Environmental Research Section A **89,** 1–11 (2002)
doi:10.1006/enrs.2002.4349, available online at http://www.idealibrary.com on IDEAL®

Neurodevelopmental Investigations among Methylmercury-Exposed Children in French Guiana

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Received May 15, 2001

French Guiana, like its neighbors, suffers from environmental pollution with methylmercury from gold mining activities, and Amerindian communities are particularly affected. A neurological and a neurospsychological evaluation were carried out in children of three Amerindian communities with various levels of pollution: 156 children from the Upper Maroni (high exposure), 69 from Camopi on the Oyapock river (median exposure), and 153 from Awala on the Atlantic coast (low exposure). Exposure to methylmercury was measured by determination of total mercury in the hair of the children and their mothers (geometric mean, 12.7 μg/g in Upper Maroni). No major neurologic signs were observed in the children examined. After adjustment for potential confounders, we found a dose-dependent association between maternal hair mercury level and increased deep tendon reflexes, poorer coordination of the legs, and decreased performance in the Stanford–Binet Copying score, which measures visuospatial organization. In this last test, the frequency of rotation errors was high in the 5–6 years age group and increased with mercury exposure. These associations depended on the sex of child and were stronger among boys. The interpretation of these results is limited mainly by the cross-sectional design of the study. It identifies specific neurological and neuropsychological deficits, in some cases modulated by sex, which are consistent with known targets of mercury neurotoxicity. © 2002 Elsevier Science (USA)

Key Words: **methylmercury; fish consumption; neurodevelopmental tests; prenatal exposure; child development.**

INTRODUCTION

Like many neighboring countries, French Guiana suffers from environmental pollution by mercury from gold mining activities. French Guiana, a French territory in South America, is located between Brazil and Surinam and is covered by the Amazonian forest. Most of its population (150,000 inhabitants in 1990) has settled along the two main rivers, the Maroni and the Oyapock, and along the coast. Several native populations still live in Guiana. They have, to various degrees, kept their traditional ways of subsistence involving fishing, hunting, and subsistence farming.

To obtain a comprehensive picture of the mercury contamination of the population, we conducted in 1994 a cross-sectional survey in which hair mercury levels were measured among 500 individuals in 13 health centers and maternity hospitals covering the whole territory and representing the main population groups living in Guiana (Cordier *et al*., 1998). This first survey demonstrated that hair mercury levels depended largely on freshwater fish consumption. In particular, the Wayana Amerindian community on the Upper Maroni river was the most exposed. Their diet is composed of up to two fish meals per day and 79% of children had hair mercury levels above 10 μg/g. Other Amerindian communities such as the Wayampi from Camopi on the Oyapock and the Galibi from Awala-Yalimapo on the coast had lower levels of exposure due to a greater diversification of their diet: the geometric means were 6.0 μg/g among children in Camopi and 2.6 μg/g among children in Awala-Yalimapo.

0013-9351/02 $35.00

A recent report from the U.S. National Research Council (2000) concluded that chronic low-dose prenatal methylmercury (MeHg) exposure from maternal consumption of fish is associated with poor performance on neurobehavioral tests, particularly those measuring attention, fine-motor function, language, visual–spatial abilities, and verbal memory. This conclusion was supported mainly by results from studies in the Faroe Islands (Grandjean *et al.*, 1997) and New Zealand (Kjellström *et al.*, 1989), although a study conducted in the Seychelles did not confirm these observations (Davidson *et al.*, 1998).

The MeHg levels observed in the Wayana community in French Guiana are in the upper range of those previously reported in populations chronically exposed through fish consumption (Grandjean *et al.*, 1997, 1999; Kjellström *et al.*, 1989; Counter *et al.*, 1998; Murata *et al.*, 1999; Marsh *et al.*, 1995; McKeown-Eyssen *et al.*, 1983). Additional reports from populations such as Amerindian communities living in a different sociocultural environment and for which mercury exposure constitutes the main toxic exposure can certainly contribute to a better knowledge of the targets of mercury toxicity.

METHODS

General Considerations

We compared the neurological and neuropsychological status of chidren in three Amerindian communities: Wayana children from five villages on the Upper Maroni (high-exposure area according to our initial survey), Wayampi children from Camopi on the Oyapock (medium exposure), and Galibi children from Awala-Yalimapo on the Atlantic coast (low exposure). The social organization of these communities is similar except that Awala is more developed and is accessible by road.

