Supplemental Material: PON1 and Neurodevelopment in Children from the CHAMACOS Study Exposed to Organophosphate Pesticides *in Utero*

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Supplemental Table 1. Mean and standard deviation (SD) of arylesterase and paraoxonase substrate-specific enzymatic activity in cord (n=266) and child's blood at age 2 years by children's *PON1*$_{-108}$ and *PON1*$_{192}$ genotypes. CHAMACOS Study, Salinas Valley, CA, 2000-2003.

Child Genotype	N (%) with cord enzyme	Cord Arylesterase Mean (SD)	Cord Paraoxonase Mean (SD)	N (%) with 2-year enzyme	2-year Arylesterase Mean (SD)	2-year Paraoxonase Mean (SD)
***PON1*$_{-108}$**						
CC	81 (31.0)	42.9 (13.6)[ab]	344.1 (178.6)[ab]	73 (29.8)	98.7 (27.4)[ab]	820.9 (429.1)[ab]
CT	127 (48.7)	31.6 (13.2)[a]	231.0 (133.9)[a]	121 (49.4)	83.2 (22.4)[a]	658.0 (346.5)[ac]
TT	53 (20.3)	27.3 (23.1)[b]	173.6 (150.3)[b]	51 (20.8)	79.6 (22.1)[b]	445.3 (282.0)[bc]
Total	*261 (100.0)*	*34.3 (16.9)****	*254.4 (164.7)****	*245 (100.0)*	87.1 (25.1)***	662.2 (383.5)***
***PON1*$_{192}$**						
RR	61 (22.9)	36.5 (12.4)	411.3 (156.8)[ab]	56 (22.7)	84.1 (22.7)	1099.3 (334.5)[ab]
QR	142 (53.4)	34.2 (18.9)	257.4 (126.9)[ac]	128 (51.8)	85.2 (25.9)	672.1 (237.2)[ac]
QQ	63 (22.9)	31.3 (15.3)	95.3 (76.7)[bc]	63 (25.5)	93.0 (25.2)	249.0 (147.2)[bc]
Total	*266 (100.0)*	*34.0 (16.8)*	*254.3 (165.0)****	*247 (100.0)*	86.9(25.2)*	661.1 (383.2)***

Difference between groups (ANOVA):
*p<0.10
** p<0.05
*** p<0.01;
Post-hoc Scheffe test differences (p<0.05) indicated by matching letters a, b, c

Supplemental Table 2. Mean and standard deviation (SD) of arylesterase and paraoxonase substrate-specific enzymatic activity in *maternal* blood (n=299) during pregnancy by maternal *PON1*$_{-108}$ and *PON1*$_{192}$ genotypes. CHAMACOS Study, Salinas Valley, CA, 2000-2003.

Maternal Genotype	N (%) with genotype	N (%) with enzyme	Arylesterase Mean (SD)	Paraoxonase Mean (SD)
***PON1*$_{-108}$**				
CC	97 (27.3)	84 (28.3)	148.8 (45.9)[ab]	1359.4 (703.5)[ab]
CT	173 (48.6)	137 (46.1)	130.0 (36.5)[a]	884.3 (470.2)[ac]
TT	86 (24.2)	76 (25.6)	119.7 (32.0)[b]	681.3 (459.0)[bc]
Total	*356 (100.0)*	*297 (100.0)*	*132.7 (39.8)****	*966.7 (601.3)****
***PON1*$_{192}$**				
RR	96 (26.9)	80 (26.8)	127.5 (37.6)	1654.3 (520.2)[ab]
QR	164 (45.9)	134 (44.8)	130.3 (36.6)	955.4 (303.0)[ac]
QQ	97 (27.2)	85 (28.4)	141.6 (45.8)	322.1 (118.2)[bc]
Total	*357 (100.0)*	*299 (100.0)*	*132.7 (39.9)***	*962.4 (601.8)****

Difference between groups (ANOVA):

** P<0.05

***p<0.01

Post-hoc Scheffe test differences (p<0.05) signified by matching letters a, b, c

Supplemental Table 3. Adjusted relationship of *maternal* PON1 genotype and Bayley Scales of Infant Development II Mental Development Index (MDI) and Psychomotor Development Index (PDI) and maternal report of pervasive developmental disorder (PDD) problems on the Child Behavior Checklist (CBCL) at age 2 years (CHAMACOS Study, Salinas Valley, CA, 2000-2003).

