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Fish consumption, mercury exposure, and their associations with scholastic achievement in the Seychelles Child Development Study☆

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ABSTRACT

Studies of neurodevelopmental outcomes in offspring exposed to MeHg from maternal consumption of fish have primarily measured cognitive abilities. Reported associations have been subtle and in both adverse and beneficial directions. Changes in functional outcomes such as school achievement and behavior in exposed children and adolescents have not been examined. We undertook an assessment of school success of children in the Seychelles Child Development Study (SCDS) main cohort to determine if there were any associations with either prenatal or recent postnatal MeHg exposure. The primary endpoints were Seychelles nationally standardized end-of-year examinations given when the cohort children were 9 and 17 years of age. A subgroup (n = 215) from the main cohort was also examined at 9 years of age using a regional achievement test called SACMEQ. Prenatal MeHg exposure was 6.8 ppm in maternal hair; recent postnatal exposure was 6.09 ppm at 9 years and 8.0 ppm at 17 years, measured in child hair. Multiple linear regression analyses showed no pattern of associations between prenatal or postnatal exposure, and either the 9- or 17-year end-of-year examination scores. For the subgroup of 215 subjects who participated in the SACMEQ test, there were significant adverse associations between examination scores and postnatal exposure, but only for males. The average postnatal exposure level in child hair for this subgroup was significantly higher than for the overall cohort. These results are consistent with our earlier studies and support the interpretation that prenatal MeHg exposure at dosages achieved by mothers consuming a diet high in fish are not associated with adverse educational measures of scholastic achievement. The adverse association of educational measures with postnatal exposure in males is intriguing, but will need to be confirmed by further studies examining factors that influence scholastic achievement.

Methylmercury (MeHg) is a known neurotoxicant present in all fish. Since the discovery that the fetus may be particularly vulnerable (Harada, 1968), there has been concern that exposure to MeHg at levels achieved by mothers who consume a diet high in fish during pregnancy may adversely affect neurodevelopment in the offspring. However the level of prenatal exposure at which adverse effects may be seen has been difficult to identify. A study from Iraq where pregnant women consumed bread baked from MeHg-treated seed grain suggested that exposures around 10 ppm in maternal hair might adversely affect development (Cox et al., 1989). Subsequently, epidemiological studies of populations with exposures from high fish or seafood consumption reported subtle neurodevelopment effects at exposures below 10 ppm (Grandjean et al., 1997; Kjellstrom et al., 1986, 1989). However, a comprehensive epidemiological study of the offspring of pregnant women exposed from consuming a diet high in fish in the Republic of Seychelles found very few associations between prenatal MeHg exposure and the children's development, some were adverse and others beneficial, and there was no consistent pattern (Davidson et al., 1998; Myers et al., 2003). Very little data are available on the developmental consequences of recent postnatal MeHg exposure (Myers et al., 2009). However, a recent study by Cao et al. (2010)

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found that very low postnatal MeHg exposure measured in child blood was not associated with IQ test scores or behavioral measures at 2, 5 and 7 years.

In general, studies of neurodevelopmental outcomes in offspring exposed to MeHg from maternal consumption of fish have primarily measured cognitive abilities. These include effects on memory, language, cognition, and sensorimotor functions. Axelrad et al. (2007) conducted a reanalysis of data from three large longitudinal cohort studies and reported that for every ppm increase of maternal hair MeHg, there was a 0.1-point drop in a measure of IQ. This report was based upon published literature, but one study estimated IQ from an abbreviated version of the Wechsler Intelligence Scale for Children, Third Edition (WISC-III). These results have not been replicated in other cohort studies. This amount of change in IQ, if true, would be associated with a 1-point loss for every 10 ppm of exposure. It is unclear whether such a small change is relevant to functional outcomes such as school achievement and behavior in exposed children. Previous studies, however, have not focused on such functional outcomes as scholastic success.

The Seychelles Child Development Study (SCDS) is a longitudinal cohort study. The main cohort consists of 779 children born to mothers who consumed sufficient fish meals during pregnancy to result in an average prenatal exposure level of 6.8 ppm in maternal hair. This exposure is substantially higher than the average exposure of 1 ppm in hair of women of child-bearing age in the US (Schober et al., 2003). In the present study we assessed school achievement of main cohort children participating in the SCDS and examined their association with prenatal or recent postnatal MeHg exposure.

1. Method

1.1. Setting

The study was conducted in the Republic of Seychelles, an Indian Ocean archipelago with about 85,000 inhabitants of mixed African, European, and East Asian origins. The Seychellois diet is varied but high in fish and fruit (Bonham et al., 2008). Human services and education are free and organizationally similar in to educational systems in western societies. The MeHg concentrations in local fish are similar to those of fish commercially available in the US (Robinson and Schroff, 2004) and sea mammals are not consumed. In all ocean fish, both MeHg and nutrient concentrations vary considerably both within and across species (Bonham et al., 2008; Robinson and Schroff, 2004). Seychellois children attend school from 5.5 years of age until around 16.5 years of age and retention in the schooling system is over 98% (Purvis, 2004). The educational system is based upon western models, and children are tested on nationally standardized achievement tests at regular intervals during primary and secondary school grades.

1.2. Cohort

The study utilized data already collected from the SCDS main cohort. This cohort was recruited in 1989 and is comprised of 779 children. The cohort children have been tested for neurodevelopmental outcomes at 6, 19, and 29 months and again at 5.5, 9, 10.5, and 17 years of age. The numbers of children with complete sets of data for each analysis varied. At age 9 years (Primary 6) they ranged between 437 and 456; at age 16 years (Secondary 3) they ranged from 351 to 384. Differences were due primarily to missing covariates or exclusions. Exclusions have been made for maternal and childhood disorders known to be highly associated with adverse neurodevelopment. The demographic characteristics of the cohort have been reported earlier (Shamlaye et al., 1995).

1.3. Study design

The aim of the current study was to test the hypothesis that scholastic achievement could be predicted by prenatal or recent postnatal MeHg exposure measured in maternal or child hair after adjustment for covariates that could independently affect achievement scores. The primary endpoints were nationally standardized subject-specific end-of-year examinations following completion of Primary 6 in 1998–1999 and Secondary 3 in 2005–2006. We also included a third endpoint consisting of scores on a curriculum-based achievement test administered to Primary 6 students in 2000. This testing was carried out by the Southern and Eastern African Consortium for Monitoring Educational Quality (SACMEQ) project. The SACMEQ Consortium is a group of 15 African and Indian Ocean nations including the Republic of Seychelles that periodically monitors learning and the conditions of primary schools and tests children for educational achievement in Reading Comprehension and Mathematics. There were 215 cohort children who took the SACMEQ tests. All endpoints were collected by the Seychelles Ministry of Education and linked to the SCDS database by an ID numbering scheme. All investigators were blinded as to the subjects' prenatal and recent postnatal MeHg hair levels.

