Supplementary Materials:

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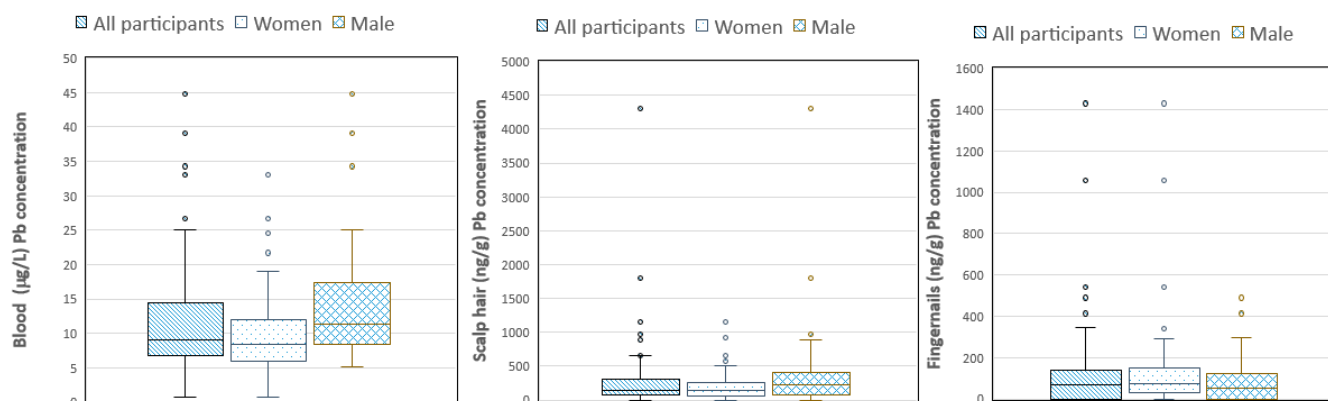
Figure S1. Box-Plots with the distribution of Pb values in analyzed biomarkers.
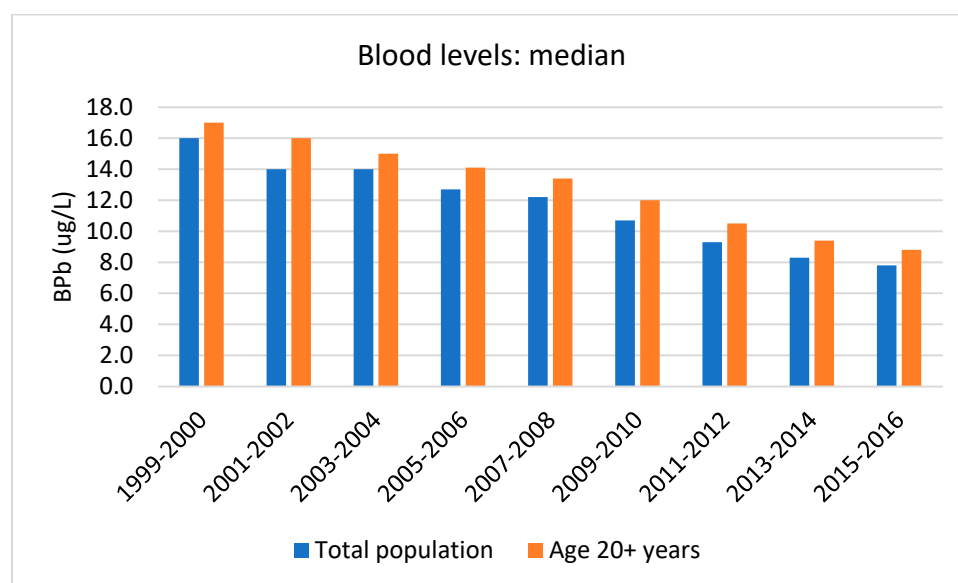

Figure S2. Decrease in blood Pb levels in the US general population from 1999 to 2016 (calculated from the Fourth National Report on Human Exposure to Environmental Chemicals (U.S. Department of Health and Human Services, 2019) [1]).

Table S1. Basal characteristics of the study population.