We carried out a standard *neurological evaluation* for all children aged 9 months to 6 years from the Upper Maroni and a random sample of the children from the other two communities, matched for age and sex. If it was not possible to match children for both age and sex, a child of the same age but the opposite sex was chosen. We applied the structured neurological examination described by Amiel-Tison and Stewart (1989) evaluating neurosensory, neuromotor, and neurobehavioral signs and functions. Specific visual functions such as visual field or color vision could not be tested because children were too young to understand properly the instructions to perform these tests. The neurological examination was carried out in March 1997 and December 1997 by two physicians who had received appropriate training for this study with C. Amiel-Tison.

The *neuropsychological investigation* was performed subsequently and concerned children aged 5 to 12 years. Camopi was not included in this second part of the study because access was difficult and high alcohol consumption proved to be a potential confounding factor. All children in the age range were eligible for inclusion in the Upper Maroni communities and a random sample of children matched for age and sex from Awala was included. In a pilot survey in Awala, the use of standard test batteries such as most of the McCarthy scales (McCarthy, 1976) proved to be inadequate in these native populations. They were too culture and language dependent and the scores of the children tested were at the low end of the range recorded for Western children, resulting in low variability in the scores. Several of the tests that we finally chose had originally been used in a similar study in Brazil (Grandjean *et al.*, 1999) and were judged by us as independent as possible from culture and education. The Finger Tapping test and McCarthy Leg Coordination measured manual motor ability and locomotor function. We used the same Finger tapper with a shortened arm adapted for small children already used by Grandjean *et al.* (1999). The Stanford–Binet Copying test (Thorndike *et al.*, 1986) measured visuospatial organization. The rules used for the subtests differed from those in the test manual in that every child was given all of the block items and all of the drawings. The study in Brazil showed that the level of difficulty set in the original American Stanford–Binet test was inappropriate for these communities. For instance, some children who were unable to perform the easier subtests of block construction well were able to draw very complex designs correctly. Stanford–Binet Bead memory (Thorndike *et al.*, 1986) was used to measure short-term memory and McCarthy Digit Span test was used to assess attention. We also measured the mother's reasoning capacity using Raven Progressive Matrices (Color) (Raven *et al.*, 1998). This specific test was designed originally for children, for anthropological studies, and for people who do not understand or speak the same language as the examiner. The evaluation of all children in December 1997 and June 1998 according to standardized procedures was shared among three psychologists experienced in the psychological evaluation of children and who were not aware of individual exposure levels.

Mothers were interviewed using a structured questionnaire recording sociodemographic information and lifestyle factors (mother's and father's age, level of education, income, smoking and drinking habits) and obstetric and medical history (parity, disease during pregnancy, disease of the child). In some centers, mothers did not speak French and this information had to be obtained from another member of the family or with the aid of an interpreter: this applied to 60% of the families in the Upper Maroni, 25% in Camopi, and 17% in Awala. Whenever possible, the characteristics of the child at birth (birth weight, gestational age) were noted from records at the local health center. Informed consent for data collection and hair sampling was obtained.

Hair samples for mercury determination were taken from both the mother and the child. Investigators obtained a lock of scalp hair, usually from the nape, approximately 0.5 cm in diameter, and stored it in a plastic bag until analysis. Chemical analysis was carried out at the Centre de Toxicologie du Québec, Canada, by cold-vapor atomic-absorption spectrometry. The results are expressed in μg/g. The reliability of the results was monitored through participation in Health Canada's interlaboratory comparison program for the determination of mercury in human air. Maternal hair mercury concentration at the time of the interview was used as a proxy for prenatal exposure. This variable had a skewed distribution so a log transformation was used. We also investigated the factors associated with the child's hair mercury concentration at the time of the examination.

Statistical Analysis

Neurological examination. The frequency of neurological signs or associations of signs was compared across three classes of maternal hair mercury concentration (≤ 5, 5–10, > 10 μg/g) and an Armitage test for trend was performed. In addition to covariables considered mandatory for this investigation (sex and age of the child, alcohol intake, and illness during childhood) we searched for potential confounding factors by selecting variables properly measured (low percentage of missing values) and associated with both mercury exposure and neurological impairment among the following: parity, maternal age at delivery, maternal education, income of the family, illness during pregnancy or at delivery, number of prenatal visits, place of birth, and duration of breast feeding. We then carried out multivariate analyses with logistic regression including mandatory confounders and potential confounders selected from the above list (i.e., place of birth).

