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Circulating Urine Phthalates Are not Associated with a Decline in Cognition in Adults and the Elderly: NHANES, 1999–2002

Ivy Shiue^{a,b}, John Starr^a

^aCentre of Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, UK; ^bThe William A. & Barbara R. Owens Institute for Behavioral Research, University of Georgia, Athens, Ga., USA

Some chemical pollutants may act as hormone mimics and thus affect the central nervous system [1]. A number of environmental pollutants have been shown to disrupt endocrine function in animals, leading to long-lasting cognitive deficits in primates [2], and are likely to reprogramme (neuro)physiological set-points and to increase susceptibility to disease later in life [3]. Phthalates, a chemical estrogen widely used in the food-packaging industry [4], leach from the polymers into food and water under normal conditions and can be detected in human urine. Animal studies have shown that chronic exposure to these, even at low doses, can alter some biological end points [5, 6]. A study in children suggests that some phthalates are detrimental to cognition development [7]. However, the effects on adults are undetermined. In this context, we aimed to study the associations of urine phthalate concentrations and cognitive function in adults ≥ 60 years old.

Methods

As described elsewhere [8], the US National Health and Nutrition Examination Surveys is a population-based multi-year cross-sectional study. Assessments on both urine phthalate concentrations and cognitive function were only available between 1999 and 2002. Information on demographics and cognitive function (using Digit Symbol Substitution test, DSS; range 0–133) [9] was obtained by household interview and people were selected (still representative) from whom urine was collected in order to measure phthalate volumes (using online solid-phase extraction, isotope dilution and high-performance liquid chromatography separation, followed by electrospray ionization and tandem mass spectrometry) [10].

The effects of circulating phthalates on cognitive function were examined by a Student *t* test and a generalized linear model, with $p < 0.05$ considered statistically significant. We adjusted first for age, sex and urine creatinine (model A) and then also for education (model B). STATA statistical software version 12.0 (STATA, College Station, Tex., USA) was used to perform all the analyses.

Results

Cognitive data was available on 1,834 subjects for the period 1999–2000 and on 1,872 for 2001–2002. After combining these with the available data on urine phthalate concentrations, the analytic sample was 462 subjects for 2001–2002 and 412 for 1999–2000. The mean DSS scores for these 2 cohorts were 42.19 ± 18.20 (range 0–100) and 39.27 ± 19.15 (range 0–117), respectively. Table 1 presents the association of each urine phthalate concentration and DSS score. There were no clear associations between urine phthalate concentrations and DSS scores after full adjustments, although a high mono-benzyl phthalate concentration was shown once to be significantly associated with a low DSS score in the crude model (Beta -0.088 ; 95% CI -0.158 to -0.018 ; $p = 0.014$) and in model A (Beta -0.097 ; 95% CI -0.174 to -0.019 ; $p = 0.014$) before education was adjusted in model B as well. The other two positive effects also disappeared after full adjustments.

Discussion

In this study, we found no evidence that urine phthalates are associated with cognitive impairment in adults over 60 years of age. A strength of this study is that it comprises a large sample from a national setting. A weakness is that only one cognitive function test was administered: future research is required to test other cognitive domains such as episodic memory. Future studies could also include other environmental chemicals that might potentially disrupt endogenous estrogen, androgen and thyroid function and so influence brain plasticity.

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Table 1. Effects of circulating urine phthalates on cognitive function

	Crude	Model A		Model B	
		beta (95% CI)	p value	beta (95% CI)	p value
NHANES, 2001–2002 (n = 462) mean ± SD, ng/ml					
Mono-n-butyl phthalate	36.97 ± 206.03	–0.001 (–0.009–0.007)	0.823	–0.0001 (–0.008–0.008)	0.986
Mono-cyclohexyl phthalate	0.54 ± 0.44	2.998 (–0.799–6.795)	0.122	3.26 (–0.457–6.976)	0.086
Mono-ethyl phthalate	498.63 ± 1443.81	–0.001 (–0.002–0.0001)	0.078	–0.001 (–0.002–0.0002)	0.109
Mono-(2-ethyl)-hexyl phthalate	7.51 ± 16.51	0.016 (–0.088–0.121)	0.762	0.008 (–0.092–0.109)	0.869
Mono-isononyl phthalate	0.98 ± 1.35	–1.070 (–2.322–0.182)	0.094	–0.789 (–1.990–0.412)	0.198
Mono-n-octyl phthalate	1.23 ± 0.34	–0.274 (–5.235–4.686)	0.914	0.297 (–4.449–5.042)	0.902
Mono-benzyl phthalate	15.18 ± 25.66	–0.088 (–0.158–0.018)	0.014	–0.097 (–0.174–0.019)	0.014
Mono-n-methyl phthalate	6.56 ± 45.23	0.023 (–0.015–0.060)	0.235	0.019 (–0.016–0.055)	0.288
Mono-(3-carboxypropyl) phthalate	4.47 ± 12.25	–0.018 (–0.157–0.121)	0.796	0.019 (–0.016–0.153)	0.783
Mono-(2-ethyl-5-hydroxyhexyl) phthalate	39.62 ± 147.82	0.012 (0.001–0.029)	0.041	0.010 (–0.001–0.022)	0.069
Mono-(2-ethyl-5-oxohexyl) phthalate	25.32 ± 82.81	0.026 (0.005–0.047)	0.015	0.022 (0.002–0.042)	0.033
Mono-isobutyl phthalate	4.08 ± 10.89	–0.092 (–0.251–0.067)	0.257	–0.142 (–0.294–0.010)	0.067
NHANES, 1999–2000 (n = 412) mean ± SD, ng/ml					
Mono-n-butyl phthalate	41.24 ± 80.15	–0.011 (–0.035–0.014)	0.404	–0.015 (–0.039–0.009)	0.218
Mono-cyclohexyl phthalate	1.73 ± 3.12	–0.130 (–0.735–0.474)	0.672	0.019 (–0.571–0.608)	0.950
Mono-ethyl phthalate	448.24 ± 1,162.69	–0.0003 (–0.002–0.001)	0.688	–0.0005 (–0.002–0.001)	0.542
Mono-(2-ethyl)-hexyl phthalate	3.71 ± 5.22	–0.078 (–0.460–0.303)	0.687	–0.165 (–0.540–0.210)	0.389
Mono-isononyl phthalate	1.54 ± 4.22	0.319 (–0.118–0.757)	0.153	0.541 (–0.032–1.114)	0.064
Mono-n-octyl phthalate	1.98 ± 5.35	0.150 (–0.198–0.497)	0.399	0.130 (–0.212–0.472)	0.457
Mono-benzyl phthalate	14.70 ± 25.19	0.038 (–0.040–0.116)	0.335	0.028 (–0.048–0.103)	0.477

Adjusted for creatinine in the crude model; for creatinine, age at examination, sex and education in model B.

Adjusted for creatinine in the crude model; for creatinine, age at examination and sex in model A, and for creatinine, age at examination, sex and education in model B.

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