	Women		Men		Total		
	n= 95		**n= 35**		**n= 130**		*p value*
Age (Mean, SD)	40.29	13.7	45.57	14.15	41.72	13.97	*0.056*
(range: min, max)	20	71	21	71	20	71	
Study level (n, %)							*0.068*
Primary education	5	5.3%	1	2.9%	6	4.6%	
Secondary Education	12	12.6%	10	28.6%	22	16.9%	
High school level	22	23.2%	8	22.9%	30	23.1%	

University studies (Bachelor's Degree)	18	18.9%	1	2.9%	19	14.6%	
University studies (University Degree)	38	40.0%	15	42.9%	53	40.8%	
Years residing (Mean, SD)	16.08	14.77	12.91	9.86	15.26	13.71	*0.242*
(range: min, max)	1	71	2	38	1	71	
Employment status							*0.072*
Employed full-time	72	75.8%	25	71.4%	97	74.6%	
Unemployed	2	2.1%	3	8.6%	5	3.8%	
Housewife	5	5.3%	0	0.0%	5	3.8%	
Retired	7	7.4%	6	17.1%	13	10.0%	
Full-time student	9	9.5%	1	2.9%	10	7.7%	
Smoking Status							*0.973*
Non-smoker	61	64.2%	23	65.7%	84	64.6%	
Former	16	16.8%	6	17.1%	22	16.9%	
Current	18	18.9%	6	17.1%	24	18.5%	
Alcohol Status							*0.005*
Never	59	62.1%	12	34.3%	71	54.6%	
Ever	36	37.9%	23	65.7%	59	45.4%	
Average of pure ethanol (g/week)							*0.006*
0 g/week	59	62.0%	12	34.3%	71	54.6%	
1-24 g/week	16	16.8%	6	17.1%	22	16.9%	
25-74 g/week	19	20.0%	14	40.0%	33	25.4%	
≥75 g/week	1	1.1%	3	8.6%	4	3.1%	

Table S2. Mean differences for Verbal Fluency test according to Pb and Mn levels in biomarkers and PM personal sampling. .

	MD*	95%	CI	*p value*
Biomarkers				
Pb Blood (>9.14 vs ≤9.14 µg/L)				
Letter P	0.53	-0.45	1.51	*0.283*
Letter M	-0.02	-0.90	0.86	*0.961*
Letter R	0.02	-0.95	0.98	*0.975*
Pb Scalp hair (>149.04 vs ≤149.04 ng/g)				
Letter P	0.13	-0.77	1.03	*0.774*
Letter M	0.20	-0.60	1.00	*0.618*
Letter R	0.26	-0.59	1.12	*0.544*
Pb Fingernails (96.04> vs ≤96.04 ng/g)				
Letter P	0.66	-0.34	1.66	*0.190*
Letter M	0.73	-0.20	1.65	*0.123*
Letter R	0.82	-0.23	1.86	*0.125*
Mn Blood (>9.58 vs ≤9.58 µg/L)				
Letter P	0.62	-0.29	1.53	*0.180*
Letter M	0.57	-0.26	1.39	*0.177*
Letter R	0.44	-0.44	1.33	*0.326*
Mn Scalp hair (>185.31 vs ≤185.31 ng/g)				
Letter P	-0.43	-1.36	0.50	*0.359*
Letter M	-0.15	-0.98	0.68	*0.727*
Letter R	-0.38	-1.27	0.52	*0.404*
Mn Fingernails (>555.28 vs ≤555.28 ng/g)				
Letter P	-0.20	-1.23	0.84	*0.709*

Letter M	-0.80	-1.79	0.20	*0.117*
Letter R	-0.48	-1.58	0.62	*0.387*
PEM Fine fraction (PM$_{2.5}$)				
Pb Bioaccessible (5.26+ vs ≤5.25 ng/m^3)				
Letter P	-0.06	-1.03	0.92	*0.907*
Letter M	-0.10	-0.98	0.79	*0.831*
Letter R	-0.37	-1.30	0.56	*0.436*
Pb Non-bioaccessible (0.38+ vs ≤0.37 ng/m^3)				
Letter P	-0.18	-1.15	0.78	*0.709*
Letter M	0.27	-0.59	1.14	*0.535*
Letter R	0.74	-0.17	1.64	*0.108*
Pb Total (Bio+Non-bio) (6.57+vs ≤6.56 ng/m^3)				
Letter P	-0.24	-1.21	0.74	*0.635*
Letter M	0.08	-0.81	0.96	*0.866*
Letter R	0.10	-0.83	1.03	*0.835*
Mn Bioaccessible (17.06+ vs ≤17.05 ng/m^3)				
Letter P	-1.21	-2.15	-0.27	*0.012*
Letter M	-1.15	-1.99	-0.30	*0.008*
Letter R	-1.18	-2.09	-0.27	*0.012*
Mn Non-bioaccessible (5.81+ vs ≤5.80 ng/m^3)				
Letter P	-0.27	-1.20	0.66	*0.566*
Letter M	-0.32	-1.15	0.52	*0.456*
Letter R	-0.41	-1.31	0.49	*0.364*
Mn Total (Bio+Non-bio) (25.01+vs ≤25.00 ng/m^3)				
Letter P	-1.36	-2.30	-0.41	*0.005*
Letter M	-1.26	-2.11	-0.41	*0.004*
Letter R	-1.20	-2.12	-0.27	*0.011*

