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Olfactory Function in Latino Farmworkers over Two Years: Longitudinal Exploration of Subclinical Neurological Effects of Pesticide Exposure

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Abstract

Objective—We compared patterns of olfactory function over two years in pesticide-exposed male Latino farmworkers and male Latino workers in industries without pesticide exposure.

Methods—At five points over two years, workers completed tests of odor threshold (16 concentrations of n-butanol) using a well-established methodology. Tests at two or more time points were completed by 156 farmworkers and 118 non-farmworkers.

Results—Farmworkers required significantly higher odorant concentrations at Contact 1 and across the two year follow-up to detect the odor. When adjusted for Contact 1, between-group differences persisted, but odor threshold performance did not worsen over time.

Conclusions—Pesticide exposure has been linked to neurodegenerative disease, as has declining olfactory function. Persistently poorer olfactory function among pesticide-exposed workers suggests the need to monitor neurological function in this vulnerable worker population.

Keywords

Neurotoxin; pesticide; community-based participatory research; occupational health; vulnerable population; environmental justice; Parkinson's Disease

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Introduction

Occupational exposure to pesticides has been linked to increased risk of neurodegenerative diseases such as Parkinson's disease and amytrophic lateral sclerosis (ALS).[1–3] Although pesticide exposure events can consist of high doses of single pesticides, as in spills at chemical manufacturing facilities or during mixing, pesticide exposure in workers in industries such as agriculture, landscaping, and cleaning is usually at low levels over long periods of time and can consist of a wide variety of pesticide classes. This latter scenario makes it difficult to link specific exposure events and specific pesticides to neurodegenerative diseases.

Migrant farmworkers in US agriculture are routinely exposed to pesticides of multiple classes, including organophosphorus, organochlorine, and pyrethroid insecticides that are neurotoxins.[4–6] Most of this exposure occurs as low dose exposure to dislodgeable pesticide residues on plants and other surfaces in fields and the worksite, with additional exposure occurring due to pesticides tracked into housing and vehicles.[7–9] Farmworkers are often unaware of their exposure, and many lack specific information on the types of pesticides used at their worksites.[10] It is difficult to identify long term outcomes of pesticide exposure in farmworkers because they frequently move from place to place and eventually seek work in other industries.[11] For such populations, it may be useful to identify subclinical disease indicators that precede the development of neurodegenerative diseases. Loss of olfactory function has been consistently identified as one such indicator, occurring early in the disease process before other symptoms occur.[12]

We have previously shown that Latino farmworkers and a comparison sample of non-farmworkers represent populations differentially exposed to pesticides over their lifetime, both considering occupational exposure and total exposure,[13] as measured by an established self-report instrument.[14] In addition, we have shown that a mixed group of male and female farmworkers demonstrate lower ability than a comparable group of non-farmworkers to detect a standard odor at a single point in time.[15] That study was unique in the occupational health literature, though the results were as expected in a population that is likely at risk for Parkinson's disease and other neurodegenerative diseases for which decline in olfactory function is an early symptom.

To date, no data using repeated measures has been available to examine whether (1) olfactory function declines over time with continued pesticide exposure, or (2) whether the observed differences between exposed and non-exposed workers in olfactory function persist over time. The goal of these analyses is to describe the patterns of olfactory function over two years in male Latino farmworkers and a comparison population of male Latino workers in occupations without pesticide exposure.

Methods

Data were collected by the PACE4 project (R01 ES008739) from 2012 to 2014. PACE4 is a community-based participatory research (CBPR) study with Latino communities to examine pesticides exposure and subclinical neurological outcomes. The study compares Latino farmworkers with Latino non-farmworkers selected for minimal occupational pesticide exposure. The protocol was approved by the Wake Forest Health Sciences Institutional Review Board. All participants gave signed informed consent.

