

# Supplementary Material

## Occupational Pesticide Exposure in Parkinson's Disease Related to *GBA* and *LRRK2* Variants

**Supplementary Table 1.** Occupational pesticide questionnaire respondents compared to non-respondents.

	LRRK2 NMC			LRRK2 PD		
	Completed N = 122	Not Completed N = 87	p	Completed N = 54	Not Completed N = 111	p
Age at baseline, Mean (SD)	62 (7)	61 (8)	0.24	64 (7)	63 (10)	0.8
Sex, n (%)			0.32			0.036
Female	73 (60)	46 (53)		21 (39)	64 (58)	
Male	49 (40)	41 (47)		33 (61)	47 (42)	
Years of PD at baseline				2.65 (2.08)	3.19 (2.10)	0.093
	GBA NMC			GBA PD		
	Completed N = 155	Not Completed N = 32	p	Completed N = 47	Not Completed N = 49	p
Age at baseline, Mean (SD)	62 (7)	63 (8)	0.2	61 (10)	62 (11)	0.6
Sex, n (%)			0.2			0.5
Female	88 (57)	25 (72)		19 (40)	24 (49)	
Male	67 (43)	9 (28)		28 (60)	25 (51)	
Years of PD at baseline				2.80 (2.53)	3.28 (2.25)	0.2

NMC, non-manifesting carriers (genetic variant present but have not been diagnosed with PD).

**Supplementary Table 2.** Reported occupations with pesticide exposure among participants who reported pesticide exposure.

	LRRK2 NMC N = 7	LRRK2 PD N = 5	GBA NMC N = 6	GBA PD N = 8
Farming or Ranching	5 (71)	4 (80)	1 (17)	2 (25)
Landscaping / Gardening	2 (29)	0 (0)	3 (50)	3 (38)
Janitorial services / building maintenance	0 (0)	0 (0)	0	1 (13)
Nursery / Greenhouse	0 (0)	0 (0)	0	1 (13)
Pest control / Exterminator	0 (0)	0 (0)	0	3 (38)
Other forms of exposure	0 (0)	1 (20)	2 (33)	2 (25)

Data shown as n (%). Note that participants may have reported multiple occupational roles in which they were exposed.

**Supplementary Table 3.** Breakdown of composite outcomes among participants with LRRK2-PD

		<b>n (%) with outcome</b>
MCI	<b>NP test</b>	
	No pesticide exposure, n = 44	4 (9.1)
	Pesticide exposure, n = 5	0 (0)
	<b>Investigator determination</b>	
	No pesticide exposure, n = 47	16 (34)
	Pesticide exposure, n = 3	3 (60)
	<b>MoCA &lt; 26</b>	
	No pesticide exposure, n = 34	12 (35)
Pesticide exposure, n = 4	1 (25)	
ADL Impairment	<b>Swallowing</b>	
	No pesticide exposure, n = 49	2 (4.1)
	Pesticide exposure, n = 5	0 (0)
	<b>Eating</b>	
	No pesticide exposure, n = 49	0 (0)
	Pesticide exposure, n = 5	0 (0)
	<b>Dressing</b>	
	No pesticide exposure, n = 49	1 (2.0)
	Pesticide exposure, n = 5	0 (0)
	<b>Hygiene</b>	
	No pesticide exposure, n = 49	0 (0)
	Pesticide exposure, n = 5	0 (0)
	<b>Speech</b>	
	No pesticide exposure, n = 49	3 (6.1)
Pesticide exposure, n = 5	0 (0)	

MCI, mild cognitive impairment composite; NP test, >1 neuropsych tests at least 1.5 standard deviations below age/sex normative mean; MoCA, Montreal Cognitive Assessment; ADLs, Activities of daily living. \*p<0.05. \*\*p<0.01.

**Supplementary Table 4.** Breakdown of composite outcomes among participants with GBA-PD

		<b>n (%) with outcome</b>
MCI	<b>NP test</b>	
	No pesticide exposure, n = 35	4 (11)
	Pesticide exposure, n = 7	1 (14)
	<b>Investigator determination</b>	
	No pesticide exposure, n = 37	19 (51)
	Pesticide exposure, n = 8	4 (50)
	<b>MoCA &lt; 26</b>	
	No pesticide exposure, n = 25	9 (36)
Pesticide exposure, n = 6	3 (50)	
ADL Impairment	<b>Swallowing</b>	
	No pesticide exposure, n = 39	2 (5.1)
	Pesticide exposure, n = 8	1 (12)
	<b>Eating</b>	
	No pesticide exposure, n = 39	1 (2.6)
	Pesticide exposure, n = 8	0 (0)
	<b>Dressing</b>	
	No pesticide exposure, n = 39	1 (2.6)
	Pesticide exposure, n = 8	1 (12)
	<b>Hygiene</b>	
	No pesticide exposure, n = 39	0 (0)
	Pesticide exposure, n = 8	0 (0)
	<b>Speech</b>	
	No pesticide exposure, n = 39	0 (0)
	Pesticide exposure, n = 8	2 (25)*

MCI, mild cognitive impairment composite; NP test, >1 neuropsych tests at least 1.5 standard deviations below age/sex normative mean; MoCA, Montreal Cognitive Assessment; ADLs, Activities of daily living. \*p<0.05. \*\*p<0.01.