1.4. Analytical methods

Prenatal and recent postnatal exposure at 9 and 17 years were used for the present study. Average maternal hair Hg during pregnancy was used as the bio-marker for prenatal MeHg exposure. Prenatal exposure was assessed by measuring the concentration of total Hg (THg) in the longest segment of maternal hair representing growth during pregnancy as described by Cernichiari et al. (1995a). Postnatal exposure was assessed by measuring the THg concentration in the 1 cm of the child's hair closest to the scalp. Methylmercury accounts for approximately 80% of THg in hair. Maternal hair THg is known to correlate with infant brain Hg levels (Cernichiari et al., 1995b) and is believed to reflect the species of Hg that is transported across the blood–brain barrier (Clarkson and Magos, 2006). Maternal hair THg during pregnancy also correlates well with maternal blood levels of MeHg (for a review, see WHO, 1990). Exposure to 28 congeners of polychlorinated biphenyls (PCBs) ranging from congener 28 to 206 were measured in serum samples from 49 main cohort children when they were 66 months of age. All samples had no detectable levels (Davidson et al., 1998). Lead, levels in 127 blood samples collected randomly from 106 pregnant women and 21 infants in the Seychelles were all below 10 μg/dl and most were below 2 μg/dl (Cernichiari et al., 1995a). Pesticides are used in the Seychelles, but measured levels have been low (Davidson et al., 1999).

1.5. Endpoints

1.5.1. Primary 6 and Secondary 3 end-of-year examinations

The Seychelles Ministry of Education conducts end-of-year comprehensive national examinations in academic subjects taught in its primary and secondary curriculum at the end of grades Primary 6 (since 1984) and Secondary 3 (since 1999). In all other grades, school-based examinations are given. The Primary 6 exam tests competencies in three languages (English, French, and Kreol), Mathematics, Social Studies, and Science. The Secondary 3 examination tests achievement in two languages (English and French), Mathematics, Geography, History, and Science. All examinations at both grades are constructed and graded centrally by a committee of teachers and administrators appointed by the Ministry. Examinations are revised annually. Each examination has at least two sections, one testing technical skills or mechanics (such as Mathematics computation or reading and writing

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comprehension) and others testing subject-specific knowledge and problem-solving. All students at each grade are required to take the examinations.

1.5.2. SACMEQ

The SACMEQ tests were developed and administered in 2000 by a consortium of National Research Coordinators of the participating nations (Botswana, Kenya, Lesotho, Malawi, Mauritius, Mozambique, Namibia, Seychelles, South Africa, Swaziland, Tanzania, Uganda, Zambia, Zanzibar, and Zimbabwe) in consultation with experts in the field of testing and educational survey. Tests were given for Reading Comprehension and Mathematics. The test content was based on analyses of the curricula, syllabi, examinations and textbooks used in SACMEQ countries. Levels of competencies were derived, and aggregated intra-nation scores were transformed to have a mean of 500 and a standard deviation of 100 (see Leste and Davidson, 2004 for a detailed description of SACMEQ).

1.6. Covariates

Covariates were selected *a priori* for their known impact on child development. The child's primary caregiver, defined as the family member with whom the child lived for at least 5 days per week were interviewed (93% of caregivers were the child's biological mother). Primary caregivers were recalled in 1999–2000 and given the Family Resource Scale (FRS) and the Henderson Environmental Learning Profile Scale (HELPS) to measure the quality of stimulation in the current home environment. They also completed the Matrices subtest of the Kaufman Brief Intelligence Test (K-Bit) to determine caregiver intelligence. The Hollingshead four factor socioeconomic score was determined using a list of Seychellois employment codes. We also included as covariates the gender of the child and the region of the Seychelles in which the child attended school (urban, suburban, rural, and off Mahé Island).

A number of measures of children's ability were also included as covariates. These included the WISC-III Full scale IQ, the long delay free recall score from the California Verbal Learning Test (CVLT), the Visual Memory subtest of the Wide Range Assessment of Memory and Learning (WRAML), and the total *T* score from the Child Behavior Checklist (CBCL). All of these scores were collected when the children were examined at 9 years of age by a team of three Seychellois child health and development professionals (a senior nurse, a child psychologist, and a special educator) as described by Myers et al. (2003). Previous reports from the SCDS documented that there were no associations between these measures and either prenatal or postnatal MeHg exposure (Myers et al., 2003). However, each variable may independently influence scholastic achievement which could obscure associations between these endpoints and MeHg exposure.

For the SACMEQ endpoint analyses only, three measures of teacher competence were available and were included as covariates in the analysis. These were collected in 2000 and included the number of years of education, the number of years of teaching experience, and the level of teacher training. These measures were not available for teachers of children who were not included in the SACMEQ cohort.

For the analysis of SACMEQ competency scores, the recent postnatal MeHg exposure measurement used in the analysis was from the 9-year examination of the cohort (Myers et al., 2003). The Primary 6 Mathematics and English Reading Comprehension subtest scores for the SACMEQ cohort were analyzed similarly to assure consistency in the SACMEQ analysis.

We have reported in the past that maternal LCPUFA levels were associated with beneficial outcomes on psychomotor development (Davidson et al., 2008; Strain et al., 2008). Recently published data from three separate randomized controlled trials indicate that children born to mothers who were supplemented with DHA rich LCPUFA scored better in a variety of cognitive tests at 9 months (Judge et al., 2007), 2.5 years (Dunstan et al., 2006) and 4 years (Helland et al., 2003) of age than children born to mothers who received placebo. These experimental studies of supplemental DHA, the $n-3$ LCPUFA plentiful in fish oil, are supported by observational studies in the UK where children of women in the large ALSPAC cohort who consumed more fish during pregnancy had higher developmental scores at age 15 months (Daniels et al., 2004) and at age 7 years (Hibbeln et al., 2007) and in the US where infants born to mothers who consumed more fish in the second trimester had greater cognitive development at 6 months and 3 years of age (Oken et al., 2005, 2008). Higher cognitive scores associated with increased LCPUFA and greater fish consumption rather than lower scores associated with MeHg suggest that negative confounding (e.g., "beneficial" associations) could be occurring. LCPUFA were not measured in this cohort, since it was recruited before the importance of nutrition when studying toxicant exposures was recognized. No adjustment was made maternal or child fish intake since these variables were not accurately collected in this cohort.