Study Sites

Participants were recruited in two areas of North Carolina. Farmworkers were recruited in east central North Carolina. Non-farmworkers were recruited from Forsyth County in the west central region of the state. Although agriculture is practiced in both locales, Forsyth County is largely urban, and agriculture is far more extensive in the east central region.

Sample

Participants were men aged 30 years and older. All self-identified as Latino or Hispanic and almost all most spoke Spanish as their primary language. Farmworkers recruited had to be currently employed as farmworkers and had to have worked in agriculture for at least three years. Non-farmworkers could not have been employed for the past 3 years in jobs that routinely expose workers to pesticides, including farm work, forestry, landscaping, grounds keeping, lawn maintenance, and pest control. Confirmatory analyses of self-reported lifetime pesticide exposure measures[14] were conducted to verify the study design's assumption of greater pesticide exposure among farmworkers than non-farmworkers. These found greater occupational and total exposure to pesticides among the farmworkers, measured in years of occupational exposure and number of exposure sources, respectively; group differences remained when corrected for participant age.[13]

Recruitment was accomplished with the assistance of community partners. Staff of community partner NC Farmworkers Project approached the farmworker camps that they served. They explained the project to the residents of each camp, including the inclusion and exclusion criteria, time commitments and incentives, and asked for volunteers. Volunteers were screened to ensure that they met the inclusion criteria. Project staff worked with Forsyth County community partner El Buen Pastor Latino Community Services and other community organizations to identify and contact potential participants. Project staff explained the project, including the inclusion and exclusion criteria, time commitments and incentives, and asked if the individual wanted to volunteer. Volunteers were screened to ensure that they met the inclusion criteria.

A total of 156 farmworkers and 118 non-farmworkers completed tests of olfactory function at multiple time points and are included in analyses presented here. Participation rates are difficult to calculate for farmworkers. Because of the communal living and working situation, groups of farmworkers were asked to volunteer. Only the number who agreed to volunteer is available; generally, all of the farmworkers in a camp who met the inclusion criteria volunteered. Farmworkers who did not want to participate could have avoided contact with the project staff or indicated that they did not meet the inclusion criteria to avoid refusing. Of the 235 farmworkers who agreed to participate, 210 completed the initial olfactory assessment at Contact 1 (see below). Among the 400 non-farmworkers contacted by project staff, 101 individuals did not to meet the inclusion criteria. Of 299 who met the inclusion criteria, 87 individuals refused to participate, for a participation rate of 70.9% (212/299). Of these 212, 163 completed the initial olfactory assessment at Contact 1.

Data Collection

Participants completed data collection in early summer of 2012, 2013, and 2014 (baseline questionnaire completion, followed by Contacts 1, 3, and 5) and fall of 2012 and 2013 (Contacts 2 and 4). Farmworker data were collected from June through September, and non-farmworker data collection from July through October. At each contact, participants completed an initial questionnaire, generally in the camp (farmworkers) or home or location such as a community center (non-farmworkers), and then attended a clinic at a central location on a Sunday for collection of clinical measures, including olfactory testing. The baseline questionnaire contained demographic and health items, and items used to construct measures of lifetime pesticide exposure. All questionnaires were developed in English and translated into Spanish. When possible, existing Spanish items were used. The Spanish and English versions were checked for comparable meaning for each item, and item wording was adjusted as needed. The Spanish versions of questionnaires were pre-tested with several native Spanish speakers, and final corrections were made. Interviewers included native Spanish speakers who completed training that addressed questionnaire content and proper technique for conducting interviews.

