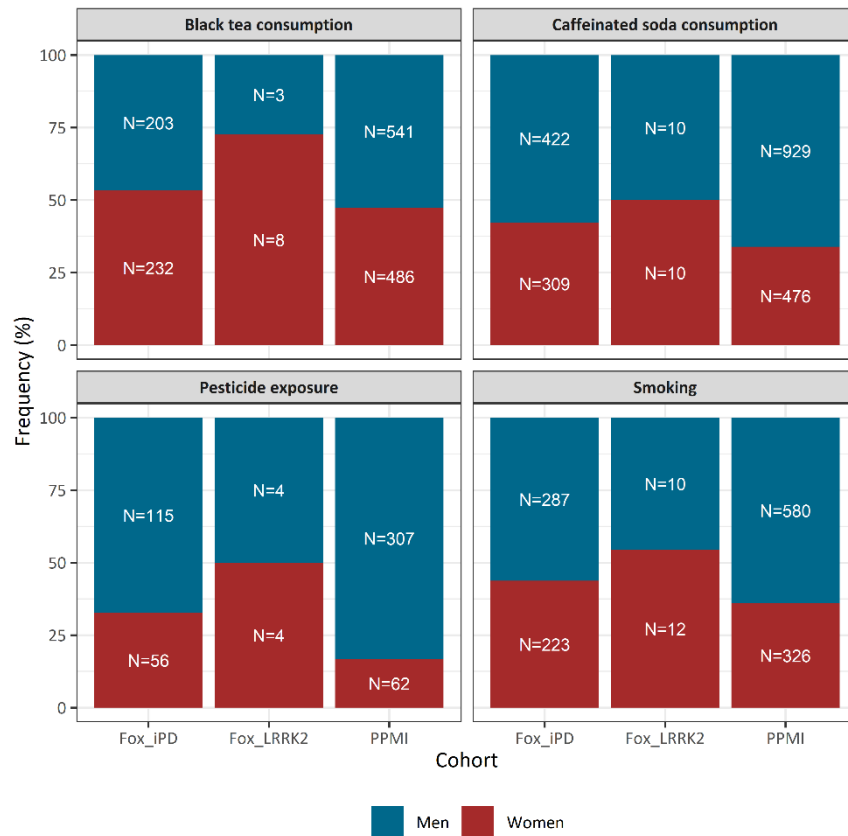
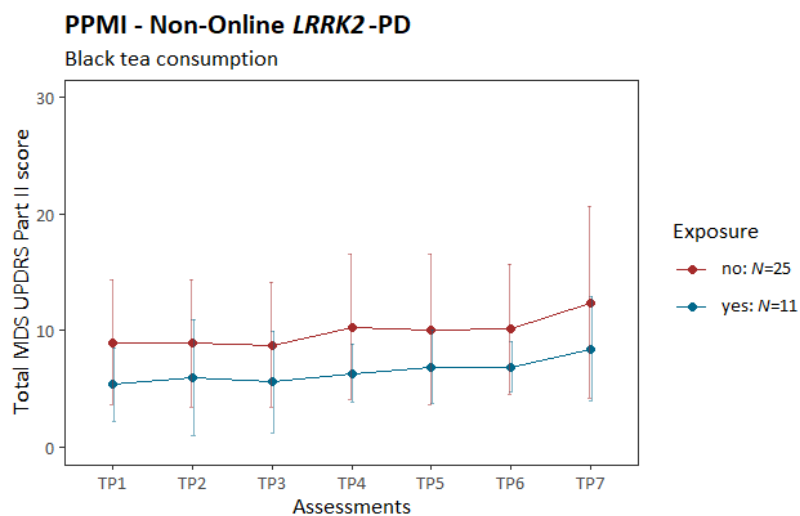


## Supplementary Material:



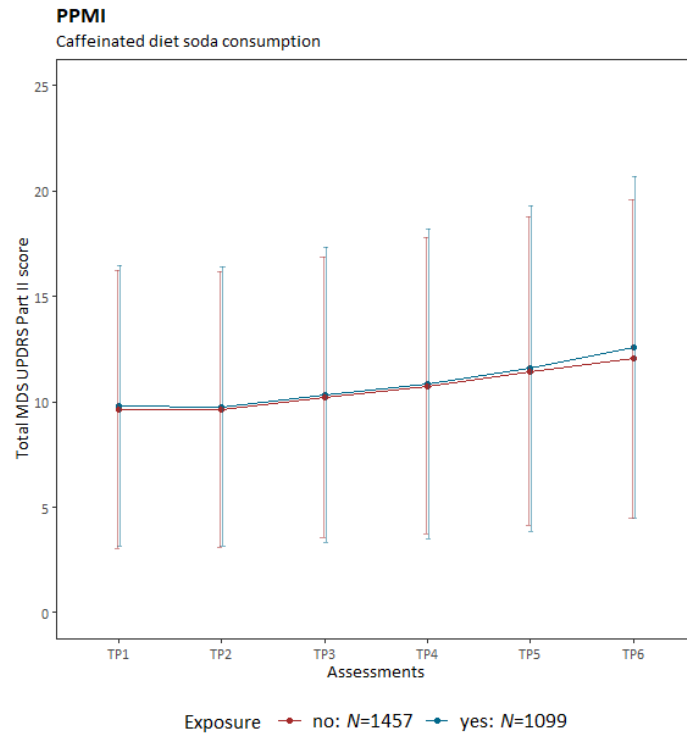
### Supplementary Figure 1. Distribution of women and men across different environmental or lifestyle factors.

