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Protective glove use and hygiene habits modify the associations of specific pesticides with Parkinson's disease

Melissa Furlong[1], **Caroline M Tanner**[2,3], **Samuel M Goldman**[3], **Grace S. Bhudhikanok**[4], **Aaron Blair**[5], **Anabel Chade**[6], **Kathleen Comyns**[3], **Jane A. Hoppin**[7], **Meike Kasten**[8], **Monica Korell**[3], **J William Langston**[4], **Connie Marras**[9], **Cheryl Meng**[2,3], **Marie Richards**[10], **G Webster Ross**[11], **David M Umbach**[12], **Dale P Sandler**[13], and **Freya Kamel**[13]

[1]University of North Carolina at Chapel Hill, Gillings School of Global Public Health, Department of Epidemiology, Chapel Hill NC

[2]San Francisco Veteran's Affairs Medical Center, Parkinson's Disease Research, Education and Clinical Center, San Francisco, CA

[3]The University of California at San Francisco School of Medicine Department of Neurology

[4]The Parkinson's Institute and Clinical Center, Sunnyvale, California

[5]National Cancer Institute, Occupational and Environmental Epidemiology Branch

[6]Favaloro University, Institute of Neuroscience, Buenos Aires, Argentina

[7]NCSU, Department of Biological Sciences, Raleigh, NC

[8]University of Lubeck, Department of Psychiatry, Lubeck, Germany

[9]University of Toronto, Toronto, Ontario, Canada

[10]Westat Inc, Durham, NC

[11]VA Pacific Islands Health Care System, Honolulu, Hawaii

[12]National Institutes of Environmental Health Sciences, Biostatistics Branch, Research Triangle Park, NC

[13]National Institutes of Environmental Health Sciences, Epidemiology Branch, Research Triangle Park, NC

Abstract

Pesticides have been associated with Parkinson's disease (PD), and protective gloves and workplace hygiene can reduce pesticide exposure. We assessed whether use of gloves and workplace hygiene modified associations between pesticides and PD. The Farming and Movement

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Corresponding Author: Melissa Furlong, furlongm@med.unc.edu; Box 7435, University of North Carolina, Gilling School of Global Public Health, Department of Epidemiology, Chapel Hill NC 27599.

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Evaluation (FAME) Study is a nested case-control study within the Agricultural Health Study. Use of protective gloves, other PPE, and hygiene practices were determined by questionnaire (69 cases and 237 controls were included). We considered interactions of gloves and hygiene with ever-use of pesticides for all pesticides with ≥ 5 exposed and unexposed cases and controls in each glove-use stratum (paraquat, permethrin, rotenone, and trifluralin). 61% of respondents consistently used protective gloves and 87% consistently used ≥ 2 hygiene practices. Protective glove use modified the associations of paraquat and permethrin with PD: neither pesticide was associated with PD among protective glove users, while both pesticides were associated with PD among non-users (paraquat OR 3.9 [95% CI 1.3, 11.7], interaction p=0.15; permethrin OR 4.3 [95% CI 1.2, 15.6] interaction p=0.05). Rotenone was associated with PD regardless of glove use. Trifluralin was associated with PD among people who used <2 hygiene practices (OR 5.5 [95% CI 1.1, 27.1]) but was not associated with PD among people who used 2 or more practices (interaction p=0.02). Although sample size was limited in the FAME study, protective glove use and hygiene practices appeared to be important modifiers of the association between pesticides and PD and may reduce risk of PD associated with certain pesticides.

Keywords

personal protective equipment; Parkinson’s disease; pesticides; neurodegenerative diseases; movement disorders

1. INTRODUCTION

Parkinson ’s disease (PD) is the second most common neurodegenerative disorder in the United States. Approximately 1% of the population over age 60 and 4% over 80 are affected in industrial nations (de Lau and Breteler 2006). Pesticide exposure has been associated with PD in some epidemiological studies and with parkinsonian symptoms in animal studies (Betarbet et al. 2000; Brown et al. 2006; Pezzoli and Cereda 2013; Priyadarshi et al. 2000). Specifically, the pesticide paraquat has been associated with PD in multiple epidemiological studies (Costello et al. 2009; Kamel et al. 2007; Liou et al. 1997; Tanner et al. 2011), whereas associations between PD and rotenone (Tanner et al. 2011), permethrin (Tanner et al. 2009), and trifluralin (Kamel et al. 2007) have been less frequently reported. Numbers of exposed cases in these studies are small (see Tanner 2011), limiting the ability to assess possible modifying factors.