1.7. Analysis plan

The analysis was based on linear regression. We first checked for collinearity within the covariates by the variance inflation factors. The analysis included Primary 6 and Secondary 3 total scores. For every endpoint, we did a maximum of three linear regression analyses for prenatal and recent postnatal MeHg levels in hair using all the covariates. All analyses were done with the SAS system, version 9. Because differential effects on males and females have been reported (Davidson et al., 1998), the first model included MeHg by gender interaction terms for both prenatal and recent postnatal MeHg levels in hair. If the overall *F*-test for the model was not significant at a two-tailed significance level of 0.05, the results of that analysis were deemed negative. If the model was significant, we examined the *p*-values of each interaction term. If both interactions were significant then results are reported for this model. If neither interaction was significant, we reran the model without interactions. If only one interaction was significant, we reran the model dropping the non-significant interaction term (thus including only a simple effect), but including the significant interaction term. The Primary 6 and Secondary 3 scores were adjusted for 9- and 17-year recent postnatal exposure respectively.

Every analysis included an assessment of residuals as a check on the assumptions of normally distributed errors with constant variance. For every analysis, we assessed the model for statistical outliers (scores with standardized residual values >3 or <-3). All models with outliers were rerun without the outliers and the results with and without outliers were compared. When there was no difference in significance of MeHg effects, we report the results with outliers.

2. Results

2.1. Methylmercury exposure

The mean prenatal MeHg level in maternal hair for the main cohort was 6.89 ppm (SD = 4.52) and for the 9-year child hair level it was 6.09 ppm (SD = 3.47) (both from Myers et al., 2003). The 17-year child MeHg hair level had a mean of 8.00 ppm (SD = 4.68). We compared the two subgroups, those with and without the SACMEQ scores, using two-sample *t*-tests. The prenatal MeHg levels were similar between the two groups, 6.77 (SD = 4.21) versus 6.95 (SD = 4.67) ppm respectively. However, the SACMEQ group had a

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Table 1
Means and standard deviations of Primary 6 and Secondary 3 test scores.

Variable	All $n = 643$		Female $n = 326$		Male $n = 317$	
Primary 6	Mean	SD	Mean	SD	Mean	SD
English	54.44	20.04	58.82	18.05	49.52	21.02
French	53.96	14.83	56.45	13.65	51.11	15.63
Kreol	56.74	18.63	61.50	16.24	51.53	19.68
Mathematics	40.99	20.37	43.24	18.98	38.55	21.55
Science	49.13	19.05	51.41	17.45	46.65	20.39
Social studies	59.02	22.07	61.60	20.04	56.19	23.81
Secondary 3						
English	52.53	17.48	55.70	16.58	48.75	17.80
French	51.30	16.87	55.90	15.18	46.14	17.21
Geography	24.73	18.61	27.16	18.36	22.09	18.55
History	32.09	17.39	34.73	17.18	29.21	17.20
Mathematics	23.99	17.17	25.27	16.46	22.49	17.90
Science	41.04	19.72	43.04	19.03	38.69	20.28

significantly higher 9-year recent postnatal hair level 7.48 (SD = 3.98) versus 5.39 (SD = 2.94) ppm, $t = 7.51$, $p < 0.0001$. There are no known reasons to suspect that the two groups would differ and we ascribe the difference to chance.

2.2. Primary 6, Secondary 3, and SACMEQ scores

The summary statistics for all Primary 6 and Secondary 3 endpoints are given in Table 1. The total score for a subject represents the sum of the weighted percent of correct responses for the component subtests. The mean total scores for Primary 6 ranged from 40% for Mathematics to 59% for Social Studies and for Secondary 3 from 23% for Mathematics to 52% for English. Table 1 shows that boys consistently scored lower than girls in all subjects. Variation around the mean total scores was substantial, reflecting distributions that tended to be bimodal.

The SACMEQ scores and teacher competence measures are summarized in Table 2. Students in the Republic of Seychelles scored near the top of all nations participating in the consortium on SACMEQ Reading Comprehension and Mathematics competencies (Leste and Davidson, 2004). But as was the case for the end-of-year examinations, the variation around the mean standard scores was large indicating substantial numbers of poor performers amongst the tested children. As with the end-of-year scores, boys scored lower than girls on the SACMEQ measures. On the whole, the Mathematics teachers were better qualified with more years of teacher training than the English teachers. However, the English teachers had more years of teaching experience than the Mathematics teachers.

2.3. Regression analysis

2.3.1. Primary 6 and Secondary 3 examinations

The results of the multiple linear regression analyses are given in Table 3. All six models examining Primary 6 outcomes and six models examining Secondary 3 outcomes were significant beyond $p = 0.0001$. In no case was the prenatal MeHg by gender interaction significant, so all 12 final models were run with only prenatal MeHg and gender main effects.

The prenatal main effect was significant in only one out of six Primary 6 examinations, and in no Secondary 3 examinations. The Primary 6 French score was adversely influenced by prenatal MeHg exposure but the effect was very small: an increase of 1 ppm of prenatal MeHg exposure was related to a 0.3% decrease in the examination score ($p = 0.043$). This result did not appear for the Secondary 3 examination.

The recent postnatal by gender interactions were significant for the Primary 6 French and Mathematics scores but no recent postnatal MeHg exposure associations were found on any Secondary 3 examination. The partial residual plots of Primary 6 and Secondary 3 French and Mathematics scores are shown in Fig. 1. For the Primary 6 French score, the female recent postnatal effect was significant, $p = 0.018$ in a "beneficial" direction without 2 outliers and $p = .055$ with outliers. The two outliers had a French score of 84 and 43 with recent postnatal MeHg hair levels of 8.24 and 12.30 ppm respectively. The effect was small, as shown in the upper left panel of Fig. 1. The French examination score improved by just over 0.2% for every 1 ppm increase in recent postnatal MeHg hair level. The lower left panel shows that this effect did not occur on the Secondary 3 French examination.