The stacked bar plots display the increased fraction of men who were exposed to pesticides, smoked and consumed caffeinated soda and the more balanced fraction of men and women who drank black tea. The fraction of men (blue) and women (red) who consume black tea, caffeinated soda, smoked or were exposed to pesticides are shown. The distribution across the three analyzed cohorts is shown (i.e., PPMI-Online, Fox Insight (iPD) and Fox Insight (*LRRK2*-PD)). *N*=number of individuals.



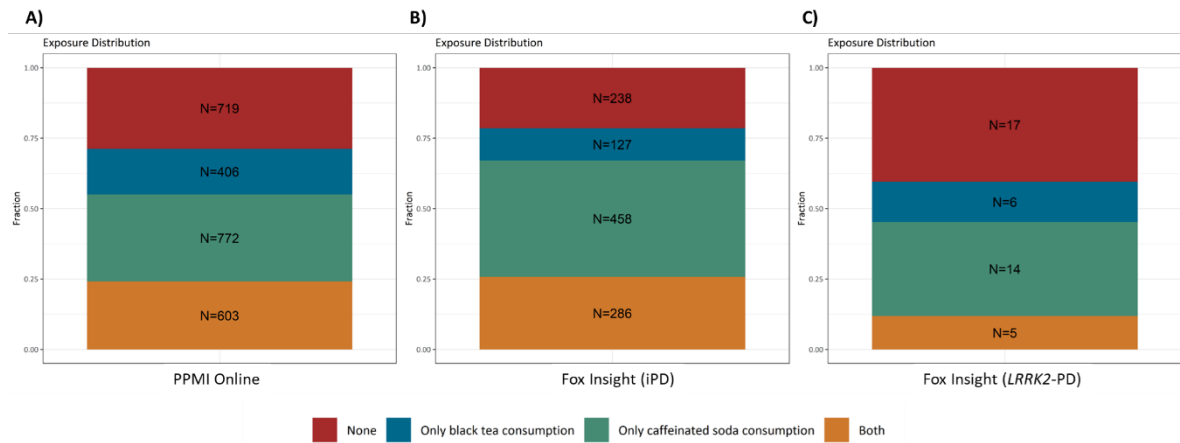
**Supplementary Figure 2. Motor aspect severity over time stratified by black tea consumption.**

The plot shows the progression of PD motor features along the longitudinal assessments. The mean cumulative MDS-UPDRS Part II score is indicated at each time period, and the error bars show the corresponding standard deviation. Patients with *LRRK2*-PD (PPMI participants that are not enrolled in the PPMI-Online study) are shown. The patients are stratified by black tea consumption. *LRRK2*-PD=Patients with PD that carry the *LRRK2* p.Gly2019Ser variant, TP=Time period,  $N$ =number of individuals.



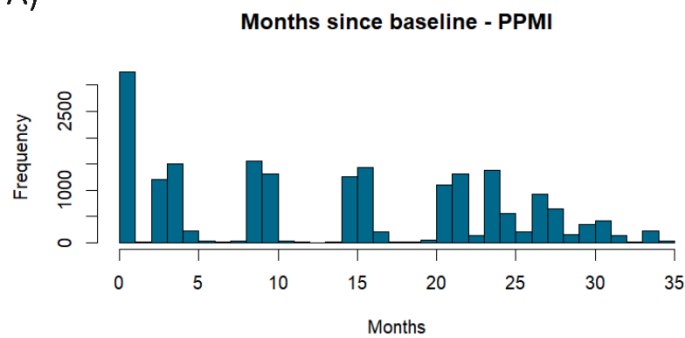
**Supplementary Figure 3. Motor aspect severity over time stratified by caffeinated diet soda consumption.**

The plots show the progression of PD motor features along the longitudinal assessments. The mean cumulative MDS-UPDRS Part II score is indicated at each time period, and the error bars show the corresponding standard deviation. Patients with iPD (PPMI-Online) are shown. The patients are stratified by caffeinated diet soda consumption. TP=Time period. N=number of individuals.