Two olfactory tests, odor identification and odor detection threshold, were conducted at the clinic in private clinic examination rooms by trained data collectors fluent in Spanish. Because no between-group differences in odor identification were found at Contact 1,[15] only odor threshold is used in the present analysis. The odor threshold test used customized "Sniffin' Sticks" kits[16] (Burghart GmbH, Wedel, Germany) developed specifically for this study and population. Odor detection threshold was assessed using the staircase method with n-butanol, a standard olfactory test odorant used in clinics and field settings worldwide.[17] Sixteen concentrations of the odor were presented one at a time from weakest to strongest dilution in a set randomly ordered with two blanks. Participants were asked to close their eyes during the test. For each set of three odor pens, the test administrator uncapped each pen and held it under the participant's nose; after all three had been presented, the participant was asked which of the three held the odor. Administration continued in an ascending staircase, forced-choice presentation until the participant could distinguish the chemical from the blanks for three consecutive presentations. The odor threshold test was administered three times.

Olfactory test data collectors underwent extensive training, followed by practice sessions to attain proper timing and dexterity with manipulating the odor pens. Prior to data collection, each was required to complete administration observed by the first author to assure proper technique and data recording.

Measures

Odor threshold was measured as the level of odor intensity at which the odor could be correctly distinguished from the blanks. Scores could range from 16 (identification at the most dilute level) to 0 (failure to identify the odor even at the most concentrated level). The results from each of the three odor threshold trials were averaged to create a single odor threshold mean and standard deviation value for each participant. Each of the three individual trials was then compared to the mean of the three trials. If any of the three trials was more than one standard deviation above or below the mean of the three trials, that individual value was determined to be an outlier and was set to missing. The remaining values were then averaged to create a single odor threshold value for each participant to use in analyses.

Participant characteristics included *age* (30 to 34 years, 35 to 44 years, 45 years and older), *education* (0 to 6 grades, 7 to 11 grades, 12 grades or more), *country of birth* (Mexico; US, including Puerto Rico; Central America, Other); *dominant language* (Spanish, English, Other); *and industry of current primary job* (farming, construction, production, food preparation/restaurant, maintenance/cleaning, sales, transportation/truck driver, mechanic, other, unemployed). *Smoking status* was measured with a series of questions about cigarette smoking. Participants who reported any cigarette smoking in the past month at the baseline visit were defined as smokers.

Data Analysis

Descriptive statistics (count, percent) were calculated by farmworker status for baseline participant characteristics of interest and Chi-Square or Fisher's Exact tests were used as appropriate to assess farmworker and non-farmworker differences. Examination of the odor threshold scores over time revealed a large learning effect between Contact 1 and Contact 2 for both farmworkers and non-farmworkers. Thus, to evaluate the differences in odor threshold scores between farmworkers and non-farmworkers over time, a linear mixed effects model was used which accounted for repeated measures across Contacts 2 through 5 with random intercepts and adjusted for participant baseline age group (3 levels), baseline smoking status (yes/no), and the odor threshold value from Contact 1. The interaction between farmworker status and Contact was examined and was not significant, thus we examined the main effects of farmworker status across time and least square means and standard errors were calculated. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC) and p-values of less than 0.05 were considered statistically significant.

Results

These analyses are based on 274 of 447 individuals who participated in the baseline data collection. These 274 individuals are those who contributed data at Contact 1, the first time olfactory data were collected, and had at least 1 additional data collection point at Contacts 2 through 5. The numbers of participants contributing data at Contacts 2 through 5 were 255, 189, 157, and 149, respectively.

By design, all participants were male. Age ranged from 30 to 70 years, with farmworkers slightly younger than non-farmworkers (Table 1). Farmworkers also had lower educational attainment, and a greater percentage had been born in Mexico (100.0% vs. 65.3%). Almost all participants in both groups reported Spanish as their preferred language, and significantly more farmworkers reported being a current smoker (29.5% vs. 15.3%) Non-farmworkers reported currently working in a wide variety of industries, but over half reported their current primary job to be in construction (39.8%) or production (18.6%).

At Contact 1, farmworkers had significantly higher olfactory threshold than non-farmworkers (5.4 [0.2] vs. 6.9 [0.3]; Least-square mean [standard error], adjusted for age and smoking status). These results indicate that farmworkers required a greater concentration of odor than non-farmworkers in order to detect it. Similar results were found at each time point, with farmworkers having significantly higher olfactory threshold at Contacts 2 through 5.