The Primary 6 Mathematics score also had a small "beneficial" female MeHg effect ($p = 0.045$). When one outlier (Mathematics score 87, female recent postnatal level 9.47 ppm) was removed, the significance remained the same ($p = 0.045$). The trends seen in Primary 6 tests do not continue in their corresponding Secondary 3 tests. The upper right panel of Fig. 1 shows that for every 1 ppm increase in recent postnatal MeHg hair level, the Mathematics examination score for girls "improved" by 0.6%, an effect that did not occur on the Secondary 3 examination score (lower right panel).

There was a main effect of recent postnatal MeHg for only the Primary 6 Social Studies score. This association was also small: every 1 ppm increase in recent postnatal MeHg hair level was associated with a 0.6% decline in the Social Studies examination score. Since a Social Studies examination is not given to Secondary 3 students, we cannot determine the persistence over grades of this result.

2.3.2. SACMEQ endpoints

The results of the multiple regression analyses of SACMEQ scores are summarized in Table 4. The overall models were

Table 2
Means and standard deviations for SACMEQ cohort endpoints and teacher characteristics ($n = 215$).

Variable	All $n = 215$		Female $n = 107$		Male $n = 108$	
	Mean	SD	Mean	SD	Mean	SD
SACMEQ English Reading Comprehension	590.36	121.07	618.21	14.74	561.68	121.27
SACMEQ Mathematics	560.50	103.47	580.95	98.24	539.43	104.96
English teacher academic qualification (years)	3.59	0.81	3.58	0.82	3.60	0.80
English teacher professional training (years)	4.86	1.01	4.86	1.05	4.87	0.97
English teacher experience (years)	22.12	11.52	22.97	11.56	21.24	11.48
Math teacher academic qualification (years)	3.91	0.50	3.91	0.46	3.91	0.53
Math teacher professional training (years)	5.36	0.97	5.55	0.81	5.16	1.07
Math teacher experience (years)	11.40	9.92	10.94	9.05	11.87	10.78
Primary 6 English Reading Comprehension (%)	53.99	18.14	57.84	15.77	49.87	19.65
Primary 6 Mathematics (%)	43.60	21.14	46.30	19.09	40.79	22.85

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Table 3
Linear regression results from primary analyses I and II: Primary 6 and Secondary 3 examinations.

Primary 6 outcome	English			French (with outliers)			French (without outliers)			Kreol		
Model significance	<.0001			<.0001			<.0001			<.0001		
R-squared	0.48			0.38			0.40			0.44		
Observations	442			439			437			445		
Independent variables	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value
Prenatal THg	[c]	[c]	[c]	−0.28	(0.13)	**[0.038]**	−0.27	(0.13)	**[0.043]**	[c]	[c]	[c]
Postnatal THg	[c]	[c]	[c]	[b]			[b]			[c]	[c]	[c]
Postnatal THg × sex	[a]					**[0.010]**			**[0.031]**	[a]		
Female postnatal THg	[a]			0.46	(0.24)	[0.055]	0.56	(0.24)	**[0.018]**	[a]		
Male × postnatal THg	[a]			[c]	[c]	[c]	[c]	[c]	[c]	[a]		
Sex			**<.0001**			[c]			[c]			**<.0001**
Female	4.87	(0.72)	**<.0001**	[c]	[c]	[c]	[c]	[c]	[c]	5.14	(0.69)	**<.0001**
Male	−4.87	(0.72)	**<.0001**	[c]	[c]	[c]	[c]	[c]	[c]	−5.14	(0.69)	**<.0001**
WISC-III full scale IQ	1.06	(0.08)	**<.0001**	0.69	(0.07)	**<.0001**	0.69	(0.07)	**<.0001**	0.84	(0.08)	**<.0001**
CVLT long recall (verbal memory)	2.66	(0.78)	**[0.001]**	3.41	(0.63)	**<.0001**	3.71	(0.62)	**<.0001**	3.80	(0.73)	**<.0001**

Primary 6 outcome	Mathematics			Science			Social studies		
Model significance	<.0001			<.0001			<.0001		
R-squared	0.42			0.51			0.42		
Observations	449			456			449		
Independent variables	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value
Prenatal THg	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]
Postnatal THg	[b]			[c]	[c]	[c]	−0.59	(0.25)	**[0.018]**
Postnatal THg × sex			[0.059]	[a]			[a]		
Female postnatal THg	0.63	(0.31)	**[0.045]**	[a]			[a]		
Male × postnatal THg	[c]	[c]	[c]	[a]			[a]		
Sex			[c]			**[0.001]**			**[0.001]**
Female	[c]	[c]	[c]	2.23	(0.66)	**[0.001]**	2.71	(0.83)	**[0.001]**
Male	[c]	[c]	[c]	−2.23	(0.66)	**[0.001]**	−2.71	(0.83)	**[0.001]**
WISC-III full scale IQ	0.96	(0.09)	**<.0001**	1.06	(0.08)	**<.0001**	1.02	(0.10)	**<.0001**
CVLT long recall (verbal memory)	2.93	(0.80)	**[0.000]**	3.78	(0.70)	**<.0001**	4.05	(0.89)	**<.0001**

Secondary 3 outcome	English			French			Geography		
Model significance	<.0001			<.0001			<.0001		
R-squared	0.42			0.46			0.47		
Observations	362			375			381		
Independent variables	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value
Prenatal THg	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]
Postnatal THg	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]
Sex			**<.0001**			**<.0001**			**[0.000]**
Female	3.58	(0.74)	**<.0001**	4.86	(0.68)	**<.0001**	2.71	(0.75)	**[0.000]**
Male	−3.58	(0.74)	**<.0001**	−4.86	(0.68)	**<.0001**	−2.71	(0.75)	**[0.000]**
WISC-III full scale IQ	0.87	(0.09)	**<.0001**	0.78	(0.08)	**<.0001**	1.03	(0.09)	**<.0001**
CVLT long recall (verbal memory)	1.89	(0.78)	**[0.016]**	2.91	(0.70)	**<.0001**	2.86	(0.78)	**[0.000]**
WRAML (spatial memory)	0.79	(0.28)	**[0.005]**	0.56	(0.26)	**[0.030]**	0.77	(0.29)	**[0.008]**