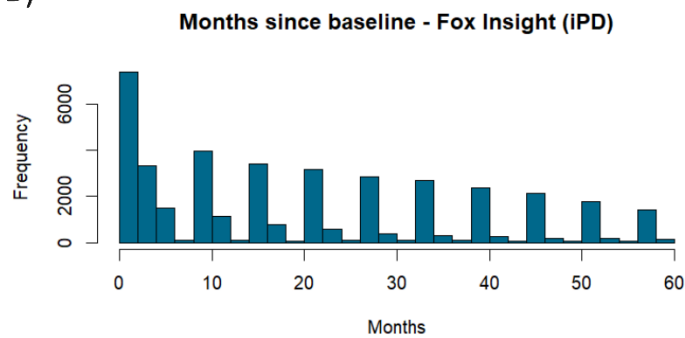
**Supplementary Figure 4. Distribution of caffeinated beverages consumption.** The stacked bar plots display the fraction of participants who consume black tea (blue), caffeinated soda (green), both beverages (orange) or none (red). There is no correlation between the two beverages, as a substantial fraction of participants consumed both beverages, only one or none. The distribution across the three analyzed cohorts is shown (i.e., PPMI-Online, Fox Insight (iPD) and Fox Insight (*LRRK2*-PD)). *N*=number of individuals.

A)



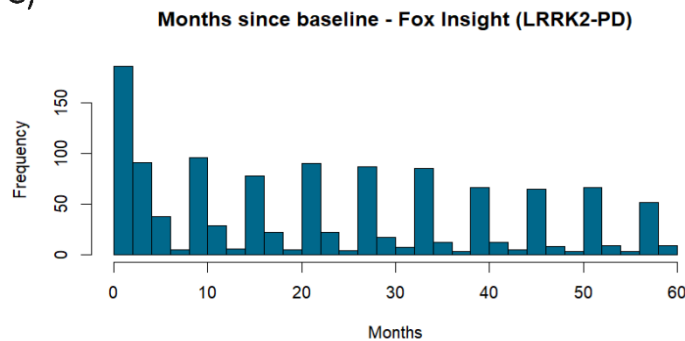
Time period	<i>N</i>
TP1 (baseline at 0 months)	2815
TP2 (0-6 months)	2673
TP3 (6-12 months)	2692
TP4 (12-18 months)	2670
TP5 (18-27 months)	2481
TP6 (27-35 months)	1160

B)



Time period	<i>N</i>
TP1 (baseline at 0 months)	2319
TP2 (0-10 months)	2103
TP3 (10-20 months)	2077
TP4 (20-30 months)	2121
TP5 (30-40 months)	1850
TP6 (40-50 months)	1267
TP7 (50-60 months)	1416

C)

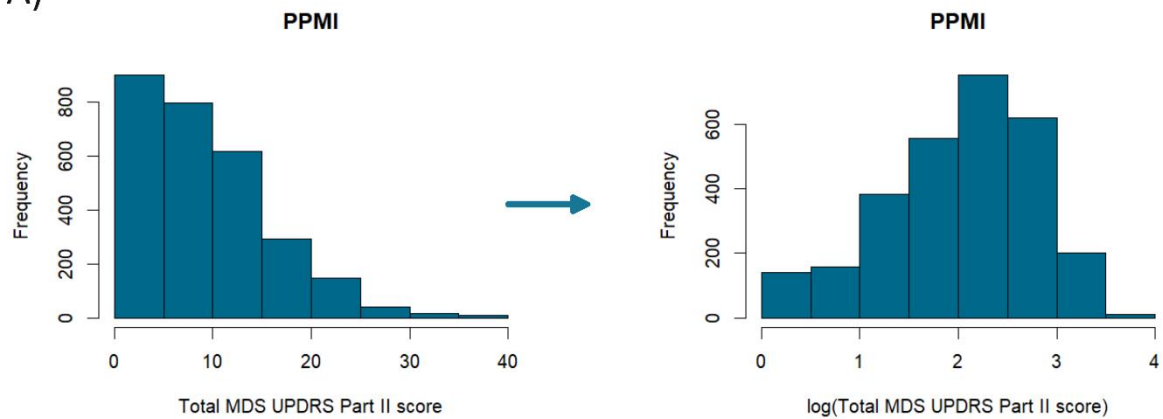


Time period-	<i>N</i>
TP1 (baseline at 0 months)	81
TP2 (0-10 months)	72
TP3 (10-20 months)	65
TP4 (20-30 months)	73
TP5 (30-40 months)	60
TP6 (40-50 months)	48
TP7 (50-60 months)	54

