-categorized into the direct exposure to pesticides group or the high exposure to pesticides group (more details, can be found in section 3.2). The rest of the participants served as the no direct exposure to pesticides group.

Table 1 presents the demographic characteristics per exposure group and table 2 shows the number of people per area of pesticide application. Written informed consent was obtained from all those who volunteered to participate and no monetary incentives were offered. Participants were treated according to the Declaration of Helsinki regarding human research participants and all procedures were approved by the institutional ethics review board of the University of Thessaly.

Procedure

Certified neurologists from the Department of Neurology of the Medical Center of the University of Thessaly and trained neuropsychologists from the School of Psychology at Aristotle University of Thessaloniki examined each participant and administered structured questionnaires in face-to-face interviews. Participants provided detailed demographic characteristics and a complete medical history (all based on self-report). Additionally, pesticide exposure and multiple related factors (e.g., types of cultivated crops, the age at which pesticide use commenced and ceased, the duration of farming, the surface area of the fields sprayed, number of pesticide applications per year, total years of pesticide use, adherence to safety practices, etc.) were assessed using a structured questionnaire [21]. All active ingredients were grouped according to the target pest/use into four major categories: 1) insecticides, 2) fungicides, 3) herbicides, and 4) soil disinfectants. According to the chemical composition, the active ingredients were grouped into three major categories: 1) carbamates, 2) organophosphates, and 3) organochlorines.

Ability to perform daily and self-care activities which require both physical and cognitive capacity, in particular memory, comprehension, mathematical skills and

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1   MRLs are the maximum acceptable levels for pesticide residuals in agricultural products as they are defined by regulation No 396/2005 of the European Commission (EC) (ec.europa.eu/).

2   Young old age: 60-69 years, middle old age: 70-79 years, advanced old age: ≥ 80 years [20].

Table 1: Demographic characteristics per pesticide-exposure group.

Sample *n* = 1943	Pesticide-exposure groups		
	No direct exposure (*n* = 1667)	Direct exposure (*n* = 208)	High exposure (*n* = 68)
Sex (% males)	34.50	74.52	85.3
Age	72.91 ± 5.90	73.84 ± 4.94	73.95 ± 4.83
Education	7.92 ± 4.91	7.14 ± 4.34	5.26 ± 3.35
No. of medications affecting cognitive, urinary and bowel function	3.95 ± 2.61	4.08 ± 2.87	3.55 ± 2.65
% of people with MiND	11.60	14.50	11.8
% of people with MaND	5.00	2.93	7.4
BDR-S total score	1.82 ± 2.10	2.04 ± 2.07	2.23 ± 1.64
BDR-S Item 1: Inability to perform household tasks	0.39 ± 0.75	0.28 ± 0.63	0.19 ± 0.57
Inability to handle small sums of money	0.05 ± 0.23	0.04 ± 0.17	0.05 ± 0.22
Inability to remember shortlist of items	0.17 ± 0.30	0.20 ± 0.31	0.23 ± 0.32
Inability to find way about indoors	0.01 ± 0.12	0.01 ± 0.09	0.00 ± 0.00
Inability to find way about familiar streets	0.04 ± 0.17	0.03 ± 0.16	0.02 ± 0.11
Inability to interpret surroundings	0.22 ± 0.13	0.01 ± 0.09	0.02 ± 0.11
Inability to recall recent events	0.11 ± 0.26	0.15 ± 0.28	0.18 ± 0.33
Tendency to dwell on the past	0.55 ± 0.45	0.68 ± 0.41	0.82 ± 0.33
Changes in eating habits	0.03 ± 0.27	0.02 ± 0.21	0.00 ± 0.00
Changes in dressing habits	0.08 ± 0.48	0.07 ± 0.47	0.06 ± 0.29
Changes in bladder-sphincter control	0.38 ± 0.87	0.55 ± 1.11	0.62 ± 1.25

Table 2: Number of participants who reported spraying their garden, fields and/or greenhouse.