Personal protective equipment (PPE) may protect workers from exposure to pesticides. In agricultural field studies, PPE use has been associated with reduced biomarkers of exposure (López et al. 2007; Quandt et al. 2006), although gloves worn during pesticide application may also serve as a reservoir of those pesticides during future use (Hines et al. 2001). Still, in the Agricultural Health Study (AHS), chemically-resistant gloves appear to provide the greatest reductions in exposure compared to other types of PPE, and AHS models predict that farmers would reduce exposure by up to 90% by wearing gloves in conjunction with several other types of PPE (Hines et al. 2011; Thomas et al. 2009).

Occupational hygiene practices may also be important in reducing exposure to pesticides (Salvatore et al. 2008). Immediately washing hands after pesticide use may reduce exposure to pesticides, with removal efficiency varying by time elapsed since exposure and specific pesticide characteristics (Fenske et al. 1998; Fenske and Lu 1994). Immediately changing clothes that were worn during mixing and applying may also reduce exposure (Grieshop et al. 1994; van Balen et al. 2011). Together, PPE and hygiene practices may account for a significant amount of variability in studies that examine the association between pesticides and PD, yet no occupational studies of pesticides and PD have evaluated these practices. Such practices, however, have been associated with reduced risk of cancer associated with pesticide exposure (Zahm et al. 1990).

Stratifying pesticide use by PPE and hygiene practices may help identify individuals with more or less exposure. For example, farmers who apply paraquat without wearing any PPE may be exposed to a greater amount of paraquat than those who apply it while wearing gloves and full body coveralls, assuming similar application and mixing methods. Thus, in the absence of measured levels of exposure, analyzing the modifying effects of PPE and hygiene may provide indirect evidence of a dose-response relationship between specific pesticides and PD and also provide information on the health benefit of employing these practices when using pesticides.

2. METHODS

2.1 Study population and questionnaires

The Farming and Agricultural Movement Evaluation (FAME) study is a case-control study nested within the Agricultural Health Study (AHS), a prospective cohort study including 52,394 private pesticide applicators, mostly farmers, and 32,345 of their spouses, recruited from 1993–1997 in Iowa and North Carolina (Tanner et al. 2011). Suspect prevalent PD cases in the AHS were identified by self-report or from state mortality files. Potential controls randomly selected from the AHS cohort were frequency-matched to cases by age at enrollment into the AHS (<40, 40–49, 50–59, 60–64, 65–69, ≥70 years), sex, and state at a ratio of approximately three controls per case. During home visits, neurologists examined living suspect cases and 5% of controls, and neurologist-trained technicians examined the remaining controls to ensure they did not have PD. Controls with evidence of parkinsonism had a second in-home examination by a neurologist. Case status was determined by agreement of two movement disorder specialists following established criteria for PD (Gelb et al. 1999) and using information from medical records, the in-home examination, and a videotaped movement evaluation conducted during the home visit. Diagnosis dates were determined from medical histories collected during in-home exams and from medical records. Proxy informants were used for subjects that were unable to complete interviews (n=16; 14 cases and 2 controls).

Cases and controls in FAME completed structured telephone interviews between 2002 and 2008 that collected information on demographics, lifestyle, medical history, a complete occupational history including details of all farm jobs, and information on PPE and hygiene practices.

2.2 Exposure assessment

2.2.1 Pesticides—The complete occupational history was used to evaluate exposure to 31 different pesticides (for a full list see Tanner (2011)) in each job held between age 14 and a reference date. The reference date for cases was age at PD diagnosis while, for controls, it was the median age of PD diagnosis for cases in the corresponding age-, sex-and state-specific stratum. The 31 pesticides were chosen based on possible mechanistic links with PD and do not necessarily include those in common use. Pesticides that were banned, had their registrations canceled, or were voluntarily pulled from the market before 1985 (aldrin, DDT, and dieldrin) were not considered, since the PPE survey only evaluated the period after 1985 (see section 2.2.2).

2.2.2 Personal protective equipment and hygiene practices—To reduce bias associated with lengthy historical recall and capture a time period before PD onset for most cases, the PPE questions focused on practices during the late 1980s and early 1990s; therefore, only individuals who used pesticides during this period were asked these questions. Of the 498 FAME subjects, 306 (237 controls, 69 cases) reported personally mixing or applying pesticides during the relevant period and completed the PPE survey; both licensed applicators and their spouses who used pesticides (but were not necessarily licensed) and responded to the PPE survey were included.

The survey included questions on use of gloves and other types of PPE more than half the time while mixing or applying pesticides (<50% gloves vs ≥50% gloves; <50% other PPE vs ≥50% other PPE) and on occupational hygiene practices. PPE and hygiene practices were not asked in relation to specific pesticides but rather were reported as general habits (PPE survey questions are in Appendix A1).

