Supplemental Material

Neurocognitive and physical functioning in the Seveso Women's Health Study

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Supplementary Table 1 – Multivariable linear regression analyses for the relationship of categorized serum TCDD (ppt) with measures of physical functioning, Seveso Women's Health Study, Italy, 1996-2008. Cutpoints based on quartiles in full SWHS cohort.

Physical Functioning

TCDD exposure level (ppt, lipid-adjusted)	Time to flip 5 coins (sec) (n=152)		Walking speed (ft/sec) (n=148)		Reach down test time (sec) (n=151)		Grip strength dominant hand (kg) (n=98)		Grip strength non-dominant hand (kg) (n=98)	
	Adj.β[a]	95% CI	Adj.β[a]	95% CI	Adj.β[a]	95% CI	Adj.β[a]	95% CI	Adj.β[a]	95% CI
3.1 – 20.0	ref		ref		ref		ref		ref	
20.1 – 47.0	-1.44*	(-2.56, -0.32)	-0.00	(-0.23, 0.22)	-0.15	(-0.63, 0.34)	1.83	(-1.80, 5.46)	3.39	(-1.01, 7.78)
47.1 – 135.0	-0.56	(-1.97, 0.86)	-0.06	(-0.29, 0.17)	-0.27	(-0.76, 0.23)	3.58*	(-0.20, 7.37)	5.42*	(0.83, 10.02)
>135	-0.10	(-1.62, 1.43)	0.02	(-0.25, 0.28)	0.04	(-0.61, 0.69)	1.01	(-3.39, 5.40)	1.92	(-2.85, 6.69)
Test for trend	p=0.39		p=0.87		p=0.96		p=0.56		p=0.49	

[a]Adjusted for age at interview, primary wage earner education in 1996, BMI in 1996

* p<0.05

Supplementary Table 2 – Multivariable linear regression analyses for the relationship of serum TCDD (log10) with measures of working memory span, stratified by exposure before peak brain development (age 25), Seveso Women's Health Study, Italy, 2008–2009.

Measurement	All women (n=457)		<25 years old in 1976 (n=299)		25+ years old in 1976 (n=158)		
	Adj.β[a]	95% CI	Adj.β[a]	95% CI	Adj.β[a]	95% CI	P_{int}
Digit Span							
Forward	0.18	(-0.09, 0.45)	0.24	(-0.10, 0.57)	0.31	(-0.18, 0.81)	0.78
Backward	0.06	(-0.22, 0.34)	0.14	(-0.21, 0.49)	-0.03	(-0.18, 0.82)	0.60
Spatial Span							
Forward	0.05	(-0.21, 0.31)	0.22	(-0.10, 0.53)	-0.19	(-0.69, 0.31)	0.23
Backward	-0.03	(-0.30, 0.24)	0.11	(-0.23, 0.44)	-0.17	(-0.68, 0.34)	0.58

[a]Models adjusted for age at interview, primary wage earner education in 2008

Supplementary Table 3 – Multivariable linear regression analyses for the relationship of serum TCDD (log10) with measures of working memory span, stratified by menopause status in 2008, Seveso Women's Health Study, Italy, 2008–2009.

Measurement	All women (n=457)		Premenopause (n=216)		Postmenopause (n=241)		P_{int}
	Adj.β[a]	95% CI	Adj.β[a]	95% CI	Adj.β[a]	95% CI	
Digit Span							
Forward	0.18	(-0.09, 0.45)	0.22	(-0.19, 0.62)	0.28	(-0.13, 0.68)	0.45
Backward	0.06	(-0.22, 0.34)	0.03	(-0.41, 0.46)	0.12	(-0.29, 0.52)	0.57
Spatial Span							
Forward	0.05	(-0.21, 0.31)	0.27	(-0.10, 0.65)	-0.02	(-0.41, 0.36)	0.56
Backward	-0.03	(-0.30, 0.24)	0.07	(-0.38, 0.52)	0.01	(-0.37, 0.39)	0.58

[a]Models adjusted for age at interview, primary wage earner education in 2008

Supplementary Table 4 – Targeted Maximum Likelihood Regression (tmle) regression analyses for the relationship of quartiles of serum TCDD (ppt) with measures of working memory span among women who completed the neuro-assessment in 2008, Seveso Women's Health Study, Italy, 2008–2009.

| TCDD exposure level | Digit span | | | | Spatial Span | | | |
| | Forward | | Backward | | Forward | | Backward | |
(ppt, lipid-adjusted)	Adj.β[a]	95% CI	Adj.β[a]	95% CI	Adj.β[a]	95% CI	Adj.β[a]	95% CI
3.1 – 20.0	ref		ref		ref		ref	
20.1 – 47.0	-0.06	(-0.85, 0.78)	-0.53	(-1.48, 0.28)	0.29	(-0.45, 1.05)	-0.22	(-1.13, 0.63)
47.1 – 135.0	0.42	(-0.33, 1.52)	-0.22	(-0.85, 0.78)	0.01	(-0.64, 0.78)	0.14	(-0.88, 1.24)
>135	0.54	(-0.21, 1.29)	-0.21	(-0.45, 1.05)	0.32	(-0.38, 1.21)	-0.23	(-1.19, 0.66)

[a]Models adjusted for age at interview, primary wage earner education in 2008