Reported use of pesticides in'	N
Garden	59 (24 men)
Fields	9 men
Greenhouse	5 (4 men)
Garden and fields	8 (5 men)
Fields and greenhouse	116 (102 men)
Garden and greenhouse	36 (27 men)
Garden, fields and greenhouse	43 (42 men)

visuospatial orientation, were measured using the Blessed Dementia Rating Scale (BDR-S) [22]. This scale's total score ranges from 0 (normal) to 22 (severe incapacity). Presence and stage severity of dementia symptoms were assessed with the Clinical Dementia Rating Scale (CDR) [23]. The scale assesses five domains of cognitive and functional performance on a five-point scale; CDR = 0 denotes no cognitive impairment, and CDR = 4 denotes severe cognitive impairment. It also provides a global rating score. Diagnostic classification of participants with Mild Neurocognitive Disorder (MiND) or Major Neurocognitive Disorder (MaND) was determined at diagnostic consensus meetings of the research group. Finally, participants were asked to provide a full list of medications they were currently taking.

Standard statistical procedures were carried out using the Statistical Package for Social Sciences (SPSS-Version 22.0).

RESULTS

Attitude towards pesticide use

To explore older farmers' attitudes and safety practices, we calculated frequencies and descriptive data associated with pesticide use among the present sample.

Participants reported applying pesticides with a mean frequency of 3.16 times per year (SD = 3.2, range = 1-20) for gardens and 3.21 times per year (SD = 2.5, range = 1-16) for fields. The mean duration of occupational pesticide exposure was 26.27 years (SD = 19.5, range = 6-70) for garden sprayers and 30.52 years (SD = 18.5, range = 6-70) for field sprayers. Analyses of frequencies of the variables age of commencement and cessation of pesticide use concerning garden spraying and crop spraying can be found in figures 1 & 2. We had no such information for the five people who applied pesticides only in a greenhouse.

In terms of the particular substances used in garden spraying, analyses showed that 52.7% of the participants could not accurately remember the commercial name of the product that they used. Most participants reported using synthetic compounds (78.3%), such as pesticides (34.7%), herbicides (30.5%) and fungicides (13.1%). The mean reported number of different products used over the past year was 1.49 (SD = 0.7, range = 1-4).

With respect to field spraying, 47.5% of the participants reported using all types of pesticides (fungicides,
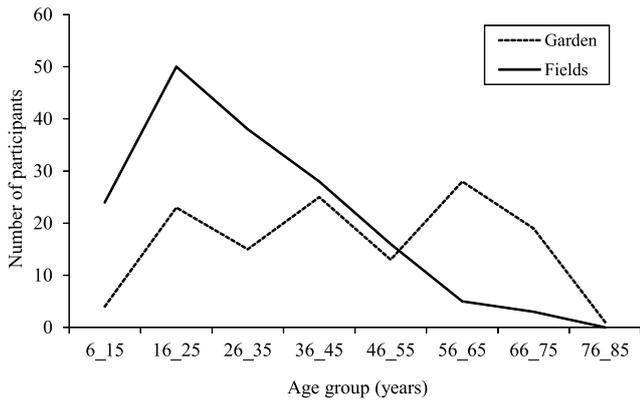
Figure 1 Number of participants who reported having commenced pesticide use in their garden or fields per age group.
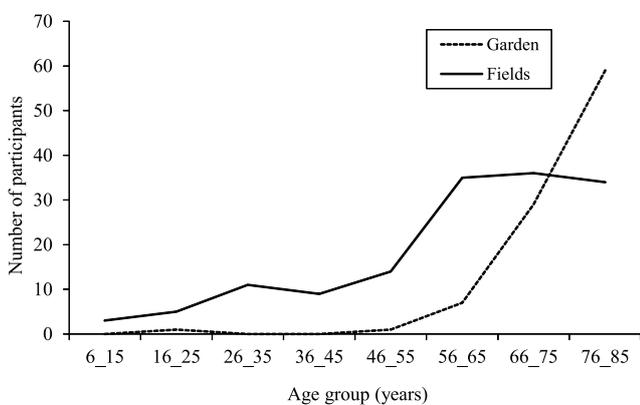
Figure 2 Number of participants who reported having ceased pesticide use in their garden or fields per age group.

insecticides, herbicides and soil disinfectants) combined while the rest reported using one or more, but not all of the aforementioned types. For the 53.10% of the farmers who could accurately recall the commercial names of the products used, further details (brand name and application per year) can be found in table 2.