Neuropsychological evaluation. For tabular presentation of test results, age-standardized mean scores were calculated for the various neuropsychological subtests and presented according to center and according to category of exposure within the high-exposure area Upper Maroni. As mentioned earlier, for some tests we adapted the entry rules toward higher tolerance to obtain greater variability in the scores. This adjustment precluded use of the standardization tables for age provided in the test manuals for most tests. We therefore constructed a standardization procedure for age, taking all of the children examined as a "standard" population: for each score, a regression equation was constructed with respect to eight age categories (5 to 12 years), adjusting for maternal mercury level. The regression coefficients estimated for the various age classes were then used to adjust each crude score, giving a score adjusted for age. For the two tests in which we strictly followed the rules of administration, we were able to compare the scores computed with this method with the standardized scores obtained with the tables in the manual: we obtained correlation coefficients of 0.95 for the Stanford–Binet Bead Memory test and 0.92 for the MSCA Leg Coordination test. The standardization was therefore applied to all scores.

In parallel, we searched for confounders in a way similar to that of the neurologic examination. Multiple linear regressions for each score were used in which age (in months), sex, and examiner, with or without Raven maternal score, were mandatory in addition to log Hg and other potential confounders selected from the above list which differed according to the test performed. The normality of residues was tested using the Shapiro–Wilk test. If the distribution was not normal, nonparametric tests were used (Spearman's rank correlation) or the score was transformed into a dichotomous variable ($<$ 25th percentile of the distribution) and logistic regression performed.

Internal analysis within the Upper Maroni. For both the neurological and the neuropsychological evaluations, internal analysis within the high-exposure area only (Upper Maroni) was performed to avoid confounding related to between-community differences and to avoid observation bias from the examiners. This analysis, however, was limited by low statistical power.

RESULTS

Overall, 156 children (and their 104 mothers) were examined in the Upper Maroni communities, 153 in Awala (115 mothers), and 69 in Camopi (51 mothers). Hair mercury levels among children were similar to those recorded in our previous survey: geometric means of 10.2 μg/g for Upper Maroni, 6.5 μg/g for Camopi, and 1.4 μg/g for Awala. The geometric mean hair mercury levels for mothers were 12.7 μg/g for Upper Maroni, 6.7 μg/g for Camopi, and 2.8 μg/g for Awala. No hair sample could be obtained for 39 mothers (14%) and 19 children (5%). There was no trend toward increasing mercury concentration with increasing age among children between 1 and 12 years old.

Neurologic Examination

Study population. One hundred and ten children between 9 months and 6 years old were eligible for the neurologic examination in the Upper Maroni communities. Various problems (one village was not accessible, several families had left for a trip), resulted in only 97 (88.2%) being finally included. We were able to examine 69 randomly selected children of 86 contacted (80.2%) in Camopi and 82 of 94 contacted (85.4%) in Awala, for the same age range. A number of sociodemographic and medical characteristics differed between the three areas: in the Maroni, it was often necessary to resort to an interpreter for the interview with the mother. Mothers in the Maroni and Camopi were less educated (71% had none or less than primary) than those from Awala (5%). The level of external resources was lower in the Maroni (390 FF per month per person versus 510 FF in Camopi and 690 FF in Awala). Almost no tobacco was consumed during pregnancy in the three regions. Alcohol consumption during pregnancy (at least once) was reported by most of the mothers in the Maroni, but was limited to celebrations and low-alcohol beverages (home-made beer called Cachiri), whereas in Camopi, regular strong drinks (rum) consumption was often reported (29%). Only 62.6% of the women in the Maroni received prenatal care (versus 96.9% in Camopi and 100% in Awala) and 26.4% of the Maroni mothers reported illness during pregnancy (mostly malaria) versus 6.4% in Camopi and 3.8% in Awala. In the Maroni and Camopi, almost half the mothers gave birth at home (6.4% in Awala). In the Maroni, a high percentage of illness during childhood was reported (30.9%), versus 19.4% in Camopi and 4.9% in Awala, mostly malaria, diarrhea, or high fever of unknown cause.

Children with severe neurological handicap not necessarily related to exposure to mercury were excluded from the analysis (two children with cerebral palsy were excluded in Camopi).