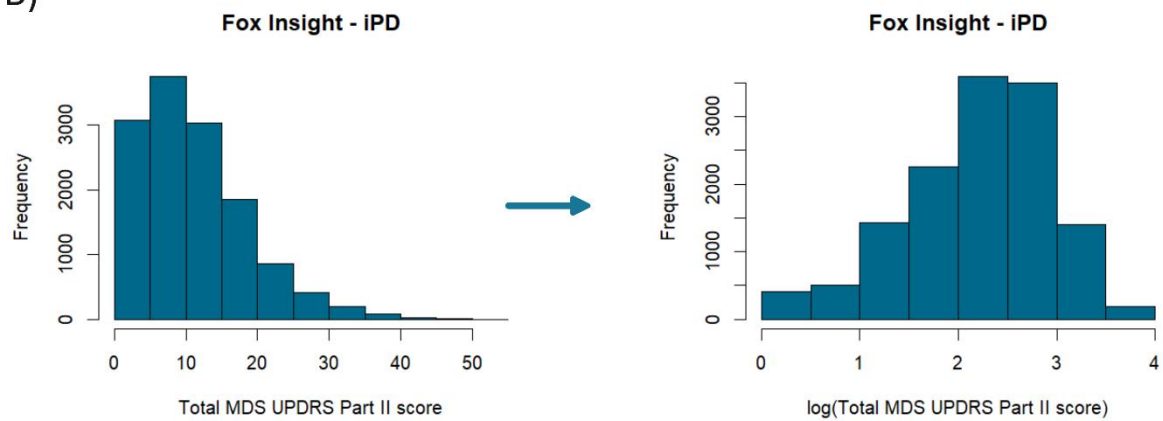
**Supplementary Figure 5. Enrollment of Patients in the PPMI-Online and Fox Insight longitudinal cohort.**

The bar charts show the number of patients with PD that longitudinally responded to the motor aspects assessment in the months since baseline. The assessments were stratified into six time periods (PPMI-Online, **A**) or seven (Fox Insight iPD and *LRRK2*-PD, **B-C**). The number of patients per assessment is also presented in the corresponding tables. *N*=Number of individuals, iPD=idiopathic Parkinson's disease, *LRRK2*-PD= Patients with PD that carry the *LRRK2* p.Gly2019Ser variant.

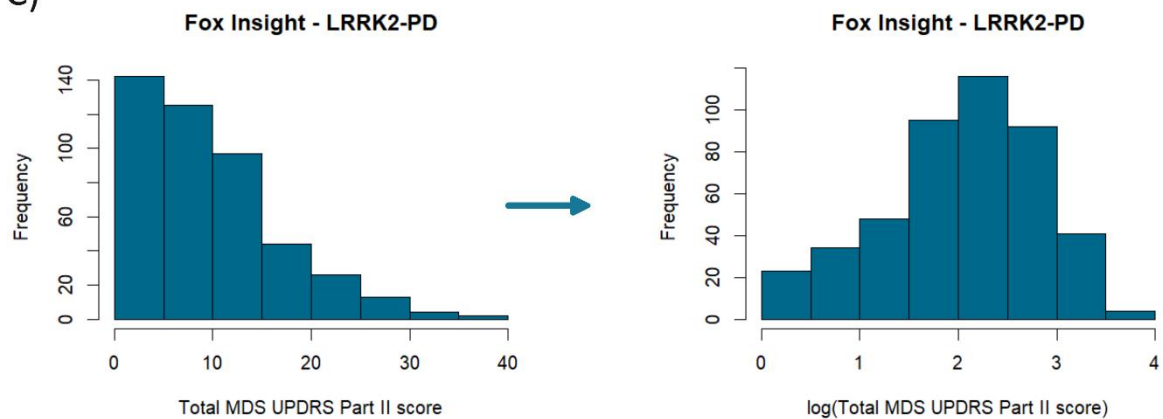
A)



B)