Overall, participants reported using a mean number of 1.71 different products per year (SD = 0.8, range = 1-4).

With the assistance of an agronomist, and by investigating the characteristics of each reported pesticide, we categorized the pesticides in terms of composition, approval of use in the EU and toxicological characteristics. The results are described in table 3.

Participants who sprayed their fields professionally worked on average for 6.81 hours/day (SD = 5.0, range = 2-20), 4.51 days/week (SD = 2.4, range = 1-7).

Regarding safety practices, 95.2% of all respondents indicated that they choose a crop protection product according to their agronomist's advice. In contrast, 26.2% of the respondents stated that they do not consult the instructions of the pesticide product and 83.1% said that they

do not consult an agronomist regarding proper pesticide application. More than half (56.6%) admitted that they never use protective equipment during pesticide application, while in smaller percentages they stated that they use protection every time (27.8%), frequently (5.2%), sometimes (8.0%) or seldom (2.4%). These percentages were slightly different for greenhouse workers, with 58.7% reporting using protective equipment always and others never (27.9%), usually (8.7%) or sometimes (4.7%).

Several participants reported smoking during (10.0%) or after (16.6%) field pesticide application and a few (8.4%) reported consuming food during spraying. Regarding proper sanitation practices, 93.1% of the respondents reported taking care of their personal hygiene (washing) after pesticide application, whereas 64.2% of them stated that they do not clean their uniform and work accessories (gloves, boots, mask, etc.). In addition, 52.2% of the farmers admitted that they keep their uniform in a storage place in their house. In fact, 7.2% of the participants reported that they store their uniform in the same shed/storage space as where they store food.

Table 3: Commercial pesticide names reported in professional spraying of fields and frequency of use/year.

Commercial Name	% of farmers reporting use	Mean (SD) of applications/year
Roundup	15.10	2.24 (1.1)
Copper	7.20	3.12 (1.7)
Gramoxone	4.10	2.57 (1.2)
Permethrin	3.30	3.00 (0.8)
Sulfur	3.20	3.50 (0.7)
Blue vitriol	2.70	2.2 (1.3)
Neotopsin	2.50	No reported frequency
Decis	2.40	1.66 (0.5)
Lindane	1.70	2.25 (1.2)
Thiodan	1.50	2.00 (1.0)
Antracol	1.40	2.50 (0.7)
Ultracide	1.10	3.33 (1.5)
Ziram	1.00	No reported frequency
Ridomil	0.90	3.33 (1.1)
Topik	0.90	Only 1 person reported frequency of use: 1 time/year
Agil	0.70	4.25 (1.5)
Granstar	0.50	1 person, 1 time/year
Aldrin	0.50	1 person, 5 times/year
Atlantis	0.50	1 person, 1 time/year
Lebaycid	0.50	1 person, 4 times/year
Systox	0.50	No reported frequency
Thiovit	0.50	1 person, 5 times/year
Parathion	0.50	1 person, 3 times/year
Thiram	0.20	1 person, 5 times/year
Dursban	0.20	1 person, 15 times/year

Subject Area(s): TOXICOLOGY

With regard to pesticide residue disposal methods, only 1.1% of the farmers stated that they return the remaining pesticide back to the agronomist, and 40.1% that they dispose of it in the soil.

Daily functioning links to pesticide exposure

To investigate the link between pesticide exposure and everyday life functioning, we performed three binary logistic regression analyses including the whole sample and utilized the BDR-S score as the main independent variable, as well as, age, gender and years of education as independent, confounding variables.

In the first analysis, the dependent variable was dichotomous: exposure to pesticides or not-exposed (assigned values 1 and 0). The analysis showed that the regression model was statistically significant overall $\chi^2(4)$ = 104.127, $p < 0.001$, $R^2 = 0.135$. The inferential goodness-of-fit test Hosmer−Lemeshow yielded a $\chi^2(8)$ of 7.105 and was insignificant ($p > 0.05$), suggesting that the model was fit to the data. However, only gender Wald(1) = 82.509, $p < 0.001$, Exp(B) = 5.750, CI = 3.942-8.386 and education Wald(1) = 18.485, $p < 0.001$, Exp(B) = 1.086, CI = 1.046-1.127 were statistically significant predictors of the odds of a participant belonging to one of the two groups (exposure and non-exposed to pesticides).