Secondary 3 outcome	Mathematics			Science			History		
Model significance	<.0001			<.0001			<.0001		
R-squared	0.40			0.45			0.43		
Observations	351			370			384		
Independent variables	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value
Prenatal THg	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]
Postnatal THg	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]	[c]
Sex			**[0.016]**			**[0.003]**			**[0.000]**
Female	1.88	(0.78)	**[0.016]**	2.44	(0.82)	**[0.003**	2.61	(0.73)	**[0.000]**
Male	−1.88	(0.78)	**[0.016]**	−2.44	(0.82)	**[0.003**	−2.61	(0.73)	**[0.000]**
WISC-III full scale IQ	0.93	(0.09)	**<.0001**	1.15	(0.10)	**<.0001**	0.85	(0.08)	**<.0001**
CVLT long recall (verbal memory)	2.26	(0.79)	**[0.005]**	2.12	(0.85)	**[0.014]**	3.01	(0.75)	**<.0001**
WRAML (spatial memory)	0.78	(0.29)	**[0.008]**	0.83	(0.31)	**[0.008]**	0.63	(0.27)	**[0.023]**

Other significant effects not shown in the table: school location for P6, Kreol ($p = 0.029$) with Urban (−3.81 (1.54) [0.014]), Urban for P6 science (−2.97 (1.46) [0.043]), Urban for S3 Mathematics (−3.80 (1.70) [0.026]; Hollingshead SES for P6 French ($p = 0.013$ with outliers, $p = 0.009$ without outliers) with professional (with outliers 3.28 (1.44) [0.024] and without outliers 3.11 (1.42) [0.029]) and semiskilled (with outliers −2.58 (0.99) [0.001] and without outliers −2.60 (0.97) [0.008]), for P6 English with professional (4.17 (1.77) [0.019]) and semiskilled (−2.53 (1.21) [0.037]); CBCL for P6 Kreol (−0.19 (0.07) [0.007]); WRAML (spatial memory) for P6 social studies (0.64 (0.31) [0.042]).

[a] Tested interaction for this model was not significant.
[b] Main effect is not relevant for this model.
[c] Non-significant.

significant beyond $p = 0.0001$ for both the SACMEQ scores and the corresponding Primary 6 Examination scores for the cohort. There were no models with a significant prenatal MeHg by gender interaction term, so all models were computed with only main effects tests for prenatal MeHg. The test for a prenatal MeHg main effect was not significant in any model.

The recent postnatal MeHg by gender interaction terms were significant for both SACMEQ endpoints ($p = 0.0001$ for Reading Comprehension and $p = 0.0038$ for Mathematics). The direction and the specificity of these effects were not consistent however. For Reading Comprehension, there was a "beneficial" effect for females and an adverse effect for males. For females, a 1 ppm

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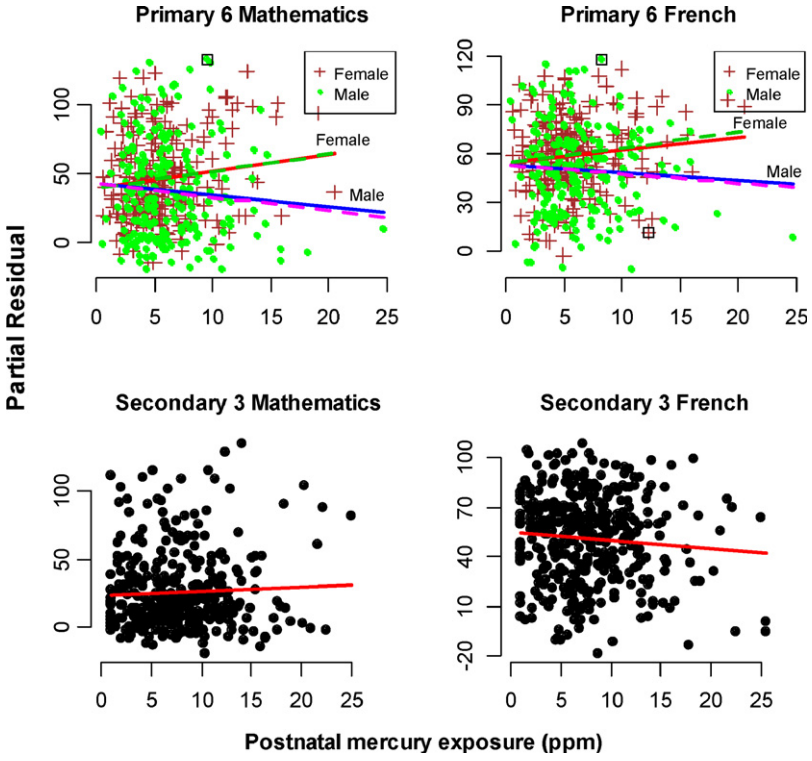

Fig. 1. Partial residuals plots from the linear regression models for Primary 6 and Secondary 3 Mathematics and French scores, with a linear trend of postnatal THg hair level for Secondary 3 and linear trends for female and male for Primary 6 adjusted for covariates. The dashed lines in plot are the lines when fitting excluding outliers.

increase in recent postnatal hair level was associated with a 5 standard score point increase in Reading Comprehension competence but their Mathematics competence was not affected as shown in the partial residual plots depicted in Fig. 2. For males, a 1 ppm increase in recent postnatal hair level was associated with declines of about 5 standard score points in both Reading Comprehension and Mathematics competence.

We further investigated the recent postnatal exposure by gender trends for the SACMEQ group on their Primary 6 Mathematics and English Reading Comprehension examination scores. Only the male adverse effect for Reading Comprehension was significant ($p = 0.003$). Fig. 2 shows that a 1 ppm increase in recent postnatal hair level was associated with a 0.5% decrease in the examination score

2.3.3. Covariate effects

Gender significantly influenced all of the Primary 6 and Secondary 3 examination scores except for Primary 6 French and Mathematics. The sign of the effect was the same with girls having higher scores than boys. The subjects' Full Scale IQ, as measured by the WISC-III, was also a significant predictor for all test scores. The WISC-III slope was always positive, as may be

Table 4
Linear regression results from primary analysis III: SACMEQ cohort.