Protective gloves included chemically resistant gloves and plastic or rubber gloves, if indicated in the “other” category of glove use. Use of leather or fabric gloves was classified as “no protective glove use,” as such materials provide little to no protection against solvents and chemicals (Frank 1994). These glove categorizations have been used in previous research on pesticide exposure reduction assessments [reviewed in (Dosemeci et al. 2002)], and in a study of 2,4-D and MCPA (Coble et al. 2005). Other PPE included chemically resistant boots or shoes, chemically resistant aprons, disposable coveralls, cartridge respirator/gas masks, and/or goggles used more than half the time.

Three hygiene questions sought information on whether respondents usually bathed or showered after mixing or applying pesticides and before continuing with other farm activities, whether they changed their clothes after using pesticides, and whether they consistently washed concentrated pesticides off their skin after exposure.

2.3 Data analysis

All analyses were performed in SAS (version 9.2, SAS Institute, Cary, NC). Participant characteristics are reported for the 306 subjects in our study population who completed the FAME PPE survey. We used logistic regression to assess whether sex, education, smoking status, age, state, or applicator status (pesticide applicator or spouse) differed between those included in the present analysis and the remainder of the FAME population. We used chi square tests to examine participant characteristics by case status. We examined the associations between PD and pesticides, PPE, and hygiene practices using unconditional logistic regression and obtained stratum-specific estimates from interaction models via the estimate statement in PROC GENMOD.

2.3.1 Covariates—Information on covariates was obtained during FAME interviews. Frequency-matching variables state, sex, and reference age were always included in analytic models. Because of low numbers in each age by sex by state matching category, we used approximate age tertiles (40–57, 58–65, and 66–85) in the data analysis. Other potential confounders previously implicated in epidemiologic studies of PD were considered using a directed acyclic graph (DAG). These included smoking (smoked>100 cigarettes before reference date), family history of PD (PD in any first-degree relative), and education (high school or less vs. some college/vocational school or higher). Applicator status (applicator or spouse) was not considered because it was almost exactly correlated with sex, a matching variable. The final covariate set for all models included reference age (tertiles), sex, state, and smoking. We also ran sensitivity analyses including either family history of PD or education. Due to the low numbers of spouses in our study, we examined results for both the whole population and the subset of applicators only.

2.3.2 Exposure variables—We created a three-category gloves-and-other-PPE variable, where the first category included people with <50% glove use (n=116), the second category included people with ≥50% glove use and <50% other PPE (n=107), and the third category included people with ≥50% glove use and ≥50% other PPE (any type) (n=76). Some participants (n=13) in the first category reported ≥50% other PPE use. However, because of concerns about small numbers, and because previous AHS studies indicate that protective glove use is the most important protective factor, we combined those 13 participants with others who reported <50% glove use. Additional three-category variables were created for each specific type of PPE (e.g., protective gloves and respirator; see Appendix A2).

For each pesticide, we created a dichotomous ever-use variable (used one or more times before reference date). For interaction analysis, we established an a priori criterion that each case/control status × pesticide use × PPE category needed to include ≥ 5 participants in order to test for an interaction, but no specific pesticide met this criterion for the three-level glove-and-PPE variable (see Appendix A3 for cell sizes). Thus, for interaction analyses, we created a dichotomous glove variable categorizing glove use into <50% glove use (n=116) or ≥50% glove use (n=183). After this, four pesticides (trifluralin, permethrin, rotenone, and paraquat) met our criterion. One pesticide, 2,4-D, had large numbers of reported users but <5 cases who did not use the pesticide so we did not analyze 2,4-D.

The hygiene practice questions queried three positive hygiene practices. We summed the number of positive practices (0–3, hereafter referred to as the hygiene sum variable) and then dichotomized this variable to indicate 2–3 hygiene practices (n=240) or 0–1 hygiene practices (n=37). We used this dichotomous variable to evaluate interactions with the same four pesticides. While this dichotomization scheme maximized the number of participants in each sub-category, a few sub-categories remained small with fewer than 5 participants.

Thus, in sensitivity analyses we used the hygiene sum variable as a continuous predictor to evaluate effect modification.

The three-category glove and PPE variable, dichotomous glove variable, dichotomous other PPE variable, and dichotomous hygiene variable were first tested for main effects, and the dichotomous glove and hygiene variables were tested for interactions with specific pesticides. To increase power for detecting interactions at the cost of a higher rate of false positives, we used $\alpha<0.20$ to indicate a notable interaction. We examined correlation odds ratios (Appendix A4) and variance inflation factors to check for collinearity, with a variance inflation factor >5 indicating collinearity.

To probe the possibility of reverse causation, whereby prodromal PD symptoms may have influenced participants' willingness to wear gloves, we also examined effect measure modification estimates after excluding cases diagnosed with PD before 1995. Thus, this method only includes cases diagnosed after the time period referenced in the PPE survey was over.