For the second and third analyses, we created a three-level, categorical variable by grouping the participants according to the number of areas in which they reported pesticide use. In detail, Group A: No direct exposure to pesticides, included participants who did not report applying pesticides to any area ($n = 1667$), Group B: Direct exposure to pesticides, included participants who reported applying pesticides only on one area (fields or garden or greenhouse) ($n = 208$) and Group C: High exposure to pesticides included participants who reported applying pesticides on two or all three aforementioned areas ($n = 68$). In the second analysis we used Group A against B as a dependent dichotomous variable and in the third, Group A against C.

The second analysis, including participants who were not occupationally exposed to pesticides and participants who used pesticides only on one area, showed that the regression model was statistically significant overall $\chi^2(4)$ = 123.907, $p < 0.001$, $R^2 = .096$ and a fit to the data (Hosmer-Lemeshow: $\chi^2(8)$ = 7.769, $p > 0.05$). Similarly, only gender Wald(1) = 94.365, $p < 0.001$, Exp(B) = 0.149, CI = 102-219 and education Wald(1) = 24.147, $p < 0.001$, Exp(B) = 0.908, CI = 0.874-0.944 were significant predictors of the variance of the dependent variable. The third analysis, including participants who were not occupationally exposed to pesticides and participants who used pesticides on two or more areas, showed that, in addition to gender Wald(1) = 53.307, $p < 0.001$, Exp(B) = 0.055, CI = 0.025-119, age Wald(1) = 4.386, $p = 0.036$, Exp(B) = 0.941, CI = 0.889-0.996 and education Wald(1) = 30.783, $p < 0.001$, Exp(B) = 0.777, CI = 0.711-0.850, BDR-S score was also a statistically significant predictor Wald(1) = 7.612, $p =$

0.006, Exp(B) = 1.160, CI = 1.044-1.289 of the variance of the dependent variable (overall model $\chi^2(4)$ = 103.814, $p < 0.001$, $R^2 = 0.256$, Hosmer-Lemeshow: $\chi^2(8)$ = 4.869, $p > 0.05$). This association disappeared, however, when the confounders were removed from the model ($\chi^2(4)$ = 2.071, $p > 0.05$). Thus, our results indicated that participants who had high occupational exposure to pesticides (by applying pesticides on two or more areas) had a higher odds ratio of presenting poor overall daily functioning, but only if we adjusted for confounding variables.

Subsequently, the same regression was conducted again, but this time controlling for medication intake associated with cognitive and urinary/bowel function[3]. For the purpose of this analysis, we created a new variable by adding the total number of such medications received per participant. On average, participants received 3.95 medications (SD = 2.64, range = 0-14). The results showed that medication intake Wald(1) = 6.903, $p = 0.009$, Exp(B) = 0.844, CI = 0.744-.958, together with number of years of education Wald(1) = 29.757, $p < 0.001$, Exp(B) = 0.777, CI = 0.710-.851 and gender Wald(1) = 50.695, $p < 0.001$, Exp(B) = 0.055, CI = 0.025-0.123 were significant predictors of the probability of a participant belonging to the high exposure or no exposure groups. Interestingly, the association with BDR-S remained significant Wald(1) = 7.771, $p = 0.005$, Exp(B) = 1.171, CI = 1.048-1.308 (overall model $\chi^2(5)$ = 103.023, $p < 0.001$, $R^2 = .268$, Hosmer-Lemeshow: $\chi^2(8)$ = 7.700, $p > 0.05$).