Maternal Genotype	**n**[b]	**Bayley MDI β (95% CI)**	***p-value trend***	**Bayley PDI β (95% CI)**	***p-value trend***	**CBCL PDD OR (95% CI)**	***p-value trend***
PON1$_{-108}$							
CC	353	Ref	*0.02*	Ref	*0.29*	Ref	*0.25*
CT		-1.3 (-4.1, 1.6)		-2.2 (-4.7, 0.3)*		1.0 (0.4, 2.3)	
TT		-3.8 (-7.1, -0.6)**		-1.5 (-4.4, 1.4)		1.6 (0.7, 3.9)	
PON1$_{192}$							
RR	354	Ref	*0.87*	Ref	*0.72*	Ref	*0.27*
QR		-1.3 (-4.2, 1.6)		-1.4 (-4.0, 1.2)		0.9 (0.4, 2.0)	
QQ		0.2 (-3.0, 3.5)		-0.5 (-3.4, 2.3)		1.6 (0.7, 3.7)	

[a]Adjusted for prenatal DAPs and age at assessment, sex, parity, breastfeeding duration, HOME score, maternal PPVT, and household poverty status (U.S. Bureau of the Census 2000). Bayley MDI and PDI models also included psychometrician and testing location; PDD models also included maternal depression.
[b]N's may vary slightly depending on the model.
* $p<0.10$
** $p<0.05$
*** $p<0.01$

Supplemental Table 4. Adjusted[a] relationship of prenatal urinary DAP concentrations and neurodevelopmental outcomes at age 2 years, stratified by *maternal* $PON1_{-108}$ and $PON1_{192}$ genotype. CHAMACOS Study, Salinas Valley, CA, 2000-2003.

Total DAPs	**N**	**Bayley MDI β (95% CI)**	***interaction p-value[b]***	**Bayley PDI β (95% CI)**	***interaction p-value[b]***	**CBCL PDD OR (95% CI**	***interaction p-value[b]***
$PON1_{-108}$ **CC**	97	-5.2 (-12.4, 2.1)	*0.52*	1.0 (-5.1, 7.0)	*0.51*	20.4 (1.0, 422.3)*	*0.51*
CT	171	-2.1 (-6.6, 2.3)		-0.7 (-4.5, 3.1)		2.6 (0.7, 9.5)	
TT	85	-5.7 (-12.2, 0.8)*		-2.6 (-9.0, 3.9)		1.4 (0.2, 8.3)	
$PON1_{192}$ **RR**	95	-3.2 (-11.7, 5.3)	*0.63*	-0.3 (-7.1, 6.6)	*0.98*	1.7 (0.2, 19.3)	*0.60*
QR	163	-3.4 (-8.1, 1.3)		-0.7 (-5.1, 3.7)		1.2 (0.3, 5.4)	
QQ	96	-4.8 (-10.0, 0.5)*		-1.4 (-6.6, 3.7)		4.2 (0.9, 19.2)*	
Dimethyl DAPs							
$PON1_{-108}$ **CC**	97	-4.7 (-11.0, 1.6)	*0.71*	0.8 (-4.5, 6.1)	*0.54*	12.9 (1.0, 161.3)**	*0.43*
CT	172	-2.8 (-6.7, 1.1)		-1.0 (-4.5, 2.4)		2.5 (0.8, 7.6)	
TT	85	-5.1 (-10.9, 0.8)*		-1.7 (-7.5, 4.0)		1.4 (0.3, 6.9)	
$PON1_{192}$ **RR**	96	-4.1 (-11.0, 2.8)	*0.67*	-1.2 (-6.8, 4.4)	*0.88*	1.6 (0.2, 10.7)	*0.88*
QR	163	-3.3 (-7.6, 1.0)		-0.3 (-4.3, 3.6)		1.4 (0.4, 5.3)	
QQ	96	-4.8 (-9.7, 0.2)*		-0.9 (-5.8, 3.9)		4.0 (1.0, 16.3)*	
Diethyl DAPs							
$PON1_{-108}$ **CC**	97	-1.1 (-8.7, 6.5)	*0.79*	2.8 (-3.5, 9.0)	*0.49*	4.8 (0.3, 69.4)	*0.59*
CT	171	-0.2 (-4.9, 4.5)		-0.9 (-4.9, 3.1)		0.8 (0.2, 2.7)	
TT	85	-2.6 (-9.3, 4.1)		-3.3 (-9.8, 3.1)		0.4 (0.1, 2.8)	
$PON1_{192}$ **RR**	95	1.4 (-6.8, 9.5)	*0.17*	0.6 (-6.0, 7.2)	*0.15*	0.2 (0.0, 2.2)	*0.73*
QR	163	0.1 (-4.8, 5.1)		0.7 (-3.8, 5.2)		0.7 (0.1, 3.0)	
QQ	96	-4.5 (-10.2, 1.3)		-5.1 (-10.5, 0.4)*		1.6 (0.3, 7.6)	