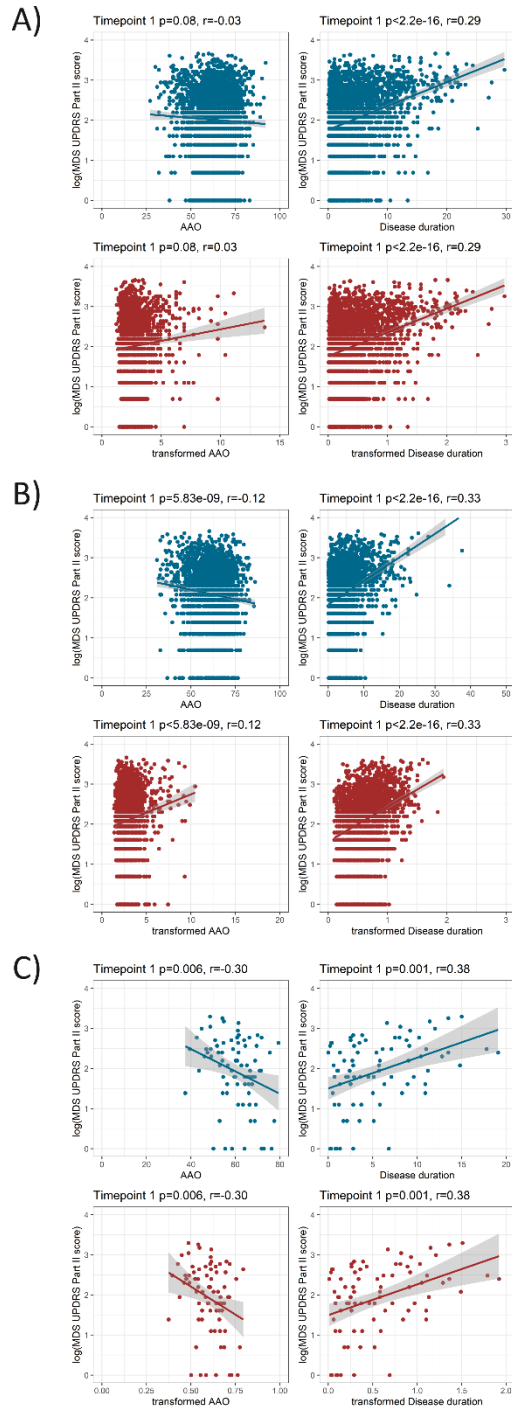


C)



**Supplementary Figure 6. Distribution of the motor aspect severity score.**

The histograms show the frequency of the cumulative MDS-UPDRS Part II score. As there is no normal distribution the score has been logarithmized. The plots show the data of patients with iPD (PPMI-Online **A** and Fox Insight in **B**) or with *LRRK2*-PD (Fox Insight in **C**). iPD=idiopathic Parkinson's disease, *LRRK2*-PD=Patients with PD that carry the *LRRK2* p.Gly2019Ser variant.



**Supplementary Figure 7. Association between age at onset or disease duration and motor aspects score.**

The scatter plots show the relationship between the age of disease onset (AAO) and disease duration with the logarithmized MDS-UPDRS part II score. The untransformed data are shown in blue, and the transformed data in red (by using fractional polynomials). The plots show the data of patients with iPD (PPMI-Online **A** and Fox Insight in **B**) or with *LRRK2*-PD (Fox Insight in **C**). iPD=idiopathic Parkinson's disease, *LRRK2*-PD=Patients with PD that carry the *LRRK2* p.Gly2019Ser variant,  $r$ =Spearman's rank correlation rho,  $p$ =Spearman's rank correlation  $p$ -value.

**Supplementary Table 1.** The association between coffee consumption and motor aspect severity over time. The motor aspect severity was evaluated longitudinally over time and assessed with a mixed linear model in the PPMI-Online and Fox Insight cohort.

	Estimate	SE	p-value
<b>PPMI-Online (iPD: yes=2059, no=548)</b>			
Time period 2	-0.002	0.01	0.844
Time period 3	0.07	0.01	$3.43 \times 10^{-12}$
Time period 4	0.12	0.01	$<2.00 \times 10^{-16}$
Time period 5	0.20	0.01	$<2.00 \times 10^{-16}$
Time period 6	0.26	0.01	$<2.00 \times 10^{-16}$
Coffee	0.05	0.03	0.157
AAO	-0.06	0.01	$8.97 \times 10^{-5}$
Disease duration	0.63	0.04	$<2.00 \times 10^{-16}$
<b>Fox Insight (iPD: yes=1054, no=312)</b>			
Time period 2	0.02	0.01	0.218
Time period 3	0.08	0.01	$1.740 \times 10^{-8}$
Time period 4	0.16	0.01	$<2.00 \times 10^{-16}$
Time period 5	0.23	0.02	$<2.00 \times 10^{-16}$
Time period 6	0.28	0.02	$<2.00 \times 10^{-16}$
Time period 7	0.32	0.02	$<2.00 \times 10^{-16}$
Coffee	0.01	0.04	0.782
AAO	-0.03	0.02	0.116
Disease duration	0.71	0.07	$<2.00 \times 10^{-16}$
OFF-episodes	0.24	0.04	$9.030 \times 10^{-11}$
<b>Fox Insight (LRRK2-PD: yes=37, no=10)</b>			
Time period 2	0.01	0.08	0.935
Time period 3	0.06	0.08	0.404
Time period 4	0.20	0.08	0.010
Time period 5	0.18	0.08	0.020
Time period 6	0.34	0.08	$4.51 \times 10^{-5}$
Time period 7	0.36	0.08	$1.59 \times 10^{-5}$
Coffee	-0.04	0.23	0.851
AAO	-0.97	1.23	0.431
Disease duration	0.48	0.24	0.051
OFF-episodes	0.68	0.20	0.002

N=Number of individuals, iPD=idiopathic Parkinson's disease, LRRK2-PD= Patients with PD that carry the LRRK2 p.Gly2019Ser variant, Formula in R (package lme4): lmer(log(Cumulative MDS-UPDRS Part II Score) ~ Assessment time periods + mfp transformed AAO + mfp transformed disease duration + Environmental/Lifestyle factor (yes/no) + Experience of OFF episodes\* + (1|Patient ID))

\*If applicable

Baseline categories: Time period=Time period 1 (i.e., assessment at enrolment)



**Supplementary Table 2.** The association between green tea consumption and motor aspect severity over time. The motor aspect severity was evaluated longitudinally over time and assessed with a mixed linear model in the PPMI-Online and Fox Insight cohort.