In order to investigate the role of cognitive impairment in this model of variables, we conducted a sensitivity analysis by excluding participants with mild (MiND) ($n = 223$) and Major Neurocognitive Disorder (MaND) ($n = 90$) from the sample. The results showed that the BDR-S score significantly predicted the probability of a participant to belong to the high pesticide exposure (application of pesticides in two or more areas) or non-exposure group, both after adjusting for confounding variables (age, gender and education) Wald(1)=11.661, $p = 0.001$, Exp(B) = 1.314, CI = 1.124-1.538 (overall model $\chi^2(4)$ = 87.204, $p < 0.001$, $R^2 = 0.270$, Hosmer-Lemeshow: $\chi^2(8)$ = 4.815, $p > 0.05$) and in the unadjusted model Wald(1) = 6835, $p = 0.009$, Exp(B) = 1.180, CI = 1.042-1.335 (overall model $\chi^2(4)$ = 5.605, $p = 0.018$, $R^2 = 0.014$, Hosmer-Lemeshow: $\chi^2(8)$ = 5.176, $p > 0.05$). Similarly, the association with BDR-S remained in this model when controlling for medication intake Wald(1) = 6.772, $p = 0.009$, Exp(B) = 1.175, CI = 1.041-1.327 (overall model $\chi^2(5)$ = 79.661, $p < 0.001$, $R^2 = 0.245$, Hosmer-Lemeshow: $\chi^2(8)$ = 3.243, $p > 0.05$).

Subsequently, we conducted the same regression analysis, this time including only the participants with MiND or MaND. The results showed that the BDR-S score was not

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3 The medications we controlled for were psychostimulants, anticholinergics, diuretics, anticonvulsants, oral estrogen supplements, oral hypoglycemics, nitrates, calcium-channel blocking agents, ACE inhibitors, statins, anticholinergics, antipsychotics, lithium, anxiolytics, cholinesterase inhibitors, rivastigmine, donepezil, galantamine, NMDA Receptors Blockers, memantine, alpha blockers, hypnotics, non-steroidal anti-inflammatory drugs, cox 2 inhibitors, narcotics, hydergine and Deprenyl/Selegiline.

a statistically significant predictor of the odds of belonging in the high exposure or non-exposure group (neither for the adjusted $\chi^2(4) = 5.605$, $p = 0.018$, $R^2 = 0.014$ nor for the unadjusted model $\chi^2(4) = 5.605$, $p = 0.018$, $R^2 = 0.014$) but only gender and education were significant predictors. The analysis yielded similar results when we also controlled for medication intake ($\chi^2(5) = 19.633$, $p < 0.001$, $R^2 = 0.261$).

Lastly, in order to explore the specific domain of everyday functioning linked to pesticide exposure, we performed 11 binary logistic regression analyses on the whole sample, with each item of the BDR-S, age, gender and years of education as independent variables, and group (high pesticide-exposure and non-exposure) as a dichotomous, dependent variable. All the models were statistically significant and exhibited a fit to the data. The results showed that the

following items significantly predicted the probability of a participant belonging to the high pesticide exposure or non-exposure group: inability to interpret surroundings (spatial orientation), inability to recall recent events (episodic memory), tendency to dwell on the past (perseveration) and bladder-sphincter incontinence.

More specifically, participants belonging to the high pesticide-exposure group had a higher odds ratio of presenting the aforementioned symptoms. Detailed results are listed in tables 4 & 5.

DISCUSSION

In the present study, we investigated the attitudes of elderly farmers towards pesticide use, their adherence to

Table 4: Composition, approval of use in EU and toxicological characteristics of the pesticides reported by elderly farmers.