MD= Mean difference adjusted for age, sex, educational level, and Pb or Mn levels respectively. PEM=Personal Environmental Monitor. *A negative MD indicates worse cognitive function (lower standardized NEURONORMA scores) among exposed to Pb or Mn higher levels. Statistically significant MDs are in bold.

Table S3. Mean differences for Trail Making Test (TMT) according to Pb and Mn levels in biomarkers and PM personal sampling.

	MD*	**95%**	**CI**	*p value*
Biomarkers				
Pb Blood (>9.14 vs ≤9.14 µg/L)				
TMT-A	-0.15	-1.28	0.98	*0.792*
TMT-B	0.37	-0.53	1.27	*0.419*
Pb Scalp hair (>149.04 vs ≤149.04 ng/g)				
TMT-A	0.19	-0.88	1.27	*0.721*
TMT-B	-0.16	-0.98	0.67	*0.71*
Pb Fingernails (96.04> vs ≤96.04 ng/g)				
TMT-A	0.50	-0.70	1.71	*0.408*
TMT-B	0.24	-0.75	1.23	*0.633*
Mn Blood (>9.58 vs ≤9.58 µg/L)				
TMT-A	0.25	-0.79	1.28	*0.640*
TMT-B	0.60	-0.22	1.42	*0.152*
Mn Scalp hair (>185.31 vs ≤185.31 ng/g)				
TMT-A	-0.27	-1.36	0.83	*0.629*
TMT-B	-0.07	-0.91	0.78	*0.876*

	MD	95%	CI	p value
Mn Fingernails (>555.28 vs ≤555.28 ng/g)				
TMT-A	-1.02	-2.21	0.17	*0.092*
TMT-B	-0.99	-1.98	0.00	*0.050*
PEM Fine fraction (PM$_{2.5}$)				
Pb Bioaccessible (>5.25 vs ≤5.25 ng/m^3)				
TMT-A	-0.11	-1.21	1.00	*0.851*
TMT-B	-0.01	-0.89	0.87	*0.980*
Pb Non-bioaccessible (>0.37 vs ≤0.37 ng/m^3)				
TMT-A	-0.28	-1.36	0.80	*0.609*
TMT-B	0.51	-0.35	1.37	*0.240*
Pb Total (Bio+Non-bio) (>6.56 vs ≤6.56 ng/m^3)				
TMT-A	-0.15	-1.26	0.96	*0.789*
TMT-B	0.10	-0.78	0.99	*0.819*
Mn Bioaccessible (>17.05 vs ≤17.05 ng/m^3)				
TMT-A	-1.00	-2.07	0.07	*0.068*
TMT-B	-0.68	-1.54	0.19	*0.123*
Mn Non-bioaccessible (>5.80 vs ≤5.80 ng/m^3)				
TMT-A	0.19	-0.86	1.23	*0.723*
TMT-B	-0.35	-1.19	0.48	*0.403*
Mn Total (Bio+Non-bio) (>25.00 vs ≤25.00 ng/m^3)				
TMT-A	-0.95	-2.03	0.14	*0.087*
TMT-B	-0.62	-1.49	0.26	*0.164*

MD= Mean difference adjusted for age, sex, educational level, and Pb or Mn levels respectively. PEM=Personal Environmental Monitor.*A negative MD indicates worse cognitive function (lower standardized NEURONORMA scores) among exposed to Pb or Mn higher levels. Statistically significant MDs are in bold.

Table S4. Mean differences for Rey Osterrieth Complex Figure (ROCF) test according to Pb and Mn levels in biomarkers and PM personal sampling.