Confounder identification. Covariables and their associations with maternal hair concentration are presented in Table 1. Much of the data, such as maternal education level and duration of breast feeding in Camopi, was difficult to obtain. Place of birth (home or maternity hospital) and parity were

TABLE 1
Maternal Mercury Concentration in Hair (μg/g) According to Various Sociodemographic and Medical Characteristics, by Center

	Upper Maroni ($N = 90$)			Camopi ($N = 63$)			Awala ($N = 77$)		
	m_{Hg}	(n)		m_{Hg}	(n)		m_{Hg}	(n)	
Sex of child									
Male	12.0	(54)	$P = 0.49$	6.2	(36)	$P = 0.09$	2.8	(38)	$P = 0.38$
Female	12.6	(36)		7.4	(27)		2.5	(39)	
Maternal age (years)									
< 20	12.6	(25)	$P = 0.05$	6.8	(21)	$P > 0.10$	2.4	(16)	$P > 0.10$
20–24	12.9	(24)		6.4	(19)		2.6	(31)	
25–29	12.5	(23)		7.3	(10)		2.6	(18)	
> 30	9.7	(16)		7.9	(9)		3.2	(9)	
Unknown		(2)			(4)			(3)	
Maternal education									
Less than primary school	11.7	(59)	$P = 0.21$	7.7	(29)	$P < 0.01$	2.4	(4)	$P = 0.37$
Primary school	13.4	(21)		5.0	(8)[a]		2.9	(38)	
Secondary or higher	14.0	(3)		5.7	(1)[a]		2.4	(34)	
Unknown		(7)			(25)			(1)	

TABLE 1—*Continued*

	Upper Maroni ($N = 90$)			Camopi ($N = 63$)			Awala ($N = 77$)		
	m_{Hg}	(n)		m_{Hg}	(n)		m_{Hg}	(n)	
Income (FF/person.month)									
< 200	11.6	(33)	$P = 0.30$	7.3	(9)	$P = 0.20$	2.7	(7)	$P = 0.76$
200–399	13.5	(15)		5.6	(18)		2.5	(11)	
400–599	11.1	(14)		6.4	(13)		3.0	(18)	
≥ 600	12.7	(19)		7.2	(15)		2.5	(37)	
Unknown		(9)			(8)			(4)	
Alcohol during pregnancy									
< Once/week	12.5	(79)	$P = 0.29$	7.4	(43)	$P < 0.001$	2.6	(55)	$P = 0.53$
≥ Once/week	17.5	(1)		5.1	(17)		2.9	(18)	
Unknown		(10)			(3)			(4)	
Illness during pregnancy									
No	12.6	(60)	$P = 0.16$	6.5	(55)	$P < 0.63$	2.7	(73)	$P = 0.44$
Yes	11.3	(22)		7.2	(4)		2.1	(3)	
Unknown		(8)			(4)			(1)	
Prenatal care (No. visits > 1)									
No	13.0	(31)	$P = 0.07$	5.0	(2)	$P > 0.10$	—	(0)	$P > 0.10$
Yes	11.5	(54)		6.8	(60)		2.7	(76)	
Unknown		(5)			(1)			(1)	
Place of birth									
Home	13.7	(44)	$P < 0.001$	6.9	(30)	$P = 0.92$	4.8	(5)	$P < 0.02$
Maternity hospital	10.9	(44)		6.8	(31)		2.5	(68)	
Unknown		(2)			(2)			(4)	
Parity									
1	13.1	(27)	$P < 0.001$	6.4	(16)	$P = 0.86$	2.1	(26)	$P < 0.01$
2–3	13.8	(29)		6.8	(21)		3.0	(26)	
≥ 4	10.4	(32)		6.4	(22)		3.4	(19)	
Unknown		(2)			(4)			(6)	
Breast feeding									
< 1 year	10.5	(9)	$P = 0.17$	6.5	(10)	$P = 0.90$	2.5	(38)	$P = 0.45$
1–2 years	11.8	(35)		6.1	(21)		3.0	(27)	
> 2 years	13.0	(38)		6.2	(9)		2.6	(9)	
Unknown		(8)			(23)			(3)	
Illness during childhood									
No	11.8	(62)	$P = 0.36$	6.4	(50)	$P = 0.09$	2.6	(73)	$P = 0.42$
Yes	12.7	(25)		7.9	(13)		3.5	(3)	
Unknown		(3)			(0)			(1)	

Note. m_{Hg}, geometric mean. Maternal hair concentration data are missing for seven children in Upper Maroni, four children in Camopi, and five children in Awala.