Commercial name and type of pesticide	Active compound and chemical group	Approved in EU	Toxicity (LD_{50})	Suspected of carcinogenesis in humans
Actelic: C, BS Insecticide	Pirimiphos-methyl organophosphate	Yes (until 2022)	Low (1260 mg/kg)	Unclassified
Agil: S, SA Herbicide	Propaquizafop aryloxyphenoxy-propionate 'FOPs'	Yes (until 2022)	Low (5000 mg/kg)	Unclassified
Aldrin: C, BS Insecticide	Aldrin organochlorine	No (since 1991)	High-Moderate (38-67 mg/kg)	Group B2 according to EPA: Probably carcinogenic
Antracol: C, SA Fungicide	Propineb dithiocarbamate	No (since 2009)	Relatively non-toxic (>5000 mg/kg)	Unclassified
Atlantis: S, SA Herbicide	Mesosulfuron-methyl sulfonylurea	Yes (until 2032)	Relatively non-toxic (>5000 mg/kg)	Not likely carcinogenic according to EPA
Benzoyl Chloride: plant growth regulator	Benzoyl chloride organic compound	Yes	Low (1900 mg/kg)	Group 2A according to IARC: Probably carcinogenic
Blue vitriol: C, BS herbicide/bactericide/enricher	Copper sulphate inorganic compound	Yes (until 2025)	Moderate (300 mg/kg)	Group E according to EPA: Probably not carcinogenic
Bordeaux Mixture: C, BS fungicide/pesticide/bactericide	Copper sulfate, Lime, Water inorganic compound	Yes (until 2025)	Moderate (300 mg/kg)	Group E according to EPA: Probably not carcinogenic
DDT: SA Insecticide	DDT organochlorine	No (since 1986)	Moderate-Low (113-800 mg/kg)	Group B2 according to EPA: Probably carcinogenic
Decis: C, BS Insecticide	Deltamethrin synthetic pyrethroid	Yes (until 2022)	Moderate-Low (128-5000 mg/kg)	Group 3 according to IARC: Not enough evidence
Dialifor: C, SA insecticide/acaricide	Dialifos organophosphate	No (since 1991)	High-Moderate (43-53 mg/kg)	Unclassified
Diazinol: C, BS insecticide/acaricide	Diazinon organophosphate	No (since 2002)	Low (1250 mg/kg)	Not likely carcinogenic according to EPA
Drazoxolon: C, SA fungicide/bactericide	Drazoxolon oxazole	No (since 2002)	Moderate (126 mg/kg)	Unclassified
Dursban: C, BS Insecticide	Chlorpyrifos organophosphate	No (since 2020)	Moderate (82-270 mg/kg)	Group E according to EPA: Probably not carcinogenic
Gramoxone: S, BS herbicide/soil disinfectant	Paraquat Dichloride dipiridilium	No (since 2009)	High-Moderate (40-200 mg/kg)	Group E according to EPA: Probably not carcinogenic
Granstar: S, BS Herbicide	Tribenuron methyl sulfonylurea	Yes (until 2034)	Relatively non-toxic (>5000 mg/kg)	Group C according to EPA: Possibly carcinogenic
Karate: C, BS Insecticide	Lambda-cyhalothrin pyrethroid	Yes (until 2023)	Moderate (56 mg/kg)	Group D according to EPA: Not classifiable as to human carcinogenicity
Lebaycid: S, BS Insecticide	Fenthion organophosphate	No (since 2004)	Moderate (180-298 mg/kg)	Group E according to EPA: Probably not carcinogenic
Lindane: C, BS Insecticide	Lindane organochlorine	No (since 2009)	Moderate (163 mg/kg)	Group B2 according to EPA: Probably carcinogenic
Malathion: C, BS Insecticide	Malathion organophosphate	Yes (until 2022)	Moderate-Relatively harmless (480->10000 mg/kg)	Group 2A according to IARC: Probably carcinogenic
Neotopsin: S, BS Fungicide	Thiophanate methyl benzimidazol	No (Since 2020)	Relatively non-toxic (>5000 mg/kg)	Group C according to EPA: Possibly carcinogenic