	MD*	**95%**	**CI**	*p value*
Biomarkers				
Pb Blood (>9.14 vs ≤9.14 µg/L)				
ROCF Copy	-0.12	-1.32	1.07	*0.840*
ROCF Delayed	0.03	-0.78	0.83	*0.949*
Pb Scalp hair (>149.04 vs ≤149.04 ng/g)				
ROCF Copy	-0.29	-1.42	0.85	*0.619*
ROCF Delayed	-0.52	-1.26	0.23	*0.174*
Pb Fingernails (96.04> vs ≤96.04 ng/g)				
ROCF Copy	0.20	-1.08	1.48	*0.754*
ROCF Delayed	-0.15	-1.08	0.77	*0.745*
Mn Blood (>9.58 vs ≤9.58 µg/L)				
ROCF Copy	-0.39	-1.48	0.70	*0.478*
ROCF Delayed	0.34	-0.40	1.08	*0.368*
Mn Scalp hair (>185.31 vs ≤185.31 ng/g)				
ROCF Copy	-0.37	-1.52	0.79	*0.528*
ROCF Delayed	0.11	-0.66	0.87	*0.784*
Mn Fingernails (>555.28 vs ≤555.28 ng/g)				
ROCF Copy	-0.18	-1.47	1.12	*0.789*
ROCF Delayed	0.24	-0.68	1.16	*0.604*
PEM Fine fraction (PM$_{2.5}$)				
Pb Bioaccessible (>5.25 vs ≤5.25 ng/m^3)				

	MD			p value
ROCF Copy	0.53	-0.61	1.68	*0.359*
ROCF Delayed	0.21	-0.58	1.00	*0.596*
Pb Non-bioaccessible (>0.37 vs ≤0.37 ng/m³)				
ROCF Copy	-0.21	-1.35	0.93	*0.719*
ROCF Delayed	0.12	-0.65	0.89	*0.759*
Pb Total (Bio+Non-bio) (>6.56 vs ≤6.56 ng/m³)				
ROCF Copy	0.67	-0.49	1.82	*0.255*
ROCF Delayed	0.26	-0.53	1.05	*0.516*
Mn Bioaccessible (>17.05 vs ≤17.05 ng/m³)				
ROCF Copy	-0.67	-1.81	0.47	*0.244*
ROCF Delayed	-0.80	-1.57	-0.04	*0.040*
Mn Non-bioaccessible (>5.80 vs ≤5.80 ng/m³)				
ROCF Copy	-0.22	-1.32	0.88	*0.692*
ROCF Delayed	-1.38	-2.08	-0.67	*<0.001*
Mn Total (Bio+Non-bio) (>25.00 vs ≤25.00 ng/m³)				
ROCF Copy	-0.88	-2.03	0.26	*0.130*
ROCF Delayed	-0.73	-1.51	0.05	*0.065*

MD= Mean Difference adjusted for age, sex, educational level, and Pb or Mn levels respectively. PEM=Personal Environmental Monitor.*A negative MD indicates worse cognitive function (lower standardized NEURONORMA scores) among exposed to Pb or Mn higher levels. Statistically significant MDs are in bold.

Table S5. Mean differences for Grooved Pegboardtest (seconds) according to Pb and Mn levels in biomarkers and PM personal sampling, in dominant and non-dominant hands.

	MD*	**95%**	**CI**	*p value*
Biomarkers				
Pb Blood (>9.14 vs ≤9.14 µg/L)				
dom hand	0.78	-2.15	3.71	*0.600*
non-dom hand	-0.86	-4.46	2.74	*0.639*
Pb Scalp hair (>149.04 vs ≤149.04 ng/g)				
dom hand	0.01	-2.77	2.79	*0.993*
non-dom hand	-0.44	-3.86	2.97	*0.798*
Pb Fingernails (96.04> vs ≤96.04 ng/g)				
dom hand	0.32	-2.64	3.29	*0.828*
non-dom hand	1.64	-2.06	5.35	*0.381*
Mn Blood (>9.58 vs ≤9.58 µg/L)				
dom hand	-2.82	-5.46	-0.19	*0.036*
non-dom hand	-2.56	-5.81	0.70	*0.123*
Mn Scalp hair (>185.31 vs ≤185.31 ng/g)				
dom hand	0.35	-2.47	3.17	*0.806*
non-dom hand	-1.18	-4.66	2.29	*0.501*
Mn Fingernails (>555.28 vs ≤555.28 ng/g)				
dom hand	0.97	-1.96	3.89	*0.514*
non-dom hand	1.29	-2.45	5.02	*0.495*
PEM Fine fraction (PM$_{2.5}$)				
Pb Bioaccessible (>5.25 vs ≤5.25 ng/m³)				
dom hand	1.34	-1.52	4.20	*0.356*
non-dom hand	0.81	-2.71	4.33	*0.650*
Pb Non-bioaccessible (>0.37 vs ≤0.37 ng/m³)				
dom hand	-1.34	-4.11	1.43	*0.341*
non-dom hand	-1.05	-4.48	2.39	*0.548*