[a] These categories were merged before testing.

the variables most strongly associated with mercury exposure in the various centers. However, for parity, opposite trends in association were observed in the Maroni and Awala. Alcohol consumption during pregnancy and illness during childhood were systematically included among the potential confounding factors due to their known effects on neurologic development.

Neurologic signs. No major neurologic signs were observed in the children examined except for two children who began to walk late in Camopi. There is no evidence of a linear increase in the prevalence of mild neurologic signs except for an increase in tendon reflexes. With boys and girls analyzed separately this increase was significant in the boys only, 2.6% for mercury levels < 5 μg/g, 13.2% between 5 and 10 μg/g and 27.9% above 10 μg/g, and was close to significance in the girls (12.5, 18.8, and 32.3%, respectively). These trends held if only children 2 years old and older were considered, for whom this sign is easier to evaluate.

Multivariate analysis. In a logistic regression model to account for the increase in tendon reflexes (dependent variable) including the confounding variables cited above, the only medical or sociodemographic characteristic found to contribute to this clinical sign was place of birth (home, hospital). The odds ratio (OR) associated with the mother's mercury level (log Hg) adjusted for age, sex, and place of birth was 5.20 (95% confidence interval (CI) 1.2–22), corresponding to the increase (multiplicative) in the risk of increased reflexes associated with a 10-μg/g increase in log mercury level. The associated OR of mercury was much higher for boys and close to 1 for girls.

The internal analysis in the Upper Maroni alone showed no statistically significant correlation between mercury level and prevalence of increased tendon reflexes either for both sexes considered together ($OR_{Hg} = 2.53$, 95% CI 0.05–124) or for boys alone, but the estimates were of the same order of magnitude as the values obtained when all centers were considered.

Reproducibility. As this observation concerns a sign (increased tendon reflexes) the evaluation of which is subjective, we investigated the reproducibility of the clinical observation: 10 children from the Upper Maroni found to have increased tendon reflexes in March 1997 were assessed again in December 1997 by another examiner who was blind to the previous results. Only 3 of the 10 children were again reported to have increased tendon reflexes. Due to the difficulties of investigation, we did not examine unaffected children again to look for an increase in reflexes in another examination. We were unable to distinguish between individual variability in responses and poor interobserver reproducibility, but poor reproducibility certainly limits interpretation of the results concerning increased tendon reflexes in this group.

Neuropsychological Investigation

Study population. One hundred and three children aged from 5 to 12 years of 128 eligible for inclusion (80.5%) in the Upper Maroni and 103 in Awala of 115 contacted (89.6%) were tested by psychologists. Mean age at examination was 8.1 ± 2.2 years (m $\pm$ SD) in the Upper Maroni and 8.7 ± 2.2 years in Awala.

The differences observed in the characteristics of the families included in the survey in Awala and the Upper Maroni were of the same nature as those previously noted in the neurologic investigation: use of an interpreter, mother's educational level, income, alcohol consumption, prenatal care, illness during pregnancy, delivery at home, and childhood illnesses. An additional indicator, the Raven score, which measures the mother's aptitude for logical reasoning, was twice as high in the Awala mothers as in the Maroni mothers (21.4 ± 6.6 versus 12.9 ± 4.0). Malaria was the predominant illness reported during pregnancy and childhood in the Maroni.

Scores. Significantly higher age-standardized scores were recorded in Awala than in the Upper Maroni for the Copying test and Digit Span (Table 2). Within the Upper Maroni, scores decreased with exposure category, with this trend statistically significant for the Leg Coordination test and close to significance for the Copying test.

Looking at sex-specific associations, a significant decrease in score correlated with exposure ($P < 0.01$) was observed for girls in the Block replication score of the Copying test, a decrease close to significance for Design Copying score on the same test and for the Digit Span test ($P < 0.10$). A significant decrease was observed for boys in the Leg Coordination test ($P < 0.01$) (data not shown).

Confounder identification and multivariate analysis. Adjustment for age, sex, and examiner was considered mandatory. Among other potentially confounding variables, only place of birth (home or hospital) was found to be related to mercury exposure level in both centers. A correlation was observed between parity and Finger Tapping score, between the Raven Score and all scores except those for the Finger Tapping and Leg Coordination tests, and between place of birth, Design score from the Copying test, Bead Memory, and Digit Span scores.