3. RESULTS

3.1 Participant characteristics

The respondents to the PPE survey in FAME (n=306, 267 controls and 69 cases) were primarily male (94%), from Iowa (73%), and between the ages of 40 and 65 (77%); distributions of these characteristics were similar in cases and controls, reflecting the frequency-matching design of the parent study (Table 1). Pesticide use was slightly more common in cases (Table 2) while use of gloves, other PPE and hygiene practices were more common among controls (Table 3).

Of all FAME participants, 153 reported that they did not personally mix or apply pesticides during the late 1980s or early 1990s, and 9 reported that they did not know; these 162 people were not included in this analysis. Completion of the PPE survey was associated with male sex and having more than a high school education, but not with case-control status, age, state, and smoking.

3.2 Association of PD with pesticide use, PPE use and hygiene practices

Overall, in this subset of FAME, rotenone and paraquat were associated with PD in models controlling for PPE, gloves, and hygiene as covariates but not as modifiers, while trifluralin and permethrin were not (Table 2). This observation is similar to previous results in the complete FAME population (Tanner et al. 2011). Pesticide associations with PD were similar in a model including all four pesticides as well as PPE and hygiene variables (Table 2). In general, these four pesticides were not highly correlated. The strongest association was between trifluralin and permethrin; the OR for this association was 2.29 (Appendix A4). However, results did not change when including multiple pesticides in one model, and variance inflation factors suggested collinearity was not a major concern.

We analyzed associations of PD with protective gloves, hygiene practices, and other PPE first in separate models (Single Protective Factor Models in Table 3) and then simultaneously in two models (Models 2 and 3 in Table 3). No collinearity was evident (all variance inflation factors were less than two) in Model 2, which simultaneously tested the dichotomous glove variable, the dichotomous hygiene variable, and the dichotomous variable for other PPE. Hygiene practices were associated with reduced odds of PD regardless of adjustment for other factors (OR 0.3 (95% CI 0.1, 0.6)). Models assessing the three-category glove and other PPE variable exhibited a dose-response relationship: wearing protective gloves only was suggestively protective while the OR for wearing gloves in conjunction with other PPE was significantly below the null. However, “other PPE” was not protective by itself (Table 3). Similarly, protective gloves alone offered some protection but not as much as protective gloves in conjunction with another specific type of PPE (Appendix A2).

3.3 Modification of PD-pesticide associations by use of PPE and hygiene practices

We tested interactions between dichotomous glove and hygiene variables and the four pesticides in separate models. Paraquat, permethrin, and trifluralin displayed notable interactions with the dichotomous protective glove variable (Table 4). Among individuals with ≥50% glove use, ORs for paraquat and permethrin were essentially 1, while among individuals with <50% glove use, permethrin had an OR of 4.7 (95% CI 1.5, 14.6), and paraquat had an OR of 3.9 (95% CI 1.5, 10.2) (Table 4). While the OR for trifluralin was elevated in <50% glove users, and decreased for ≥50% glove users, neither stratum-specific OR was significantly different from the null despite the notable interaction. The OR for rotenone, while elevated in both strata of glove users, was reduced among >50% glove users relative to <50% users, although confidence intervals displayed substantial overlap and the p for interaction was >0.2. Adding hygiene to the glove models did not generally alter results (Model 3 in Table 4). Results in models restricted to only pesticide applicators (excluding 17 spouses) were similar, although there was some loss of precision (not shown).

There was a notable interaction of trifluralin with hygiene practices (p interaction = 0.02). Although confidence intervals were quite wide, trifluralin was associated with increased odds of PD among people who used 0 or 1 hygiene practices (OR 5.5, 95% CI 1.1, 27.1), but not among those who used 2–3 hygiene practices (OR 0.6, 95% CI 0.3, 1.3) (Table 4). We were unable to test the interaction between permethrin and the dichotomous hygiene variable due to empty cells in some sub-categories (see Appendix A3). However, there was no interaction between permethrin and the hygiene sum variable (p interaction = 0.7). Neither rotenone nor paraquat displayed notable interactions with either the dichotomous hygiene variable or the hygiene sum variable. Although the OR for rotenone was reduced among those who used ≥2 hygiene practices, the confidence intervals again displayed substantial overlap and the p for interaction was 0.4.

Excluding participants with proxy interviews (n=16; 14 cases and 2 controls) from the interaction analyses resulted in findings similar to those in Table 4. Excluding cases (n=30) who received a PD diagnosis before 1995 also resulted in similar findings to those reported for the full case-control population.

4. DISCUSSION

This study of pesticides and PD is the first that takes into account the modifying effects of PPE use and hygiene practices. We found that overall, among all users of all pesticides, these factors were associated with reduced risk of PD. Further, the strength of association between several pesticides and PD varied according to PPE or hygiene.