	Estimate	SE	p-value
<b>PPMI-Online (iPD: yes=385, no=2164)</b>			
Time period 2	-0.004	0.01	0.660
Time period 3	0.07	0.01	$1.34 \times 10^{-11}$
Time period 4	0.12	0.01	$<2.00 \times 10^{-16}$
Time period 5	0.20	0.01	$<2.00 \times 10^{-16}$
Time period 6	0.26	0.01	$<2.00 \times 10^{-16}$
Green tea	0.04	0.04	0.360
AAO	-0.06	0.01	$7.41 \times 10^{-5}$
Disease duration	0.62	0.04	$<2.00 \times 10^{-16}$
<b>Fox Insight (iPD: yes=189, no=943)</b>			
Time period 2	0.01	0.02	0.356
Time period 3	0.08	0.02	$2.23 \times 10^{-7}$
Time period 4	0.16	0.02	$<2.00 \times 10^{-16}$
Time period 5	0.23	0.02	$<2.00 \times 10^{-16}$
Time period 6	0.28	0.02	$<2.00 \times 10^{-16}$
Time period 7	0.31	0.02	$<2.00 \times 10^{-16}$
Green tea	-0.03	0.05	0.557
AAO	-0.02	0.02	0.274
Disease duration	0.67	0.07	$<2.00 \times 10^{-16}$
OFF-episodes	0.25	0.04	$3.18 \times 10^{-10}$
<b>Fox Insight (LRRK2-PD: yes=9, no=34)</b>			
Time period 2	-0.01	0.08	0.889
Time period 3	0.09	0.08	0.260
Time period 4	0.22	0.08	0.006
Time period 5	0.23	0.08	0.005
Time period 6	0.39	0.09	$1.19 \times 10^{-5}$
Time period 7	0.40	0.08	$4.65 \times 10^{-6}$
Green tea	-0.23	0.25	0.358
AAO	-0.65	1.32	0.625
Disease duration	0.45	0.25	0.080
OFF-episodes	0.54	0.22	0.018

N=Number of individuals, iPD=idiopathic Parkinson's disease, LRRK2-PD= Patients with PD that carry the LRRK2 p.Gly2019Ser variant, Formula in R (package lme4): lmer(log(Cumulative MDS-UPDRS Part II Score) ~ Assessment time periods + mfp transformed AAO + mfp transformed disease duration + Environmental/Lifestyle factor (yes/no) + Experience of OFF episodes\* + (1|Patient ID))

\*If applicable

Baseline categories: Time period=Time period 1 (i.e., assessment at enrolment)

**Supplementary Table 3A.** The association between pesticide exposure and motor aspect severity over time. The motor aspect severity was evaluated longitudinally over time and assessed with a linear mixed model in the PPMI-Online and Fox Insight cohort.

	Estimate	SE	p-value
<b>PPMI-Online (iPD: yes=369, no=2098)</b>			
<b>Time period 2</b>	0.001	0.01	0.891
<b>Time period 3</b>	0.07	0.01	$4.18 \times 10^{-13}$
<b>Time period 4</b>	0.12	0.01	$<2.00 \times 10^{-16}$
<b>Time period 5</b>	0.20	0.01	$<2.00 \times 10^{-16}$
<b>Time period 6</b>	0.27	0.01	$<2.00 \times 10^{-16}$
<b>Pesticide exposure</b>	0.19	0.04	$1.24 \times 10^{-6}$
<b>AAO</b>	-0.06	0.01	$1.48 \times 10^{-4}$
<b>Disease duration</b>	0.64	0.04	$<2.00 \times 10^{-16}$
<b>Sex: Men</b>	0.14	0.03	$9.94 \times 10^{-7}$
<b>Fox Insight (iPD: yes=171, no=630)</b>			
<b>Time period 2</b>	0.01	0.02	0.610
<b>Time period 3</b>	0.09	0.02	$1.350 \times 10^{-05}$
<b>Time period 4</b>	0.15	0.02	$5.510 \times 10^{-14}$
<b>Time period 5</b>	0.22	0.02	$<2.00 \times 10^{-16}$
<b>Time period 6</b>	0.27	0.02	$<2.00 \times 10^{-16}$
<b>Time period 7</b>	0.30	0.02	$<2.00 \times 10^{-16}$
<b>Pesticide exposure</b>	0.08	0.06	0.146
<b>AAO</b>	-0.02	0.02	0.484
<b>Disease duration</b>	0.76	0.09	$<2.00 \times 10^{-16}$
<b>OFF-episodes</b>	0.25	0.05	$2.150 \times 10^{-7}$
<b>Sex: Men</b>	0.18	0.05	$1.590 \times 10^{-4}$