For all scores except Finger Tapping and Leg Coordination, β coefficients of the log Hg exposure level, adjusted for the variables listed above, are presented in Table 3 with or without additional adjustment for the Raven score, because in our study, performance in the Raven test was highly correlated to the region and consequently to mercury exposure. We observed a negative correlation between Design score from the Copying test and mercury level, in both sexes. With the Upper Maroni and each sex studied separately, a negative correlation was observed in boys between mercury exposure level and Leg Coordination score and in girls between mercury level and Block Design score. A positive association was also observed between the mercury

TABLE 2

Mean Age-Standardized Scores (± Standard Error) in the Various Tests by Region and Category of Mercury Concentration in Maternal Hair (μg/g)

				Upper Maroni only			
Test	Awala	Upper Maroni	P_1	< 11.5	11.5–14.4	≥ 14.5 μg/g	P_2
Finger tapping (age ≥ 7)							
N	71	71		21	20	17	
Preferred hand	47.2 ± 1.3	47.7 ± 1.3	0.77	49.6 ± 2.8	47.2 ± 2.3	48.6 ± 2.7	0.84
Other hand	43.1 ± 1.1	43.0 ± 0.9	0.92	43.7 ± 1.2	42.2 ± 2.0	41.8 ± 1.6	0.42
Stanford–Binet							
N	103	103		28	33	26	
Copying test: block score	8.8 ± 0.2	8.6 ± 0.2	0.31	9.0 ± 0.3	8.8 ± 0.4	8.1 ± 0.5	0.11
Copying test: design score	10.9 ± 0.2	8.9 ± 0.3	< 0.001	9.6 ± 0.4	8.4 ± 0.5	8.2 ± 0.5	0.08
Bead memory	13.5 ± 0.4	12.5 ± 0.5	0.09	10.8 ± 1.0	13.4 ± 1.0	12.5 ± 0.7	0.29
McCarthy							
N	103	103					
Digit span							
Forward	5.2 ± 0.1	4.8 ± 0.2	0.06	5.4 ± 0.3	4.4 ± 0.4	4.6 ± 0.4	0.22
Backward	2.2 ± 0.1	1.5 ± 0.2	0.006	1.5 ± 0.3	1.1 ± 0.3	1.8 ± 0.3	0.11[a]
Leg Coordination (5–8.5 years)							
N	55	54		12	21	16	
Mean score	12.5 ± 0.1	12.5 ± 0.2	0.94	13.0 ± 0.1	12.9 ± 0.2	11.8 ± 0.4	0.12[a]
% < 25th percentile	26.4% (14)	23.6% (13)	0.74	8.3% (1)	20.0% (4)	50% (8)	0.01

Note. P_1, degree of significance (comparison between Awala and Upper Maroni); P_2, degree of significance (test for trend in the Upper Maroni only).

[a] Spearman's rank correlation test.

exposure level and the Bead memory score among boys.

Rotation errors. In the Copying test, one error appeared repeatedly during the course of the scoring: the design to be reproduced was rotated by 90°, usually from horizontal to vertical. We scored this type of error specifically, without knowledge of exposure status, and compared its frequency (at least one rotation during the whole Copying test) across exposure categories. Results are presented in Table 4. We found a steep increase in the frequency of this error with mercury exposure, which was more pronounced among boys. This error mainly affected younger children (66% of affected children in the Upper Maroni were 5–6 years old): in the highest exposure category, almost all children made this error at least once. In our data we could check that the frequency of this error was not related to the examiner ($P = 0.94$) or to one particular location (similar frequency in the four villages of Upper Maroni; $P = 0.90$).

Child's hair memory concentration. Overall, a strong correlation was observed between the mercury hair concentrations of the mother and those of the child ($r = 0.82$, $P < 0.001$). This correlation, however, results at least in part from the large differences in environmental mercury levels in the three regions. With Upper Maroni considered separately, the correlation holds but is weaker ($r = 0.30$, $P < 0.01$). Therefore we attempted to evaluate the independent effect of the child's mercury exposure (reflecting postnatal exposure) on the various neuropsychological scores in the Upper Maroni only.

There was a strong negative association for girls only with the Bead Memory score ($\beta = -19.3$, $P = 0.03$) and the Digits Span score ($\beta = -4.9$, $P = 0.03$). Maternal and child mercury concentrations were independently associated with the Leg Coordination score for boys. For this last score, with both maternal and child mercury concentrations included in a multivariate model, the association was stronger with maternal hair concentration and became not statistically significant with the child mercury concentration.