Our findings associating the four pesticides with PD are generally in accord with previous reports in the literature. Associations of paraquat and rotenone with PD have previously been reported in the parent Agricultural Health Study (Kamel et al. 2007) and in FAME (Tanner et al. 2011); our population and is a subset of FAME, which is nested within the Agricultural Health Study. Paraquat has been associated with PD in other populations (Costello et al. 2009; Liou et al. 1997) and in a recent meta-analysis (Pezzoli and Cereda 2013), although some studies have reported no effect (Engel et al. 2001; Hertzman et al. 1994). Relationships with trifluralin and permethrin have mainly been identified in experimental models. An association between permethrin and PD in humans was reported in one previous study, although the authors noted that precision was poor (OR 3.61, 95% CI 0.65, 15.80) (Tanner et al. 2009). In animal models, pyrethroid pesticides may alter dopamine transporter-mediated uptake (Elwan et al. 2006) and cause oxidative stress (Nasuti et al. 2007), two biological processes associated with PD in humans. An association between trifluralin and incident self-reported PD was previously reported in the AHS (Kamel et al. 2007), and an in vitro study showed that trifluralin induces conformational alterations in α-synuclein, a protein implicated in PD pathophysiology, and accelerates the rate of formation of α-synuclein fibrils (Uversky et al. 2002).

4.1 Gloves, PPE, and PD

Modification of the associations of PD with paraquat and permethrin by use of protective gloves may have several explanations. The first is that protective glove use is a determinant of actual dermal exposure, and people who infrequently used protective gloves received a higher pesticide dose than people who frequently used them (although both groups likely experience some degree of exposure). If this explanation is correct, it suggests that a dose-response relationship exists between exposure to pesticides and likelihood of developing PD, and adds to the current literature reporting associations between PD and paraquat or permethrin. Moreover, failure to consider protective effects of gloves may mask associations of PD with pesticides in populations where PPE use is relatively common. Second, people who consistently use protective gloves and other PPE may generally handle pesticides more safely in all respects, including avoiding spills when mixing/applying, avoiding spray drift, opting for safer application techniques, avoiding touching their faces with their hands, and other behaviors not captured in this survey. While this set of behaviors would still suggest that people who use gloves have lower pesticide exposure, it is possible that the association is not driven exclusively by protective gloves but rather by safer pesticide handling habits in general. Finally, the apparent effect modification could be spurious. Although the number of exposed cases in FAME is higher than in most previous studies, it is still small, and the confidence intervals are relatively wide.

We report no modifying effect of protective gloves on the association between rotenone and PD. Fewer participants reported using rotenone than any of the other three pesticides, and so the failure to detect an interaction may be due to limited power. Alternatively, the lack of an interaction with rotenone may be due to the fact that rotenone was marketed as an organic pesticide, and farmers may have equated organic with “non-toxic” and not used protective gloves or other PPE when working with this pesticide. The survey did not ask about pesticide-specific habits, but rather gathered data about overall habits while mixing and applying pesticides. While this limitation applies to all pesticides in the study, it may have been more of an issue with rotenone due to possible perceptions about non-toxicity. Finally, the EPA has reported that rotenone displays low acute toxicity through dermal routes of exposure and high acute toxicity through inhalation or ingestion (EPA 2007). Since wearing protective gloves primarily reduces dermal exposure, this type of PPE may be ineffective in reducing rotenone toxicity, particularly since rotenone is commonly applied as dust or granules. The toxicity of rotenone with regard to PD in humans may be dependent on exposure route.

4.2 Hygiene and PD

Hygiene practices did not modify associations of paraquat, rotenone, and permethrin use with PD. This may be attributable to several factors. First, counts in some sub-categories for these analyses were small (see Appendix A3). However, in analyses where hygiene was treated as a continuous sum variable rather than as a dichotomous variable, the results remained the same. That is, only the association with trifluralin was reduced by use of hygiene practices, suggesting that small sample size may not entirely account for the failure to detect effect modification. Additionally, using hygiene practices is different from wearing protective gloves and is more complicated to assess. Some farmers may be quite careful during mixing and applying and may minimize splashing or use methods that reduce splashing, thus obviating the need for washing or altering the perception of a need for washing. Other farmers who were less careful, and thus felt greater need to wash, may have in fact been exposed to greater doses of pesticides overall. Thus, the hygiene variable may not adequately classify participants into higher and lower levels of exposure. These results do not necessarily imply that hygiene practices are not protective, as the overall main effect of hygiene appeared quite protective. Instead, these practices may minimize the effects of some although not all pesticides. The important finding is that trifluralin displayed no association among participants with consistent hygiene practices, and an adverse association among subjects without consistent hygiene practices. While the strataspecific trifluralin associations are in accordance with hypotheses, the association could be spurious, and there could be unknown confounders that are specific to trifluralin. The wide confidence intervals do indicate uncertainty, and further research should be done to replicate this association.