	SACMEQ Reading Comprehension			SACMEQ Mathematics			Primary 6 Reading Comprehension			Primary 6 Mathematics		
Model significance	<.0001			<.0001			<.0001			<.0001		
R-squared	0.68			0.58			0.60			0.46		
Observations	179			179			156			151		
Independent variables	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value	Estimate	St. err.	*p*-Value
Prenatal THg	[a]	[a]	[a]	[a]	[a]	[a]	[a]	[a]	[a]	[a]	[a]	[a]
Postnatal THgsex			**[0.001]**			**[0.004]**			**[0.011]**			**[0.016]**
Female × postnatal THg	5.09	(2.14)	**[0.019]**	3.59	(2.03)	[0.079]	[a]	[a]	[a]	[a]	[a]	[a]
Male × postnatal THg	−5.59	(2.21)	**[0.012]**	−5.10	(2.13)	**[0.018]**	−0.59	(0.20)	**[0.003]**	[a]	[a]	[a]
WISC-III full scale IQ	5.21	(0.63)	**<.0001**	5.03	(0.59)	**<.0001**	0.37	(0.06)	**<.0001**	0.91	(0.16)	**<.0001**
CVLT short delay (verbal memory)[c]	24.37	(6.70)	**[0.000]**	18.97	(6.42)	**[0.004]**	1.69	(0.58)	**[0.004]**	5.10	(1.61)	**[0.002]**
Maths teacher experience	[b]			1.42	(0.63)	**[0.025]**	[c]			0.47	(0.18)	**[0.009]**
English teacher training	20.27	(7.06)	**[0.005]**	[b]			1.06	(0.60)	[0.078]	[c]		
English teacher experience	2.55	(0.55)	**<.0001**	[b]			0.20	(0.05)	**[0.000]**	[c]		

Mother's Ravens progressive matrices, given at 29-month examination was used due to missing values of the KBIT for the SACMEQ cohort. Other significant effects not shown in table: Henderson early learning profile for SACMEQ Reading Comprehension (1.58 (0.72) [0.030]); CBCL for SACMEQ Reading Comprehension (−1.61 (0.64) [0.012]) and SACMEQ Mathematics (−1.55 (0.61) [0.012]); Hollingshead SES (Overall) was significant for Primary 6 Reading Comprehension ($p = 0.031$); SES professional for SACMEQ Reading Comprehension (28.14 (13.43) [0.038]) and Primary 6 Reading Comprehension (3.72 (1.26) [0.004]).

[a] Non-significant.
[b] Covariate is not relevant for this model.
[c] Short delay used due to large numbers of missing long delay scores for SACMEQ cohort.

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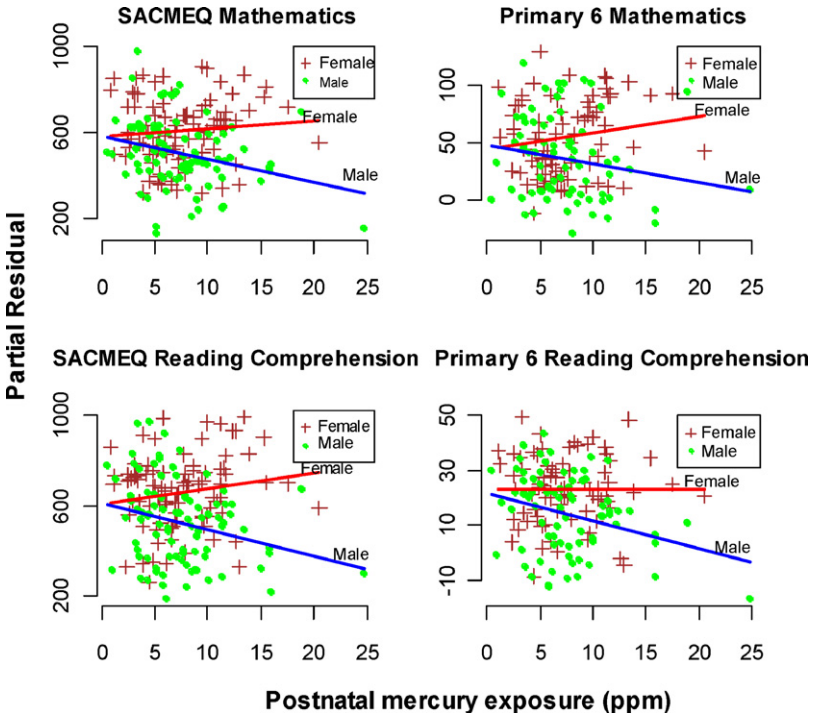

Fig. 2. Partial residuals plot from the linear regression models for SACMEQ Cohort boys and girls. The left panel shows regression results for SACMEQ tests for Mathematics (upper graph) and Reading Comprehension (lower graph). The right panel shows the Primary 6 end-of-year examination Mathematics (upper graph) and Reading Comprehension (lower panel) results for the SACMEQ subjects. All analysis results are plotted with a linear trend of postnatal THg hair level adjusted for covariates.

expected, indicating that a higher IQ score results in better academic achievement. The only other ability score showing significance across most test scores was our measure of verbal recall, the CVLT long delay. It significantly affected all Primary 6 and Secondary 3 examination scores with the slope estimates all positive. Effects of other cognitive, behavioral, or learning environment covariates were not strong and were inconsistent.

3. Discussion

Our results for Primary 6 and Secondary 3 end-of-year examinations indicated no consistent pattern of association between prenatal or recent postnatal MeHg hair levels and any outcome, either at the end of primary school or in mid-high school. In all, we studied 12 end-of-year examination scores, six at the end of Primary 6 and six at the end of Secondary 3. We found one association between prenatal MeHg exposure and 11 out of 12 achievement scores, and no association between recent postnatal exposure and 11 out of 12 examination scores. At the end of Primary 6, we found a significant negative association between prenatal exposure and achievement in French and another significant negative association between recent postnatal exposure and Social Studies achievement. These findings may not have statistical or biological meaningfulness given the lack of associations in these content areas at other time points and may have resulted by chance alone. Taken together, they do not indicate any pattern of either adverse or beneficial MeHg effects on end-of-year achievement test scores.

The results of our analysis of the SACMEQ achievement scores from a subgroup of 215 main cohort children differed from the end-of-year examination results. We found no evidence of associations between prenatal MeHg hair level and outcomes in either subject examined. However, we did find significant adverse associations between recent postnatal MeHg hair level and outcomes in both subjects examined in boys only. These results are different from the subjects' scores on the Primary 6 end-of-year exams and could also have resulted by chance alone. The mean prenatal MeHg exposure for these 215 subjects was similar to that for the overall subgroup. But the mean recent postnatal MeHg exposure level for the 215 subjects was nearly 2 ppm higher than for the overall subgroup. We cannot discern any reason to explain the difference in recent postnatal exposure. The adverse associations with slightly higher exposure on the SAQMEC exams may be significant if they can be replicated in a larger cohort. Previous studies have indicated that 10 ppm in maternal hair may be the lower end of a threshold effect from prenatal exposure (Cox et al., 1989; Huang et al., 2005). There are very limited data on recent postnatal MeHg effects on cognition in children. Recently, Myers et al. (2009) reported some adverse effects of recent postnatal MeHg exposure on some but not all cognitive endpoints. Our findings appear to extend that report to scholastic achievement scores. These findings are sporadic and not consistent, but do suggest that further work is needed on recent postnatal exposure, both as a separate exposure source and as a potential effect modifier to prenatal MeHg exposure.