DISCUSSION

This study shows an association between the level of exposure to mercury of the mother and the

TABLE 3

Regression β Coefficients for the Mother's Hair Mercury Concentration in Multivariate Analysis for the Total Sample and the Upper Maroni Alone, by Sex

	Total sample						Upper Maroni					
	All children[a]		Boys only[b]		Girls only[b]		All children[a]		Boys only[b]		Girls only[b]	
Test	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*	*β*	*P*
Finger tapping												
Preferred hand	[c] 1.27	0.64	2.93	0.33	– 4.60	0.40	– 3.73	0.79	– 2.70	0.87	– 14.4	0.60
Other hand	[c] – 1.63	0.44	– 1.20	0.64	– 2.77	0.50	– 0.76	0.92	– 8.28	0.41	0.02	1.00
Stanford–Binet												
Copying test:												
Block score	– 0.55	0.18	– 0.20	0.69	– 1.16	0.11	– 1.45	0.47	3.03	0.31	– 6.04	0.03
	[d] 0.01	0.98	0.27	0.70	– 0.44	0.60	– 1.79	0.38	2.51	0.41	– 5.89	0.04
Copying test:												
Design score	[e] – 2.98	< 0.0001	– 2.90	0.0004	– 2.17	0.02	– 2.83	0.34	– 1.39	0.72	– 3.84	0.41
	[d,e] – 2.11	0.007	– 2.02	0.04	– 1.68	0.19	– 3.30	0.30	– 2.33	0.59	– 4.52	0.38
Bead Memory	[e] 0.11	0.92	0.09	0.95	– 0.06	0.98	9.73	0.05	11.7	0.07	6.02	0.43
	[d,e] 0.56	0.67	0.23	0.89	0.62	0.78	10.2	0.05	12.5	0.07	7.81	0.38
McCarthy												
Digits Forward	[e] 0.04	0.93	– 0.59	0.25	1.19	0.10	– 0.08	0.97	1.07	0.67	– 0.91	0.77
	[d,e] 0.07	0.89	– 0.10	0.88	0.64	0.43	0.007	1.00	0.56	0.84	0.23	0.94
Leg coordination	– 0.15	0.62	– 0.50	0.26	0.03	0.92	– 3.72	0.006	– 5.96	0.02	– 2.12	0.08

Note. *P*, degree of significance of regression coefficient (two-sided).

[a] Adjusted for age, sex, examiner.

[b] Adjusted for age, examiner.

[c] Additional adjustment for parity.

[d] Additional adjustment for Raven score.

[e] Additional adjustment for place of birth.

TABLE 4
Frequency of Rotation Errors (at Least One) in the Copying Test, by Center, Category of Exposure, and Sex

Rotation error	Awala	Upper Maroni	P_1	Upper Maroni < 11.5	11.5–14.4	≥ 14.5 μg/g	P_2
Both sexes							
N	103	103		28	33	26	
% Yes	8.7% (9)	32.0% (33)	< 0.001	17.9% (5)	36.4% (12)	46.2% (12)	0.027
5–6 Years old							
N	32	32		7	13	9	
% Yes	25.0% (8)	65.6% (21)	< 0.001	42.9% (3)	69.2% (9)	88.9% (8)	0.049
Girls only							
N	39	44		11	18	9	
% Yes	7.7% (3)	25.0% (11)	0.036	27.3% (3)	22.2% (4)	33.3% (3)	0.799
Boys only							
N	64	59		17	15	17	
% Yes	9.4% (6)	37.3% (22)	0.001	11.8% (2)	53.3% (8)	52.9% (9)	0.014

Note. P_1, comparison between Awala and Upper Maroni: degree of significance; P_2, degree of significance of test for trend (Upper Maroni only).

increased deep tendon reflexes, the poorer coordination of the legs, and a deficit in the Copying test score, a test that nonspecifically measures reasoning and visuospatial organization. These associations held if the population was restricted to that in the exposed region, but with a lower degree of significance, and they seemed to depend on the sex of the child. Although drawing errors in copying designs are part of normal development, frequent rotation errors after age 6 years are likely to result from insult in the parietal lobes of the brain. Support for this localization of error type is given by the results of research in dyslexic children who often have smaller superior parietal lobes on brain imaging and show rotation errors into the primary school years (Rumsey *et al*., 1992). Since the brain areas often involved in mercury exposure are parietal and occipital lobes, our observation is consistent with current knowledge of mercury toxicity (Sullivan, 1999).