4.3 Other PPE

An interesting finding was that when considering the three level PPE variable in main effects analyses, wearing gloves alone was not significantly protective. Rather, a significant association was only seen for protective gloves in conjunction with other PPE. However, no specific type of PPE appeared to be more protective than any other, perhaps because of sample size limitations. This observation could also arise because farmers pick the most convenient PPE or the most protective type of PPE according to pesticide warning labels. Furthermore, farmers who use other types of PPE may be more wary of the possible negative impacts of pesticides on health and thus may tend to be more careful regarding all aspects of pesticide handling and wear gloves more consistently.

4.4 Study limitations and strengths

Like any study, this one has inherent limitations. The small sample size imposes limitations, especially when making inferences regarding effect modification. We used $p<0.20$ to identify interactions, to maximize our ability to detect interactions at the risk of increasing false positives. Additionally, although the number of exposed cases is generally higher in FAME than in other PD studies, cell sizes still remain small and confidence intervals are fairly wide, particularly for trifluralin. Sparse data may lead to inflated effect estimates.

Aspects of study design may also entail possible bias. FAME relied on participants' recall to characterize exposures and protective habits (including glove use and hygiene habits), which could create bias if cases and controls differentially recall these behaviors. Cases may be less likely to accurately report glove use if they seek an explanation for their disease – to our knowledge, no studies have reported on recall bias specifically in regards to the use of personal protective equipment or hygiene habits. However, reliability studies, including one performed in the AHS, show farmers do reliably report history of pesticide use (Blair et al. 2000; Blair and Zahm 1993), and the use of a complete occupational history should minimize recall errors (reviewed in (Teschke et al. 2002)).

Reverse causation is also a possibility. Participants with prodromal parkinsonian symptoms such as tremor may have been less willing or able to consistently wear protective gloves, which tend to be cumbersome and limit dexterity. However, excluding cases diagnosed before 1995 (n=30) resulted in similar results for all models, suggesting that failure of participants with early PD symptoms to use gloves were not driving the results. Furthermore, PPE use did not differ among cases diagnosed before or after 1995. Together, these findings suggest that reverse causation does not account for our findings, although it is possible that there may be some residual bias present.

Another limitation is that pesticide use was evaluated over the lifetime up to a referent year, while PPE use was only evaluated in the narrow time frame from the 1980s to the 1990s. However, since there is an internal control group, any misclassification of pesticide use during this time period resulting from this approach is likely to be non-differential. PPE use and hygiene habits were also only evaluated generally, rather than according to each specific pesticide. Inferences were thus based on the assumption that habits were constant across different pesticides.

This occupational case-control study had several notable strengths. FAME overcame limitations of some previous studies of pesticides and PD by focusing on an agricultural population with high numbers of exposed cases, thereby increasing the power to examine both some less-studied pesticides and modifying practices. Further, FAME collected highly detailed historic information on pesticides and unique data on PPE, allowing for the first time the examination of protective gloves and hygiene as modifiers of the pesticide-PD association. The nested case-control design minimized confounding by using an internal control group of farmers. Finally, outcome misclassification should be minor, as all cases were confirmed by movement disorder specialists.

4.5 Public health significance

Trifluralin and paraquat are widely used in agricultural settings, and permethrin is widely used in both residential and agricultural settings. In 2007, trifluralin and paraquat were two of the top fifteen most commonly used herbicides in the United States (EPA 2011). Of note, 41% of the two million pounds of permethrin that are used yearly in the United States are applied residentially by homeowners (EPA 2009). Permethrin is also the active ingredient in first-line scabies and lice treatment in children, some flea and tick medicines for dogs, and in pesticideimpregnated clothing. The widespread adoption of permethrin for pest control in multiple settings is largely based on the assumption that permethrin is low-risk with minimal side effects, although to date no studies have been published on the potential long-term consequences of dermal exposure to permethrin in non-occupational settings, for example on home gardens, pets, treated clothing, and for scabies and lice treatment. Occupational exposure to permethrin was associated with PD in this and one other epidemiologic study (Tanner et al 2009). Clearly, further research is necessary to establish this association, which is not a widely reported finding, and may be spurious or specific to agricultural pesticide users. However, the use of protective gloves is relatively inexpensive and may have substantial protective effects in occupational or other settings. Given that use of permethrin is widespread, especially among residential pesticide applicators, use of appropriate PPE with permethrin both occupationally and by homeowners should be emphasized in public health messages while we await further studies.