Our results for prenatal exposure associations are consistent with our previous findings (Davidson et al., 1998; Myers et al., 2003) with respect to cognitive functions. Cognitive functions such as IQ or memory are expected to individually influence achievement, which they did in this study, but the impact was not related to prenatal MeHg. Cognitive functions were related to socioeconomic and geographic variables such as SES and school district setting (as a proxy for classroom size and teacher attention), which are independently associated with achievement.

The gender effects present in this analysis are intriguing. The analysis of outcomes at the conclusion of Primary 6 indicated evidence of gender effects. In most cases, girls outperformed boys. In almost all cases these results were independent of either prenatal or recent postnatal MeHg exposure. But in one case (French), there was a significant positive association between prenatal MeHg and achievement for girls only. Again, this outcome does not constitute evidence of any pattern of associations

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between MeHg and achievement. There are a number of reports in the literature that suggest a greater vulnerability to neurotoxic effects on cognition in males (Vahter et al., 2007). There may be many reasons for this outcome, including metabolic differences favoring females in excretion, distribution and retention of both organic and inorganic forms of Hg (Thomas et al., 1986, 1987) and in the activity of antioxidant defenses (Borras et al., 2003) which some studies have linked to estrogen receptors (Olivieri et al., 2002). The consistency of better scores among girls across both ages and most academic subjects reinforces previous reports from the Government of Seychelles that identified pervasive gaps between girls and boys in both Primary and Secondary educational outcomes (Leste and Davidson, 2004). The reasons for these gaps are unclear and warrant further examination.

The achievement scores at both ages were noticeably low across all subjects. This outcome has been noted in recurrent examination reports produced by the Assessment and testing section in the Ministry of Education (Benstrong, E., personal communication). There is concern that a number of factors may influence the average scores on end-of-year exams, including teacher competency including the mechanics of teaching and associated subject knowledge, curriculum design, and the correlation between end-of-year test content and what is actually taught in classrooms across the educational system. In particular, administrators in the Ministry of Education have suspected that teacher competency may account in part for the very low Mathematics competency among Seychellois young people (Leste and Davidson, 2004). More recent intervention strategies to improve classroom practice of Mathematics teachers in primary schools have led to some improvement in student average scores in some schools (Leste, A., personal communication). The identification and coding of effective teaching practices are important factors to be included in further examination of scholastic achievement.

Achievement outcomes at both ages were directly influenced by covariates that typically would be expected to influence school achievement in general. For example, almost all outcomes were positively correlated with child IQ and with scores on tests of spatial and verbal memory. Cultural variables, including SES and home environment, less consistently affected achievement, perhaps as should be expected for pre-adolescent and adolescent children.

The strengths of this study were that the sub-cohorts for each evaluation were of substantial size, extensive data were available on the individual subjects, and both the end-of-year examinations and the SAQMEC test were standardized. In addition, the SACMEQ examinations were normed across all participating nations, for two endpoints data were available on the subjects' teachers, and there was no co-exposure to other toxicants. The study also has limitations. Not all of the main cohort children had data available. Norms did not exist for the tests administered at Primary 6 and Secondary 3; consequently, some of the variability in educational achievement could be related to the fact the children were enrolled in multiple schools with teachers who varied in training, ability, and motivation. In addition, the inclusion of measures of cognitive ability in our models could have increased the probability of over control.

4. Summary

This study is the first time scholastic achievement scores have been related to either prenatal or postnatal MeHg exposure from fish consumption and we found no consistent pattern of associations. These results are consistent with findings from our earlier studies that reported prenatal MeHg exposure to dosages present in frequent fish consumers are not associated with consistent detectable effects on child development. The adverse associations found with recent postnatal MeHg exposure are intriguing, but will need confirmation by further studies that include educational factors before being accepted.

Conflict of interest statement

None.

References

Axelrad DA, Bellinger DC, Ryan LM, Woodruff TJ. Dose–response relationship of prenatal mercury exposure and IQ: an integrative analysis of epidemiologic data. Environmental Health Perspectives 2007;115:609–15.

Bonham MP, Duffy EM, Wallace JMW, Robson PJ, Myers GJ, Davidson PW, et al. Habitual fish consumption does not prevent a decrease in LCPUFA status in pregnant women (the Seychelles child development nutrition study). Prostaglandins Leukotrienes and Essential Fatty Acids 2008;78:343–50.

Borras C, Sastre J, Garcia-Sala D, Lloret A, Pallardo FV, Vina J. Mitochondria from females exhibit higher antioxidant gene expression and lower oxidative damage than males. Free Radical Biology and Medicine 2003;34:546–52.

Cao Y, Chen A, Jones RL, Radcliffe J, Caldwell KL, Deitrich K, et al. Does background postnatal methylmercury exposure in toddlers affect cognition and behavior? NeuroToxicology 2010;31:1–9.

Cernichiari E, Toribara TY, Liang L, Marsh DO, Berlin M, Myers GJ, et al. The biological monitoring of mercury in the Seychelles study. NeuroToxicology 1995a;16:613–28.

Cernichiari E, Brewer R, Myers GJ, Marsh DO, Lapham LW, Cox C, et al. Monitoring methylmercury during pregnancy maternal hair predicts fetal brain exposure. NeuroToxicology 1995b;16:705–10.

Cox C, Clarkson TW, Marsh DO, Amin-Zaki L, Tikriti S, Myers GJ. Dose–response analysis of infants prenatally exposed to methylmercury: an application of a single compartment model to single-strand hair analysis. Environmental Research 1989;49:318–32.

Clarkson TW, Magos L. The toxicity of mercury and its chemical compounds. Critical Reviews of Toxicology 2006;36:609–62.

Daniels JL, Longnecker MP, Rowland AS, Golding J. ALSPAC Study TeamUniversity of Bristol Institute of Child Health. Fish intake during pregnancy and early cognitive development of offspring. Epidemiology 2004;15(July (4)):394–402.