The level of development of the populations studied and difficulties in communication restricted our choice to tests independent of language and culture and made it impossible to use psychological tests similar to those currently used in other populations exposed to methylmercury, in the Seychelles and Faroe Islands, for example (Grandjean *et al*., 1997; Davidson *et al*., 1998). For this reason, only certain areas of the child's neuropsychological and neurological development could be explored. However, the tests used proved pertinent and sensitive for the evaluation of neurological or neuropsychological impairment in the Amerindian populations of Guiana. Our study also suggests several effect modifiers in the associations found, mainly region and sex of the child. Although the tests chosen were as independent as possible from language and education, an influence on performance of the more "learned" environment in Awala is probable, and, similarly, regular outdoor activity in the Upper Maroni may account for the high average performance in the motor coordination test. Thus, internal analysis within the high-exposure region was justified.

Various associations were observed according to the sex of the child. This may result from multiple testing or may be due to the choice of subtests designed to assess areas of development such as motor coordination and visuospatial orientation that develop differently in the two sexes in this age group; it may also reflect genuine gender specificity of mercury toxicity in humans.

This study inherently contains several uncertainties and a lack of precision. The retrospective nature of the investigation (due to the low number of births annually) resulted in children of different ages being assessed, which introduces heterogeneity into the examination despite the standardization for age. In addition, it is difficult to identify exactly who the children included in the study represent at a given age with respect to the corresponding birth cohort: deaths are likely to have occured but are poorly recorded if at all, especially in the Upper Maroni and particularly in the village of Antecume-Pata, where there is no family allowance and therefore no obligation to register births.

If we assume that the period of maximum risk associated with exposure is the prenatal period, then the mercury content of the mother's hair at the time of the examination (that is, up to 12 years after the pregnancy) only imperfectly reflects the exposure level during pregnancy. Two conditions are necessary for this indicator to be accurate: the concentrations of mercury in the environment and in fish must have remained stable over the last 10 years and the mother's diet (in particular, her consumption of fish) must not have changed significantly. These two hypotheses are corroborated by the very close mercury hair concentrations measured in our previous survey in 1994 (Cordier *et al*., 1998) and in the present survey: geometric means of 11.7 μg/g (95% CI 10.5–13.1) among adults in Upper Maroni in 1994 compared to 12.7 μg/g in 1997, 6.7 μg/g (5.3–8.5) in Camopi in 1994 compared to 6.7 μg/g in 1997, and 3.8 μg/g (3.0–4.9) in Awala in 1994 compared to 2.8 μg/g in the present survey.

The retrospective evaluation of potentially important covariables such as prematurity, malaria during pregnancy, and alcohol consumption was also made difficult by having to use an interpreter in many situations and by the lack of information concerning the birth for women who gave birth at home, particularly in the village of Antecume-Pata in the Upper Maroni. There was a significant association between place of birth (home, maternity hospital) and mercury level, and this variable was taken into consideration for comparisons, but there is no evident association between mercury level and prematurity or malaria for the women for whom we had this information.

Other toxicants that may be present in the Guianese environment and known neurotoxicants, such as PCB and lead, may also be related to exposure to mercury but industrialization is virtually absent, rendering this problem unlikely.

One of the strong points of this investigation is the high rate of participation: 88% for the neurologic study and 81% for the neuropsychological study in the Upper Maroni. In addition, within each region, the physicians and psychologists worked without knowing the individual exposure level. This blindness to exposure status was respected in scoring the results of the neuropsychological tests.

CONCLUSION

The results obtained show a link between the exposure to mercury and a number of perturbations of the child's neurological and neuropsychological development. The deficiencies observed were mild and it is difficult to assess their prognostic value. However, these results, obtained in the Amerindian populations of Guiana, are consistent with those of most of the studies of other populations exposed to methylmercury elsewhere in the world. In addition, they point at specific subtests which may prove sensitive in the evaluation of neuropsychological deficits in these native populations.

ACKNOWLEDGMENTS

We thank the families, health agents, and school teachers in Antecume-Pata, Awala, Cayode, Camopi, Elahe, Taluhen, and Twenke and the different administrations of Guiana for their active participation and their help all through this investigation. We also thank Gina Muckle, Philippe Grandjean, and Maria de Agostini for constructive discussions during the different phases of the study, Alain LeBlanc from the Centre de Toxicologie du Québec for performing the mercury analyses, and Jo Ann Cahn for revising the manuscript. This study was supported by a grant from the French National Network of Public Health (RNSP).

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