5. Conclusions

In the FAME study, protective gloves and hygiene practices appeared to be important modifiers of the association between pesticides and PD, and these practices may reduce risk of PD associated with use of paraquat, permethrin, and trifluralin.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations and definitions

AHS	Agricultural Health Study
FAME	Farming and Movement Evaluation Study
NIEHS	National Institute of Environmental Health Sciences
PPE	personal protective equipment
PD	Parkinson’s disease
OR	Odds Ratio
CI	Confidence Interval

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Highlights

- Associations between occupational pesticide use and PD were modified by work habits
- Overall, consistent glove and hygiene use were associated with reduced odds of PD
- Among inconsistent glove users, paraquat and permethrin were associated with PD
- Among those with inconsistent hygiene habits, trifluralin was associated with PD
- Rotenone remained associated with PD regardless of glove use or hygiene habits

Table 1

Characteristics of FAME PPE Study Population[a]

Characteristic	Category	Total N (%)	Controls N (%)	Cases N (%)	p value[b]
Age[c] (years)	40–57	119 (39)	90 (38)	29 (42)	0.83
	58–65	118 (39)	93(39)	25(36)	
	66–85	69 (23)	54(23)	15(22)	
Gender	Female	18 (6)	16 (7)	2 (3)	0.38
	Male	288 (94)	221 (93)	67 (97)	
State	North Carolina	84 (27)	66 (28)	18 (26)	0.77
	Iowa	222 (73)	171 (72)	51 (74)	
Smoking	Non smoker	172 (56)	126 (53)	46 (67)	0.05
	Smoker	134 (44)	111 (47)	23 (33)	
Education	>HS	150 (49)	120 (51)	30 (43)	0.30
	HS or less	156 (51)	117 (49)	39 (57)	
Applicator/Spouse	Spouse	17 (6)	16 (7)	1 (1)	0.13
	Pesticide Applicator	289 (94)	221 (93)	68 (99)	

[a] Study population (n=306) includes FAME participants who reported personally mixing or applying pesticides during the 1980s/1990s and completed the PPE survey

[b] We used a t-test for the continuous age variable and chi square tests for categorical variables to test if participant characteristics varied by case status for variables with >5 observations in all cells. For variables with ≤5 observations, we report Fisher's exact p values.

[c] Age is reference age; for cases this was age at PD diagnosis while for controls, it was the median age of PD diagnosis for cases in the matched age-, sex-and state-specific stratum

Table 2

Associations of PD with Pesticide Use

	Controls N (%)	Cases N (%)	OR (95% CI)[a]	OR (95%CI)[b]	OR (95%CI)[c]
Never use paraquat	182 (79)	40 (65)	1	1	1
Ever use paraquat	48 (21)	22 (35)	2.5 (1.3, 4.8)[¥]	2.4 (1.1, 5.1) [¥]	2.6 (1.1, 6.1) [¥]
Missing	7	7			
Never use permethrin	192 (83)	48 (75)	1	1	1
Ever use permethrin	39 (17)	16 (25)	1.5 (0.8, 3.0)	1.5 (0.7, 3.5)	1.2 (0.5, 3.0)
Missing	6	5			
Never use rotenone	207 (91)	51 (76)	1	1	1
Ever use rotenone	21 (9)	16 (24)	3.7 (1.7, 8.1)[£]	3.8 (1.5, 9.6) [£]	5.5 (2.0, 15.3) [£]
Missing	9	2			
Never use trifluralin	104 (45)	26 (40)	1	1	1
Ever use trifluralin	129 (55)	39 (60)	1.1 (0.6, 2.0)	1.0 (0.5, 2.0)	0.9 (0.4, 2.1)
Missing	4	4			

[a] Adjusted for state, smoking, sex, and age

[b] Adjusted for three-category glove variable, dichotomous hygiene variable, state, smoking, sex, and age

[c] Adjusted for three-category glove variable, dichotomous hygiene variable, state, smoking, sex, age, and the three other pesticides

[£] p <0.01

[¥] p <0.05

Table 3

Association of PD with use of PPE and Hygiene practices

				OR (95% CI) [a]			
		Controls N (%)	Cases N (%)	Single Protection Factors	Model 2	Model 3	Model 3, Cases dx after 1994
Binary Glove Variable	≤ 50% Gloves[b]	83(36)	33 (49)	1	1		
	>50% Gloves only	149 (64)	34 (51)	0.5 (0.3, 0.9)$^{£}$	0.5 (0.3, 1.1)		
	Missing	5	2				
	≤ 50% Non-glove PPE	163 (70)	51 (75)	1	1		
Other PPE	> 50% Any non-glove PPE	73 (31)	17 (25)	0.7 (0.4, 1.3)	1.0 (0.5, 2.0)		
	Missing	1	1				
Three Category Glove Variable	≤ 50% Gloves	83 (36)	33 (49)	1		1	1
	>50% Gloves only	83 (36)	24 (36)	0.6 (0.3, 1.2)		0.7 (0.3, 1.4)	1.1 (0.5, 2.6)
	>50% Gloves & Other PPE	66 (28)	10 (15)	0.3 (0.1, 0.7) $^{£}$		0.4 (0.2, 1.0) $^{£}$	0.3 (0.1, 1.1)
	Missing	5	2				
	<2 hygiene practices	21(9)	16 (29)	1	1	1	1
Hygiene	2–3 hygiene practices	201(91)	39 (71)	0.2 (0.1, 0.5) $^{£}$	0.3 (0.1, 0.6) $^{£}$	0.3 (0.1, 0.6)$^{£}$	0.3 (0.1, 0.7)$^{£}$
	Missing	15	14				