**Supplementary Table 5.** Cognitive and motor outcomes based on duration of pesticide exposure, LRRK2-PD

	<b>H&amp;Y 3</b>				
<b>n/N (%) developed outcome</b>	<b>No, N = 37</b>	<b>Yes, N = 12</b>	<b>aHR</b>	<b>95% CI</b>	<b>p</b>
<b>No Pesticide Exposure</b>	34 (92)	11 (92)	—	—	
<b>Pesticide Exposure ≤ 5 y</b>	1 (2.7)	0 (0)	0.00	0.00, Inf	>0.9
<b>Pesticide Exposure &gt; 5 y</b>	2 (5.4)	1 (8.3)	5.71	0.45, 71.8	0.2
	<b>Cognitive Impairment (composite)</b>				
<b>n/N (%) developed outcome</b>	<b>No, N = 32</b>	<b>Yes, N = 19</b>	<b>aHR</b>	<b>95% CI</b>	<b>p</b>
<b>No Pesticide Exposure</b>	30 (94)	17 (89)	—	—	
<b>Pesticide Exposure ≤ 5 y</b>	1 (3.1)	0 (0)	0.00	0.00, Inf	>0.9
<b>Pesticide Exposure &gt; 5 y</b>	1 (3.1)	2 (11)	5.06	0.85, 30.2	0.075
	<b>Impairment in ADLs</b>				
<b>n/N (%) developed outcome</b>	<b>No, N = 47</b>	<b>Yes, N = 6</b>	<b>aHR</b>	<b>95% CI</b>	<b>p</b>
<b>No Pesticide Exposure</b>	43 (91)	6 (100)	—	—	
<b>Pesticide Exposure ≤ 5 y</b>	1 (2.1)	0 (0)	0.00	0.00, Inf	>0.9
<b>Pesticide Exposure &gt; 5 y</b>	3 (6.4)	0 (0)	0.00	0.00, Inf	>0.9

**Supplementary Table 6.** Cognitive and motor outcomes based on duration of pesticide exposure, GBA-PD

	<b>H&amp;Y 3</b>				
<b>n/N (%) developed outcome</b>	<b>No, N = 34</b>	<b>Yes, N = 12</b>	<b>HR</b>	<b>95% CI</b>	<b>p</b>
<b>No Pesticide Exposure</b>	28 (82)	10 (83)	—	—	
<b>Pesticide Exposure ≤ 5 y</b>	3 (8.8)	1 (8.3)	0.47	0.05, 5.71	0.6
<b>Pesticide Exposure &gt; 5 y</b>	3 (8.8)	1 (8.3)	0.14	0.01, 2.00	0.15
	<b>Cognitive Impairment (composite)</b>				
<b>n/N (%) developed outcome</b>	<b>No, N = 22</b>	<b>Yes, N = 23</b>	<b>aHR</b>	<b>95% CI</b>	<b>p</b>
<b>No Pesticide Exposure</b>	18 (82)	19 (83)	—	—	
<b>Pesticide Exposure ≤ 5 y</b>	2 (9.1)	2 (8.7)	1.11	0.23, 5.31	>0.9
<b>Pesticide Exposure &gt; 5 y</b>	2 (9.1)	2 (8.7)	0.48	0.09, 2.41	0.4
	<b>Impairment in ADLs</b>				
<b>n/N (%) developed outcome</b>	<b>No, N = 40</b>	<b>Yes, N = 7</b>	<b>aHR</b>	<b>95% CI</b>	<b>p</b>
<b>No Pesticide Exposure</b>	35 (88)	4 (57)	—	—	
<b>Pesticide Exposure ≤ 5 y</b>	3 (7.5)	1 (14)	2.09	0.14, 30.6	0.6
<b>Pesticide Exposure &gt; 5 y</b>	2 (5.0)	2 (29)	54.1	1.81, 1,604	0.021

**Supplementary Table 7.** Relevant prior studies exploring *LRRK2* and *GBA* variants and pesticide exposure.

Reference	Gene variant studied	Population	Main finding	Comments
<b>Human Studies</b>				
Reynoso et al. [1]	<i>GBA</i> variants E326K, T369M, and N370S	People with PD (n = 2,953) vs. healthy controls (n = 88,186)	No interaction between <i>GBA</i> variant and use of pesticides in the home / garden a typical month	High prevalence of exposure in both populations (~40%) may suggest large variability in duration and timing
Simitsi et al. [2]	Multiple <i>GBA</i> variants	People with <i>GBA</i> -PD (n = 35) and people with PD without a <i>GBA</i> or <i>SNCA</i> variant (n = 35)	Higher prevalence of pesticide exposure in people with <i>GBA</i> -PD	Population of individuals with a <i>GBA</i> variant without PD not available for comparison
Chung et al. [3]	<i>LRRK2</i> rs2404835	People with PD (n = 1,098) vs healthy controls (n = 1,098)	No pair-wise interaction found between <i>LRRK2</i> variant and pesticide exposure	People with <i>LRRK2</i> G2019S not included in analysis
Desplats et al. [4]	<i>LRRK2</i> G2019S	<i>LRRK2</i> G2019S knock-in vs. wild type mice	<i>LRRK2</i> knock-in mice showed greater changes in neuronal precursors and gene expression after maneb and paraquat co-exposure	
<b>Animal Studies</b>				
Lin et al. [5]	Multiple <i>LRRK2</i> variants, not including G2019S	People with PD (n = 453) vs. healthy controls (n = 291)	No interaction between <i>LRRK2</i> and pesticide exposure	People with <i>LRRK2</i> G2019S not included in analysis
Dwyer et al. [6]	<i>LRRK2</i> G2019S	<i>LRRK2</i> G2019S knock-in vs wild-type mice	<i>LRRK2</i> knock-in mice may have more robust microglial activation after LPS and paraquat administration	Unclear effect of paraquat alone

## REFERENCES

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