[a]Adjusted for age at assessment, sex, parity, breastfeeding duration, HOME score, maternal PPVT, and household poverty status (U.S. Bureau of the Census 2000). Bayley MDI and PDI models also included psychometrician and testing location; PDD models also included maternal depression.

[b]Interaction p-value was calculated using a post-estimation combined F-test (or chi-square test) for the two interaction variables between genotype and DAPs (e.g., 192_{QR}*DAP and 192_{QQ}*DAP). Conclusions regarding interaction were similar if a single interaction term with the number of C or Q alleles (0, 1, 2) was used instead.

* $p<0.10$

** $p<0.05$

*** $P<0.01$

Supplemental Table 5. Adjusted[a] relationship of prenatal urinary DAP concentrations and neurodevelopmental outcomes at age 2 years, stratified by tertile of PON1 enzyme activity in *cord* blood. CHAMACOS Study, Salinas Valley, CA, 2000-2003.

	Tertile	n[b]	Bayley MDI β (95% CI)	*p-value* interaction	Bayley PDI β (95% CI)	*p-value* interaction	CBCL PDD OR (95% CI)	*p-value* interaction
ARYase (cord)								
Total DAPs	**1**	89	-5.4 (-11.9, 1.1)	*0.89*	-2.4 (- 8.3, 3.4)	*0.46*	3.7 (0.5, 30.8)	*0.48*
	2	88	-4.3 (-11.6, 3.0)		-1.8 (- 8.3, 4.6)		2.5 (0.3, 25.0)	
	3	88	-1.2 (- 8.7, 6.4)		1.2 (- 5.7, 8.1)		1.8 (0.3, 11.8)	
Dimethyls	**1**	89	-5.4 (-11.4, 0.5)*	*0.72*	-1.1 (- 6.5, 4.3)	*0.41*	3.1 (0.5, 20.2)	*0.43*
	2	88	-4.5 (-11.2, 2.3)		-3.2 (- 9.2, 2.8)		2.8 (0.3, 24.3)	
	3	88	-0.5 (- 7.0, 6.1)		1.7 (- 4.3, 7.7)		2.0 (0.4, 11.4)	
Diethyls	**1**	89	-3.2 (- 9.7, 3.3)	*0.23*	-5.0 (-10.7, 0.7)*	*0.42*	1.7 (0.3, 11.4)	*0.24*
	2	88	0.2 (- 6.8, 7.2)		1.6 (- 4.5, 7.8)		1.3 (0.2, 10.6)	
	3	88	2.7 (- 5.2, 10.5)		1.6 (- 5.6, 8.8)		0.9 (0.1, 8.2)	
POase (cord)								
Total DAPs	**1**	91	-6.6 (-12.9, -0.2)**	*0.72*	-4.7 (-10.6, 1.3)	*0.69*	13.2 (1.4, 128.3)**	*0.88*
	2	85	-1.0 (- 7.9, 5.9)		0.0 (- 6.6, 6.7)		0.4 (0.0, 3.9)	
	3	87	-5.8 (-13.9, 2.2)		1.5 (- 5.4, 8.4)		4.7 (0.5, 41.6)	
Dimethyls	**1**	91	-6.7 (-12.6, -0.8)**	*0.97*	-4.1 (- 9.6, 1.4)	*0.59*	7.3 (0.9, 56.9)*	*0.90*
	2	85	-0.9 (- 7.2, 5.4)		0.4 (- 5.7, 6.5)		0.8 (0.1, 6.2)	
	3	87	-4.2 (-11.2, 2.9)		1.4 (- 4.6, 7.4)		4.5 (0.7, 30.4)	
Diethyls	**1**	91	-3.0 (-10.0, 3.9)	*0.68*	-4.7 (-11.1, 1.6)	*0.35*	7.0 (0.8, 58.0)*	*0.15*
	2	85	-1.7 (- 7.8, 4.5)		-2.5 (- 8.3, 3.4)		0.4 (0.1, 3.1)	
	3	87	-0.5 (- 8.5, 7.6)		3.7 (- 3.1, 10.5)		0.7 (0.1, 6.6)	

[a]Adjusted for prenatal DAPs and age at assessment, sex, parity, breastfeeding duration, HOME score, maternal PPVT, and household poverty status (U.S. Bureau of the Census 2000). Bayley MDI and PDI models also included psychometrician and testing location; PDD models also included maternal depression.