[a] All models adjusted for age, state, smoking, and sex. “Gloves ≤ 50%” refers to protective glove use reported less than half the time during mixing and applying pesticides, and includes both people who used protective gloves < 50% of the time and those who did not use protective gloves at all.

[b] ”Gloves” here refers to protective gloves, which includes chemically resistant gloves, plastic gloves, and rubber gloves ORs reported under “single protection factors” are results from four separate models that do not adjust for the other protective factors.

Model 2 reports ORs for the binary glove variable, hygiene, and other PPE when they are all included in one model.
Model 3 reports main effect ORs for the three category glove-variable and hygiene when they are included together in one model.
Other PPE includes any of the following: chemically resistant boots, chemically resistant apron, disposable coveralls, cartridge respirator, gas mask, or goggles.
Model 3, cases dx after 1994 reports ORs for the model used in Model 3,but only including cases diagnosed in 1995 and after.

£ $p<0.01$

¥ $p<0.05$

Table 4

Modification of PD-pesticide association by use of PPE and hygiene practices

		Paraquat OR (95% CI)	**Permethrin OR (95% CI)**	**Rotenone OR (95% CI)**	**Trifluralin OR (95% CI)**
Model 1 Gloves	≤ 50%	3.9 (1.5, 10.2)[£]	4.7 (1.5 ,14.6) [£]	5.5 (1.5, 19.4) [£]	1.5 (0.6, 3.9)
	>50%	1.6 (0.6, 4.2)	0.8 (0.3, 2.3)	3.0 (1.0, 8.4) [¥]	0.7 (0.3, 1.6)
	p interaction	0.20	0.02	0.46	0.20
Model 2 Hygiene Practices	<2	2.2 (0.5, 10.5)	-	6.8 (1.0, 46.1) [¥]	5.5 (1.1, 27.1) [¥]
	2–3	2.3 (1.0, 5.3)[¥]		2.8 (1.0, 7.6) [¥]	0.6 (0.3, 1.3)
	p interaction	0.96		0.41	0.02
Model 3 Gloves, controlling for hygiene	≤ 50%	3.9 (1.3, 11.7)[¥]	4.3 (1.2, 15.6) [¥]	5.3 (1.3, 20.5) [¥]	1.7 (0.6, 4.7)
	>50%	1.3 (0.5, 3.9)	0.8 (0.3, 2.4)	2.6 (0.8, 8.6)	0.6 (0.2, 1.5)
	p interaction	0.15	0.05	0.44	0.13
Model 4 Glove use, Cases dx after 1994	≤ 50%	5.3 (1.4, 20.7) [¥]	5.1 (1.0, 25.8) [¥]	5.6 (1.2, 27.3) [¥]	1.5 (0.4, 5.4)
	>50%	1.1 (0.3, 4.2)	1.1 (0.3, 3.9)	3.4 (0.9, 13.1)	0.4 (0.1, 1.1)
	p interaction	0.10	0.14	0.64	0.09
Model 5 Hygiene, Cases dx after 1994	<2	2.6 (0.5, 14.4)	-	8.0 (0.9, 71.6)	5.4 (0.9, 33.1)
	2–3	2.0 (0.7, 5.7)		3.3 (1.0, 10.7) [¥]	0.3 (0.1, 1.0)[¥]
	p interaction	0.80		0.48	.01

[a] All models control for age, sex, state, and smoking. Model 1 estimates the effect of each pesticide at each level of protective gloves by using an interaction term between the pesticide and the binary glove variable. Model 2 estimates the effect of each pesticide at each level of hygiene use by using an interaction term between the pesticide and the dichotomous hygiene variable. Model 3 estimates the effect of each pesticide at each level of protective gloves while controlling for the main effect of the dichotomous hygiene variable. In Model 3, the main effects for hygiene were significant and protective (ORs for hygiene range from 0.25 to 0.35, p values range from <0.01 to 0.01). Model 4 excludes cases diagnosed before 1995 and controls for the dichotomous sanitation variable. Model 5 excludes cases diagnosed before 1995 and controls for the dichotomous glove variable.

[£] p<0.01

[¥] p<0.05