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Parathion: C, BS Insecticide	**Parathion** organophosphate	No (since 2005)	High (2-30 mg/kg)	Group 2B according to IARC: Possibly carcinogenic
Ridomil: S, BS Fungicide	**Metalaxyl-M** alanine	Yes (until 2035)	Low (670 mg/kg)	Group E according to EPA: Probably not carcinogenic
Roundup: S, BS herbicide/soil disinfectant	**Glyphosate** glycine	Yes (until 2022)	Relatively non-toxic (5.600 mg/kg)	Group 2A according to IARC: Probably carcinogenic
Systhane: S, BS Fungicide	**Myclobutanil** triazol	No (since 2021)	Low (2000-3000 mg/kg)	Group E according to EPA: Probably not carcinogenic
Systox: C, SA insecticide/acaricide	**Demeton-S-methyl** organophosphate	No (since 2002)	High-Moderate (35-129 mg/kg)	Unclassified
Thiram: C, BS Fungicide	**Thiram** dithiocarbamate	No (since 2009)	Low (560-1000 mg/kg)	Group 3 according to IARC: Not enough evidence
Thiodan: C, BS acaricide/insecticide	**Endosulfan** organochlorine	No (since 2012)	Moderate (80-110 mg/kg)	Group E according to EPA: Probably not carcinogenic
Thiovit: C, SA Fungicide	**Sulphur** inorganic compound	Yes (until 2022)	Relatively non-toxic (>5000 mg/kg)	Unclassified
Topik: C, BS Herbicide	**Clodinafop-propargyl** aryloxyphenoxy-propionate 'FOPs'	Yes (until 2022)	Low (>5000 mg/kg)	Likely carcinogenic according to EPA
Ultracide: S, BS Insecticide	**Permethrin** synthetic pyrethroid	No (since 2009)	Moderate-Low (430-4000 mg/kg)	Group 3 according to IARC: Not enough evidence
	Pyriproxyfen synthetic pyrethroid	Yes (until 2035)	Relatively non-toxic (>5000 mg/kg)	Group E according to EPA: Probably not carcinogenic
	Pyrethrins natural pyrethroid	Yes (until 2022)	Moderate-Low (80-2600 mg/kg)	According to EPA: Possible carcinogenic in high doses
Ziram: C, BS Fungicide	**Ziram** carbamates	Yes (until 2022)	Low (1400 mg/kg)	Group 3 according to IARC: Not enough evidence

S: Systemic, C: Contact[2], BS: Broad Spectrum, SA: Selective Action[3], EPA: US Environmental Protection Agency, IARC: International Agency for Research on Cancer, Table references: [25-31]

(Footnotes)

1 LD_{50} refers to the maximum dose per kg that can be lethal through ingestion for a specific organism [24].

2 Contact pesticides are applied to the foliage of plants and act when they come into contact with the pathogenic organism. Systemic pesticides are sprayed near the roots of plants and/or on the foliage but are absorbed by the nervous system and transported to all the parts of the plant. Systemic pesticides are more effective, but also more toxic [32,33].

3 Selective-action pesticides target a specific type of organism, while broad spectrum pesticides are lethal to a wide variety of pests, including non-target ones. The latter category includes organophosphates, organochlorines and carbamates. Broad spectrum pesticides are generally considered more dangerous for the environment than selective ones [34].

Table 5: Summary of logistic regression results for variables predicting pesticide exposure.

Main independent variables in the model (OR, p)		Background independent variables (OR, p)					
		Age	Gender	Years of education	χ^2	df	p
1. Inability to perform household tasks	1.06, >.05	.954, >.05	.061, <.001**	.782, <.001**	105.306	4	<.001
2. Inability to handle small sums of money	.893, >.05	.960, >.05	.061, <.001**	.787, <.001**	77.911	4	<.001
3. Inability to remember shortlist of items	1.46, >.05	.963, >.05	.062, <.001**	.787, <.001**	78.489	4	<.001
4. Inability to find way about indoors	0.00, >.05	.957, >.05	.060, <.001**	.781, <.001**	79.383	4	<.001
5. Inability to find way about familiar streets	1.42, >.05	.960, >.05	.061, <.001**	.787, <.001**	78.042	4	<.001
6. Inability to interpret surroundings	**60.58, <.001****	.951, >.05	.051, <.001**	.780, <.001**	86.639	4	<.001
7. Inability to recall recent events	**9.27, <.001****	.958, >.05	.053, <.001**	.775, <.001**	89.591	4	<.001
8. Tendency to dwell on the past	**6.74, <.001****	.959, >.05	.060, <.001**	.817, <.001**	96.011	4	<.001
9. Changes in eating habits	0.00, >.05	.961, >.05	.061, <.001**	.786, <.001**	78.345	4	<.001
10. Changes in dressing habits	1.02, >.05	.960, >.05	.061, <.001**	.786, <.001**	77.905	4	<.001
11. Changes in bladder-sphincter control	**1.50, .004***	.948, >.05	.055, <.001**	.789, <.001**	85.229	4	<.001

safety practices and the relationship between pesticide exposure and daily functioning capacity.