[b]N's may vary slightly depending on the model.

* p<0.10

** p<0.05

*** P<0.01

Supplemental Table 6. Adjusted[a] relationship of prenatal urinary DAP concentrations and neurodevelopmental outcomes at age 2 years, stratified by tertile of *maternal* PON1 enzyme activity. CHAMACOS Study, Salinas Valley, CA, 2000-2003.

	Tertile	n[b]	Bayley MDI β (95% CI)	*p-value interaction*	Bayley PDI β (95% CI)	*p-value interaction*	CBCL PDD OR (95% CI)	*p-value interaction*
ARYase (maternal)								
Total DAPs	**1**	102	-5.6 (-11.9, 0.7)*	*0.49*	-5.3 (-11.0, 0.4)*	*0.27*	1.6 (0.3, 7.4)	*0.70*
	2	101	-1.3 (- 6.9, 4.2)		1.4 (- 3.5, 6.3)		1.5 (0.3, 7.6)	
	3	99	-6.7 (-13.0, -0.4)**		1.3 (- 4.4, 7.0)		4.4 (0.5, 37.1)	
Dimethyls	**1**	102	-3.9 (- 9.7, 1.8)	*0.21*	-3.9 (-9.1, 1.4)	*0.35*	1.4 (0.3, 5.6)	*0.63*
	2	101	-0.5 (- 5.5, 4.6)		1.1 (-3.3, 5.5)		1.8 (0.4, 7.3)	
	3	99	-8.2 (-13.8, -2.6)***		0.8 (-4.4, 6.1)		4.5 (0.6, 33.5)	
Diethyls	**1**	102	-3.8 (-10.3, 2.6)	*0.46*	-3.7 (-9.5, 2.1)	*0.76*	1.0 (0.2, 4.4)	*0.46*
	2	101	-2.0 (- 7.7, 3.7)		1.2 (-3.8, 6.2)		0.3 (0.0, 2.3)	
	3	99	1.6 (- 4.9, 8.1)		-0.1 (-5.9, 5.7)		1.5 (0.1, 14.8)	
POase (maternal)								
Total DAPs	**1**	102	-6.0 (-11.2, -0.9)**	*0.87*	-2.1 (-6.8, 2.7)	*0.42*	2.5 (0.7, 8.8)	*0.68*
	2	101	-1.7 (- 7.9, 4.4)		0.9 (-5.0, 6.8)		1.6 (0.2, 11.5)	
	3	99	-5.4 (-13.9, 3.1)		-1.1 (-8.1, 5.9)		4.7 (0.3, 74.0)	
Dimethyls	**1**	102	-5.8 (-10.6, -1.0)**	*0.98*	-1.5 (-6.0, 2.9)	*0.62*	2.4 (0.7, 8.0)	*0.62*
	2	101	-1.3 (- 6.9, 4.4)		1.3 (-4.2, 6.7)		2.0 (0.3, 11.8)	
	3	99	-5.8 (-13.1, 1.4)		-1.1 (-7.3, 5.0)		4.7 (0.4, 63.7)	
Diethyls	**1**	102	-4.4 (-10.1, 1.3)	*0.23*	-4.3 (-9.4, 0.9)	*0.10*	0.9 (0.2, 4.0)	*0.84*
	2	101	-0.2 (- 6.3, 5.9)		0.6 (-5.2, 6.4)		0.5 (0.1, 3.5)	
	3	99	2.0 (- 5.8, 9.8)		1.7 (-4.8, 8.2)		1.2 (0.1, 11.4)	

[a]Adjusted for prenatal DAPs and age at assessment, sex, parity, breastfeeding duration, HOME score, maternal PPVT, and household poverty status. Bayley MDI and PDI models also included psychometrician and testing location; PDD models also included maternal depression.

[b]N's may vary slightly depending on the model.

* $p<0.10$

** $p<0.05$

*** $P<0.01$