N=Number of individuals, iPD=idiopathic Parkinson's disease, Formula in R (package lme4): lmer(log(Cumulative MDS-UPDRS Part II Score) ~ Assessment time periods + mfp transformed AAO + mfp transformed disease duration + Environmental/Lifestyle factor (yes/no) + Experience of OFF episodes\* + Sex + (1|Patient ID))

\*If applicable, Tested for significance at  $\alpha = 0.017$

Baseline categories: Time period=Time period 1 (i.e., assessment at enrolment), Sex=Women

**Supplementary Table 3B.** The association between smoking and motor aspect severity over time. The severity of motor aspect was evaluated longitudinally over time and assessed using a linear mixed model in the PPMI-Online.

	Estimate	SE	p-value
<b>PPMI-Online (iPD: yes=906, no=1670)</b>			
<b>Time period 2</b>	0.001	0.01	0.911
<b>Time period 3</b>	0.07	0.01	$1.970 \times 10^{-11}$
<b>Time period 4</b>	0.12	0.01	$<2.00 \times 10^{-16}$
<b>Time period 5</b>	0.20	0.01	$<2.00 \times 10^{-16}$
<b>Time period 6</b>	0.26	0.01	$<2.00 \times 10^{-16}$
<b>Smoking</b>	0.12	0.03	$3.170 \times 10^{-5}$
<b>AAO</b>	-0.05	0.01	0.001
<b>Disease duration</b>	0.64	0.04	$<2.00 \times 10^{-16}$
<b>Sex: Men</b>	0.17	0.03	$8.620 \times 10^{-10}$

N=Number of individuals, iPD=idiopathic Parkinson's disease, Formula in R (package lme4): lmer(log(Cumulative MDS-UPDRS Part II Score) ~ Assessment time periods + mfp transformed AAO + mfp transformed disease duration + Environmental/Lifestyle factor (yes/no) + Experience of OFF episodes\* + Sex + (1|Patient ID))

\*If applicable

Baseline categories: Time period=Time period 1 (i.e., assessment at enrolment), Sex=Women

**Supplementary Table 3C.** The association between black tea consumption and motor aspect severity over time. The motor aspect severity was evaluated longitudinally over time and assessed using a linear mixed model in the Fox Insight cohort (*LRRK2*-PD)

	Estimate	SE	p-value
<b>Fox Insight (<i>LRRK2</i>-PD: yes=11, no=31)</b>			
<b>Time period 2</b>	-0.01	0.08	0.855
<b>Time period 3</b>	0.09	0.08	0.296
<b>Time period 4</b>	0.22	0.08	0.006
<b>Time period 5</b>	0.23	0.08	0.006
<b>Time period 6</b>	0.39	0.09	$1.420 \times 10^{-5}$
<b>Time period 7</b>	0.40	0.09	$5.830 \times 10^{-6}$
<b>Black tea</b>	-0.53	0.23	0.028
<b>AAO</b>	-0.90	1.31	0.495
<b>Disease duration</b>	0.37	0.24	0.138
<b>OFF-episodes</b>	0.58	0.21	0.009
<b>Sex: Men</b>	-0.08	0.21	0.718

N=Number of individuals, *LRRK2*-PD= Patients with PD that carry the *LRRK2* p.Gly2019Ser variant, Formula in R (package lme4): lmer(log(Cumulative MDS-UPDRS Part II Score) ~ Assessment time periods + mfp transformed AAO + mfp transformed disease duration + Environmental/Lifestyle factor (yes/no) + Experience of OFF episodes\* + Sex + (1|Patient ID))

\*If applicable

Baseline categories: Time period=Time period 1 (i.e., assessment at enrolment), Sex=Women

**Supplementary Table 3D.** The association between caffeinated soda consumption and motor aspect severity over time. The motor aspect severity was evaluated longitudinally over time and assessed with a linear mixed model in the PPMI-Online and Fox Insight cohort.