Pb Total (Bio+Non-bio) (>6.56 vs ≤6.56 ng/m³)

	MD	95%	CI	p value
dom hand	0.67	-2.20	3.55	*0.645*
non-dom hand	0.36	-3.17	3.89	*0.841*

Mn Bioaccessible (>17.05 vs ≤17.05 ng/m³)

dom hand	3.36	0.60	6.11	*0.018*
non-dom hand	3.13	-0.28	6.54	*0.072*

Mn Non-bioaccessible (>5.80 vs ≤5.80 ng/m³)

dom hand	1.72	-0.97	4.41	*0.208*
non-dom hand	0.37	-2.95	3.70	*0.825*

Mn Total (Bio+Non-bio) (>25.00 vs ≤25.00 ng/m³)

dom hand	2.39	-0.43	5.21	*0.096*
non-dom hand	2.38	-1.09	5.85	*0.178*

MD= Mean difference adjusted for age, sex, educational level, and Pb or Mn levels respectively. Dom= dominant. Non-dom= non-dominant. PEM=Personal Environmental Monitor. *A positive MD indicates worse motor function (higher time to complete the test) among exposed to higher Pb or Mn levels. Statistically significant MDs are in bold.

Table S6. Mean differences for Finger Tapping Test (FTT) (number of taps in 10 seconds) according to Pb and Mn levels in biomarkers and PM personal sampling, in dominant and non-dominant hands.

	MD*	95%	CI	*p value*
Biomarkers				
Pb Blood (>9.14 vs ≤9.14 µg/L)				
dom hand	-1.71	-5.88	2.47	*0.420*
non-dom hand	0.18	-4.17	4.54	*0.934*
Pb Scalp hair (>149.04 vs ≤149.04 ng/g)				
dom hand	0.02	-3.84	3.87	*0.994*
non-dom hand	0.87	-3.11	4.85	*0.666*
Pb Fingernails (96.04> vs ≤96.04 ng/g)				
dom hand	0.28	-4.42	4.97	*0.908*
non-dom hand	-1.12	-6.06	3.83	*0.656*
Mn Blood (>9.58 vs ≤9.58 µg/L)				
dom hand	1.58	-2.25	5.41	*0.416*
non-dom hand	2.20	-1.78	6.19	*0.275*
Mn Scalp hair (>185.31 vs ≤185.31 ng/g)				
dom hand	2.58	-1.36	6.51	*0.197*
non-dom hand	2.01	-2.02	6.05	*0.325*
Mn Fingernails (>555.28 vs ≤555.28 ng/g)				
dom hand	-2.82	-7.48	1.84	*0.232*
non-dom hand	-2.45	-7.36	2.46	*0.324*
PEM Fine fraction (PM2.5)				
Pb Bioaccessible (>5.25 vs ≤5.25 ng/m³)				
dom hand	-1.09	-5.20	3.02	*0.602*
non-dom hand	-0.12	-4.35	4.11	*0.955*
Pb Non-bioaccessible (>0.37 vs ≤0.37 ng/m³)				
dom hand	0.26	-3.77	4.29	*0.899*
non-dom hand	1.61	-2.56	5.77	*0.447*
Pb Total (Bio+Non-bio) (>6.56 vs ≤6.56 ng/m³)				
dom hand	-0.69	-4.81	3.44	*0.742*
non-dom hand	0.26	-3.99	4.52	*0.903*
Mn Bioaccessible (>17.05 vs ≤17.05 ng/m³)				
dom hand	0.19	-3.85	4.23	*0.925*

non-dom hand	-1.87	-6.04	2.31	*0.378*
Mn Non-bioaccessible (>5.80 vs ≤5.80 ng/m³)				
dom hand	0.28	-3.62	4.17	*0.888*
non-dom hand	1.30	-2.74	5.33	*0.526*
Mn Total (Bio+Non-bio) (>25.00 vs ≤25.00 ng/m³)				
dom hand	0.73	-3.36	4.81	*0.726*
non-dom hand	-0.80	-5.04	3.43	*0.708*

MD= Mean difference adjusted for age, sex, educational level, and Pb or Mn levels respectively. PEM=Personal Environmental Monitor. *A negative MD indicates worse motor function (lower number of taps in 10 seconds) among exposed to higher Pb or Mn levels. Statistically significant MDs are in bold.

Reference

1. U.S. Department of Health and Human Services; Centers for Disease Control and Prevention. In *National Center for Environmental Health. Division of Laboratory Sciences. Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables*; *National Center for Environmental Health. U.S.* 2019; Volume 1.