The findings suggest negligence towards pesticide use and frequent unsafe practices, such smoking or eating during pesticide application, not consulting an agronomist for instructions, not using protective equipment and storing work clothes in food sheds. Additionally, many elderly farmers in Greece have a low level of education or no education at all, which may further compromise their ability to comprehend the instructions provided on pesticide labels [18,35]. Surprisingly, exploration of the toxicological characteristics of the products used showed that the majority of them were highly hazardous and have been linked to adverse effects on human health [36-38]. Participants reported using active substances such as DDT, Lindane,

Aldrin, Endosulfan, Permethrin, Parathion, Demeton-S-Methyl, Dialifos, Fenthion, Paraquat Dichloride, which are prohibited in the EU. In fact, some products, such as Aldrin and Dialifos, were banned 26 years previously and DDT has been banned since 1986. The present findings are alarming, considering that the older farmers in the present study reported not only using chemical cocktails but also, disposing the remaining substance in the soil as a common practice.

Finally, the present study provided evidence that cumulative pesticide exposure has an impact on everyday functioning, potentially hindering an elderly individual's ability to live independently. In fact, detailed analyses showed that exposure to pesticides in the present sample was linked to the inability to interpret one's surroundings, the tendency to dwell on the past and the inability to recall recent events, and, additionally, changes in bladder/sphincter control. These symptoms are associated with cognitive dysfunction, namely impaired episodic memory and spatial orientation and perseveration and also, neurological deficits.

Indeed, several previous studies have shown that pesticide exposure is linked to muscle or neurological deficits [39,40] and in this context, bladder-sphincter control may be affected, as well, since its function is associated with spinal cord and brain regions. Previous studies have shown that acute pesticide poisoning may lead to diarrhea, and loss of reflexes and sphincter control [41], but the present study is the first, to our knowledge, confirming a link to long-term pesticide exposure. Furthermore, a review of the relevant literature suggested that cognitive abilities are closely associated with daily functioning [42-44]. However, the overall findings of our study suggest that everyday functioning impairments associated with pesticide exposure are prominent mainly in healthy, older adults and not adults with neurocognitive disorders.

Given the aforementioned results, we speculate that deficits in everyday functioning associated with high and long-term pesticide use could be preceding the noticeable symptoms associated with the diagnosis of MiND, MaND or other neurological conditions. This hypothesis is supported by recent research findings [45] showing that specific cognitive and neurological signs are present even before the formal diagnosis of MiND. This is an important finding contributing in recent research efforts to enhance the diagnostic criteria towards the assessment of neurocognitive disorders early on.

In addition, the pattern of deficits emerging in our study indicates that pesticide exposure may be associated with a specific neurological deficit that affects bladder-sphincter control, episodic memory, spatial orientation, and perseveration. This speculation could be supported by research data suggesting that bladder control, and specifically control of the urge to urinate, is mediated by the anterior cingulate gyrus and the prefrontal cortex.

Both areas are typically affected in neurological disorders, such as Parkinson 's disease [46]. Likewise, the ability to recall details of recent events (episodic memory) is highly dependent on the function of the prefrontal and cingulate cortex [47,48] two areas important for spatial orientation and ability to disengage from tasks, as well [49]. Thus, our results may provide a basis for a theory that imprudent long-term exposure to chemical agents may structurally or functionally affect specific brain regions and, consequently, the functions mediated by them. Recent studies support this theory [50] although further research is required, in order to draw robust conclusions.

The insidious nature of pesticide links to health status is disconcerting. Genetic susceptibility either in metabolism, in the elimination and transport of pesticides or in the extent of mitochondrial dysfunction, oxidative stress and neuronal loss may increase some individuals' risk of developing neurodegenerative diseases when exposed to pesticides [51]. The relevant evidence, however, is currently limited and conflicting. Therefore, it is important that such potential interactions are considered in future studies, which may provide a better understanding of the pathogenic mechanisms of diseases such as Parkinson's.

LIMITATIONS

In our research, as in all epidemiological studies, the instrument used to measure pesticide exposure was a self-report questionnaire, and, hence, subject to confounds (such as social desirability effects or poor memory). We might assume, however, that in terms of subjectivity, the participants were likely to have reported safer and more acceptable pesticide handling practices than those reported; thus, their attitudes and practices with respect to pesticide use may in fact be even more dangerous than what was delineated by our findings.

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