To evaluate differences in olfactory threshold over time, a linear mixed effects model was evaluated adjusting for the Contact 1 value, as well as age and smoking status (Figure 1; Table 2). The overall difference between farmworkers and non-farmworkers remained significant (p=0.0214), with non-farmworkers performing better across time. There was no increase or decrease in the difference over time; odor threshold scores remained relatively stable (p=0.2692).

Discussion

This study shows that farmworkers and non-farmworkers, with different lifetime and current pesticide exposure, maintain differences in olfactory threshold performance over two years. Non-farmworkers were able to detect odors at significantly weaker concentrations than were farmworkers throughout the course of the study. However, the study also showed that there was no progression in olfactory function. That is, farmworkers, despite continued exposure to pesticides,[18] did not show a decline in olfactory function over time. Their olfactory function was worse than that of non-farmworkers consistently over the course of the study.

This result is somewhat unexpected. The logic behind the analysis proposes a dose-response relationship, with farmworkers having cumulatively higher doses over time and therefore showing progressively poorer olfactory function. This logic is supported by a recent meta-analysis of occupational pesticide exposure that examined cognitive and motor neurobehavioral outcomes.[19] Although the neurotoxic effects explored in such studies are different from the olfactory function in the present study, the principle of neurotoxicity resulting in progressively declining function is the same. The meta-analysis found significant performance effects for both cognitive and motor performance in adults.

Several factors can account for the continued, but steady, difference between farmworkers and non-farmworkers. It may be that two years is too short a time for a substantial decline in function to occur. Neurodegenerative processes are assumed to progress slowly, and the doses in the current study are likely chronic, but low. Another reason is suggested, based on the neurodegeneration found in of amyotrophic lateral sclerosis (ALS).[20] This work notes that difference mechanisms appear to exist in ALS for initiating disease onset and for the subsequent progression of the disease. The same may be true of neurodegeneration related specifically to pesticide exposure. That is, pesticides may have initiated some degeneration of the olfactory nerve, but some additional factor is necessary for the neurodegenerative effects to progress.

This study should be interpreted in light of its limitations. It is based on farmworkers in North Carolina, and results may not be the same in other groups of farmworkers or other worker populations exposed to pesticides. The sample size declined from 373 to 149 over the course of the two years. Workers who were lost to follow up in either the farmworker or non-farmworker sample may have been lost in a non-random way creating bias that affected the study results.

Nevertheless, the results are consistent over the two years with farmworkers, who had both lifetime and current pesticide exposure greater than non-farmworkers demonstrating poorer olfactory threshold performance. Farmworkers who work hand-cultivated and hand-harvested crops in conventional agriculture are chronically exposed to a diverse assortment of pesticides that include several classes of neurotoxins.[4–6] Because workers are rarely aware of this exposure and mandated safety training focuses more on acute exposures than chronic, workers may not take measures to protect themselves. Although exposures may take years to progress to develop into neurodegenerative diseases, and, for many workers, will not progress, farmworkers need to be informed about the potential for delayed work-related health effects from their work environment.

Conclusions

Differences in olfactory function between farmworkers, who are occupationally exposed to pesticides, and a sample of non-farmworkers selected to avoid those in pesticide-exposing jobs persist over two years. Farmworkers have and maintain significantly poorer ability to detect a test odorant. It is possible that, while pesticides can precipitate initial injury to the olfactory nerve, other factors determine whether there is further neurodegenerative progression. Additional research is needed to confirm these findings in other worker populations and to determine factors that lead to neurodegenerative diseases in pesticide-exposed populations.