	Estimate	SE	p-value
<b>PPMI-Online (iPD: yes=1405, no=1154)</b>			
Time period 2	0.0004	0.01	0.966
Time period 3	0.07	0.01	$1.180 \times 10^{-12}$
Time period 4	0.12	0.01	$<2.00 \times 10^{-16}$
Time period 5	0.20	0.01	$<2.00 \times 10^{-16}$
Time period 6	0.26	0.01	$<2.00 \times 10^{-16}$
Caffeinated soda	0.13	0.03	$2.080 \times 10^{-6}$
AAO	-0.06	0.01	$2.600 \times 10^{-5}$
Disease duration	0.64	0.04	$<2.00 \times 10^{-16}$
Sex: Men	0.17	0.03	$1.520 \times 10^{-9}$
<b>Fox Insight (iPD: yes=731, no=357)</b>			
Time period 2	0.01	0.02	0.751
Time period 3	0.08	0.02	$4.490 \times 10^{-6}$
Time period 4	0.15	0.02	$<2.00 \times 10^{-16}$
Time period 5	0.23	0.02	$<2.00 \times 10^{-16}$
Time period 6	0.28	0.02	$<2.00 \times 10^{-16}$
Time period 7	0.31	0.02	$<2.00 \times 10^{-16}$
Caffeinated soda	0.07	0.04	0.119
AAO	-0.02	0.02	0.220
Disease duration	0.72	0.07	$<2.00 \times 10^{-16}$
OFF-episodes	0.25	0.04	$4.920 \times 10^{-10}$
Sex: Men	0.20	0.04	$2.040 \times 10^{-7}$
<b>Fox Insight (LRRK2-PD: yes=20, no=23)</b>			
Time period 2	-0.01	0.08	0.881
Time period 3	0.09	0.08	0.259
Time period 4	0.22	0.08	0.006
Time period 5	0.23	0.08	0.005
Time period 6	0.39	0.09	$1.160 \times 10^{-5}$
Time period 7	0.40	0.08	$4.890 \times 10^{-6}$
Caffeinated soda	0.35	0.22	0.111
AAO	-1.18	1.37	0.394
Disease duration	0.46	0.25	0.069
OFF-episodes	0.42	0.23	0.080
Sex: Men	0.07	0.21	0.749

N=Number of individuals, iPD=idiopathic Parkinson's disease, LRRK2-PD= Patients with PD that carry the LRRK2 p.Gly2019Ser variant, Formula in R (package lme4):  $\text{lmer}(\log(\text{Cumulative MDS-UPDRS Part II Score}) \sim \text{Assessment time periods} + \text{mfp transformed AAO} + \text{mfp transformed disease duration} + \text{Environmental/Lifestyle factor (yes/no)} + \text{Experience of OFF episodes}^* + \text{Sex} + (1|\text{Patient ID}))$

\*If applicable

Baseline categories: Time period=Time period 1 (i.e., assessment at enrolment), Sex=Women

**Supplementary Table 4.** The association between black tea consumption and motor aspect severity over time. The motor aspect severity was evaluated longitudinally over time and assessed with a mixed linear model in patients with *LRRK2*-PD PPMI participants who are not enrolled in the PPMI-Online study.

	Estimate	SE	p-value
<b>PPMI – Non-Online (iPD: yes=11, no=25)</b>			
<b>Time period 2</b>	-0.04	0.11	0.735
<b>Time period 3</b>	-0.01	0.11	0.948
<b>Time period 4</b>	0.27	0.12	0.019
<b>Time period 5</b>	0.28	0.12	0.018
<b>Time period 6</b>	0.35	0.12	0.004
<b>Time period 7</b>	0.40	0.12	0.001
<b>Black tea</b>	-0.41	0.18	0.026
<b>AAO</b>	-0.51	1.16	0.665
<b>Disease duration</b>	0.14	0.04	0.001

N=Number of individuals, iPD=idiopathic Parkinson's disease, *LRRK2*-PD= Patients with PD that carry the *LRRK2* p.Gly2019Ser variant, Formula in R (package lme4): lmer(log(Cumulative MDS-UPDRS Part II Score) ~ Assessment time periods + mfp transformed AAO + mfp transformed disease duration + Environmental/Lifestyle factor (yes/no) + Experience of OFF episodes\* + (1|Patient ID))

\*If applicable

Baseline categories: Time period=Time period 1 (i.e., assessment at enrolment)

**Supplementary Table 5.** Overview of patients with iPD and *LRRK2*-PD that are also affected by type 2 diabetes (T2DM), stratified by caffeinated soda consumption within Fox Insight.

PD subtype	Caffeinated soda	T2DM (N)	No T2DM (N)	NA (N)
<b>iPD</b>	<b>yes</b>	16	217	609
	<b>no</b>	8	11	283
<b><i>LRRK2</i>-PD</b>	<b>yes</b>	1	4	8
	<b>no</b>	0	8	12

N=Number of individuals, iPD=idiopathic Parkinson's disease, *LRRK2*-PD= Patients with PD that carry the *LRRK2* p.Gly2019Ser variant, NA=Information not available