Davidson PW, Myers GJ, Cox C, Axtell CD, Shamlaye CF, Sloane-Reeves J, et al. Effects of prenatal and postnatal methylmercury exposure from fish consumption at 66 months of age: the Seychelles child development study. JAMA 1998;280:701–7.

Davidson PW, Myers GJ, Shamlaye CF, Cox C, Gao P, Axtell C, et al. Association between prenatal exposure to methylmercury and developmental outcomes in Seychelles children: effects modifications by social and environmental factor. NeuroToxicology 1999;20:833–42.

Davidson PW, Strain JJ, Myers GJ, Thurston SW, Bonham MP, Shamlaye CF, et al. Neurodevelopmental effects of maternal nutritional status and exposure to methylmercury from eating fish during pregnancy. NeuroToxicology 2008;29(5):767–75.

Dunstan JA, Simmer K, Dixon G, Prescott SL. Cognitive assessment of children at age 2(1/2) years after maternal fish oil supplementation in pregnancy: randomised controlled trial. Archives of Disease in Childhood Fetal and Neonatal edition 2006;93(January (1)):F45–50.

Grandjean P, Weihe P, White RF, Debes F, Araki S, Yokoyama K, et al. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. Neurotoxicology and Teratology 1997;19(6):417–28.

Harada Y. Congenital (or fetal) Minamata disease. In: Study group of Minamata disease, editor. Minamata disease. Kumamoto, Japan: Kumamoto University; 196893–118.

Helland IB, Smith L, Saarem K, Saugstad OD, Drevon CA. Maternal supplementation with very-long-chain n-3 fatty acids during pregnancy and lactation augments children's IQ at 4 years of age. Pediatrics 2003;11(January (1)):e39–44.

Hibbeln JR, Davis JM, Steer C, Emmett P, Rogers I, Williams C, et al. Maternal seafood consumption in pregnancy and neurodevelopmental outcomes in childhood (ALSPAC study): an observational cohort study. Lancet 2007;369(February 17 (9561)):578–85.

Huang S-L, Cox C, Myers GJ, Davidson PW, Cernichiari E, Shamlaye CF, et al. Exploring nonlinear association between prenatal methylmercury exposure from fish consumption and child development: evaluation of the Seychelles child development study nine-year data using semiparametric additive models. Environmental Research 2005;87:100–8.

Judge JP, Harel O, Lammi-Keefe CJ. Maternal consumption of a doscosahexaenoic acid-containing functional food during pregnancy: benefit for infant performance on problem-solving but not on recognition memory tasks at age 9 months. American Journal of Clinical Nutrition 2007;85(Jun (6)):1572–7.

Kjellstrom T, Kennedy P, Wallis S, Mantell C. Physical and mental development of children with prenatal exposure to mercury from fish. Stage 1. Preliminary tests at age 4. Solna, National Swedish Environmental Board, Report 3080; 1986.

Kjellstrom T, Kennedy P, Wallis S, Stewart A, Friberg L, Lind B et al. Physical and mental development of children with prenatal exposure to mercury from fish. Stage 2. Interviews and psychological tests at age 5. Solna, National Swedish Environmental Board, Report 3642; 1989.

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Leste A, Davidson PW. Monitoring the educational achievement of primary school children: an international collaboration. Seychelles Medical and Dental Journal 2004;7:114–20.
Myers GJ, Davidson PW, Cox C, Shamlaye CF, Palumbo D, Cernichiari E, et al. Prenatal methylmercury exposure from ocean fish consumption in the Seychelles child development study. Lancet 2003;361:1686–92.
Myers GJ, Thurston SW, Pearson A, Davidson PW, Cox C, Shamlaye CF, et al. Postnatal exposure to methyl mercury from fish consumption: a review and new data from the Seychelles child development study. NeuroToxicology 2009;30:338–49.
Oken E, Wright RO, Kleinam KP, Bellinger D, Amarasiriwardena CJ, Hu H, et al. Maternal fish consumption, hair mercury, and infant cognition in a U.S. cohort. Environmental Health Perspectives 2005;113(October (10)):1376–80.
Oken E, Radesky JS, Wright RO, Bellinger DC, Amarasiriwardena CJ, Kleinman KP, et al. Maternal fish intake during pregnancy, blood mercury levels, and child cognition at age 3 years in a US cohort. American Journal of Epidemiology 2008;167(May 15 (10)):1171–81.
Olivieri G, Novakovic M, Savaskan E, Meier F, Baysang G, Brockhaus M, et al. The effects of beta-estradiol on SHSY5Y neuroplastoma cells during heavy metal induced oxidative stress, neurotoxicity and beta-amyloid secretioin. Neuroscience 2002;113:849–55.
Purvis M-T. Education in the Seychelles: an overview. Seychelles Medical and Dental Journal 2004;7:46–51.
Robinson I, Schroff J. The fishing sector in Seychelles: an overview, with emphasis on artisanal fisheries. Seychelles Medical and Dental Journal 2004;7:52–5.
Schober SE, Sinks TH, Jones RL, Bolger PM, McDowell M, Osterloh J, et al. Blood mercury levels in US children and women of childbearing age, 1999–2000. Journal of the American Medical Association 2003;289(13):1667–74.
Shamlaye CF, Marsh DO, Myers GJ, Cox C, Davidson PW, Choisy O, et al. The Seychelles child development study on neurodevelopmental outcomes in children following in utero exposure to methylmercury from a maternal fish diet: background and demographics. NeuroToxicology 1995;16:597–612.
Strain JJ, Davidson PW, Bonham MP, Duffy EM, Stokes-Riner A, Thurston SW, et al. Associations of maternal long chain polyunsaturated fatty acids, methyl mercury, and infant development in the Seychelles Child Development and Nutrition Study. NeuroToxicology 2008;29(5):776–82.
Thomas DJ, Fisher HL, Sumler MR, Marcus AH, Mushak P, Hall LL. Sexual differences in the distribution and retention of organic and inorganic mercury in methyl mercury-treated rats. Environmental Research 1986;41:219–34.
Thomas DJ, Fisher HL, Sumler MR, Mushak P, Hall LL. Sexual differences in the excretion of organic and inorganic mercury in methyl mercury-treated rats. Environmental Research 1987;43:203–16.
Vahter M, Akesson A, Lidén C, Ceccatelli S, Berglund M. Gender differences in the disposition and toxicity of metals. Environmental Research 2007;104:85–95.
World Health Organization. International programme on chemical safety. Geneva: Environmental Health Criteria 101 Methylmercury; 1990.

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