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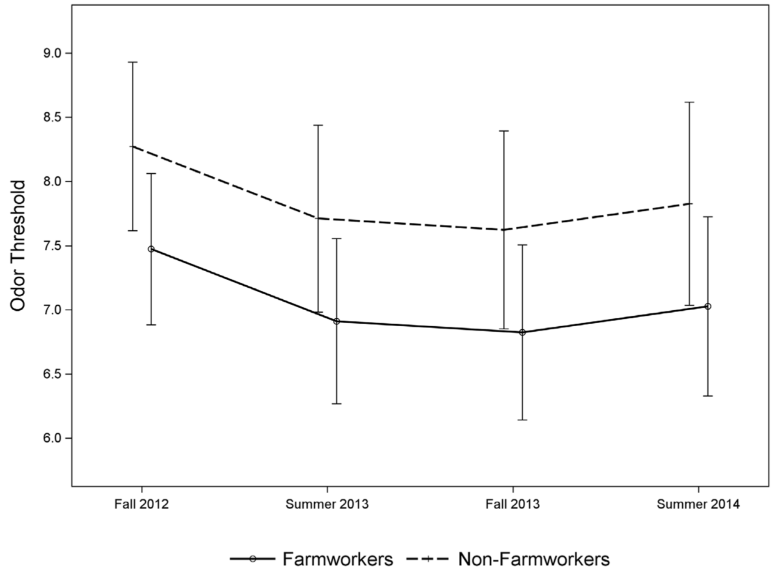

Figure 1.
Odor threshold over time, adjusted for smoking status, age, and Contact 1 score, in farmworkers and non-farmworkers selected for lack of pesticide exposure.

Table 1

Description of the sample, Latino farmworkers and non-farmworkers, North Carolina, 2012.

Participant Characteristics	Farmworkers n=156		Non-farmworkers n=118		p-value[a]
	n	%	n	%	
Age					0.1118
30–34 years	56	35.9	32	27.1	
35–44 years	58	37.2	41	34.8	
45+ years	42	26.9	45	38.1	
Education					<.0001
0–6 grade	66	42.3	39	33.1	
7–11 grade	75	48.1	39	33.1	
12 grade or more	15	9.6	40	33.9	
Country of birth					<.0001
Mexico	156	100	77	65.3	
United States/Puerto Rico			3	2.5	
Central America			28	23.7	
Other			10	8.5	
Preferred language					0.4307
Spanish	156	100	117	99.2	
Other			1	0.8	
Current Smoker	46	29.5	18	15.3	0.0058
Industry of current job					NA
Farm work	210	100			
Construction			47	39.8	
Production			22	18.6	
Maintenance/cleaning			12	10.2	
Food preparation/restaurant			9	7.6	
Mechanic			7	5.9	
Sales			7	5.9	
Transportation/Truck driver			4	3.4	
Other			3	2.5	

Participant Characteristics	Farmworkers n=156		Non-farmworkers n=118		p-value[a]
	n	%	n	%	
Unemployed			7	5.9	

[a]Based on Chi-Square or Fisher's Exact test, as appropriate

Table 2

Odor threshold least-square means and standard errors for four time points, comparing Latino farmworkers and non-farmworkers, North Carolina 2012–2014[*]

	LSMEANS (SE)		
	Farmworkers	**Non-Farmworkers**	**Overall**
Contact 2	7.47 (0.30)	8.27 (0.34)	7.87 (0.27)[‡]
Contact 3	6.91 (0.33)	7.71 (0.37)	7.31 (0.30)[‡]
Contact 4	6.82 (0.35)	7.62 (0.39)	7.22 (0.33)[‡]
Contact 5	7.03 (0.36)	7.83 (0.40)	7.43 (0.34)[‡]
Overall	7.06 (0.23)[†]	7.86 (0.29)[†]	

[*]adjusting for baseline values of: age (3-level category), current smoking status (smoker/nonsmoker), and odor threshold at Contact 1.

[†]p-value for farmworker status difference = 0.0214

[‡]p-value for Contact difference = 0.2692