Published in final edited form as:
Int J Hyg Environ Health. 2009 July ; 212(4): . doi:10.1016/j.ijheh.2008.09.004.

Nephrotoxicity, Neurotoxicity, and Mercury Exposure among Children with and without Dental Amalgam Fillings

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Abstract

Purpose—A scientific review panel for the U.S. Food and Drug Administration (FDA) recently identified the need for more data on the health risk of mercury exposure from dental amalgam among susceptible populations. We evaluated impacts of low level mercury exposure on renal function and neurobehavioral and neuropsychological performance among children.

Methods—Dental histories for 403 children aged 7-11 years in five schools from Xuhui, Shanghai were checked by dentists. Of them, 198 with confirmed amalgam fillings were recruited (exposure group). Reference children (N=205) were those who never had dental amalgam treatment. In May 2004, each child provided a urine sample for measurements of total mercury, n-acetyl-β-D-glucosaminidase activity, microalbumin, and creatinine (Cr). The Child Behavior Checklist, Eysenck Personality Questionnaire, and an intelligence screening test were administered.

Results—The geometric mean urinary mercury concentration was 1.6 μg/g Cr for children with and 1.4 μg/g Cr for children without amalgam fillings. No differences were found between children with and without fillings for either renal function biomarker, or on neurobehavioral, neuropsychological, or intelligence tests.

Conclusions—Although urinary mercury concentration was slightly elevated among children with amalgam fillings, we found no evidence of adverse effects on the outcomes evaluated. These results agree with those from recent trials in developed countries.

Keywords

dental amalgam; mercury; nephrotoxicity; neurotoxicity

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1. Introduction

Dental amalgams containing approximately 50% elemental mercury have been used for dental restoration for more than 150 years because they are malleable, durable, and more affordable than gold or composites. Dental amalgam fillings can release elemental mercury (Hg^0), causing an elevated body burden of mercury (Vimy et al., 1990; Khordi-Mood et al., 2001; Counter and Buchanan, 2004). Hg^0 is known to be neurotoxic and nephrotoxic, even at low levels (International Program on Chemical Safety, 2003; Counter and Buchanan, 2004; Clarkson and Magos, 2006). Concerns about adverse health effects of mercury exposure after dental amalgam filling have existed since the introduction of amalgams to dentistry (Eley, 1997; Bates, 2006).

Children are especially vulnerable to environmental toxicants such as mercury (Tamburlini et al., 2002; World Health Organization, 2006). Some countries have limited the use of dental amalgams for pregnant women and children (Beazoglou et al., 2007). Two recent clinical trials have shown no statistically significant differences in neurobehavioral or neuropsychological performance between children with and without dental amalgam fillings, although urinary total mercury levels were higher among those with dental amalgams (Bellinger et al., 2006; DeRouen et al., 2006; Bellinger et al., 2007; Woods et al., 2007). Children with amalgam fillings in one of two trials, however, had higher mean urinary concentration of albumin and increased microalbuminuria compared with children without amalgam fillings (Bellinger et al., 2006; Barregard et al., 2008).

A recent FDA staff draft white paper stated no scientific studies have demonstrated harm from dental amalgams (Food and Drug Administration, 2006). This conclusion, however, was questioned by a scientific advisory panel, which recommended a more extensive review, including data from other countries (Food and Drug Administration, 2006).

This issue is of special importance to policy makers in developing countries because use of alternative materials for restoration may be less feasible in their countries due to cost, storage, and dental expertise. This paper reports the results of a study on renal function, and neurobehavioral and neuropsychological performance of children with and without dental amalgams in Shanghai, China.

2. Materials and Methods

2.1. Subjects

The targeted population comprised all 435 students in grades 3 and 4 (age range: 7-11 years) as of May of 2004 in five elementary schools in Xuhui, Shanghai. Medical records containing annual medical and dental examination results were reviewed by school physicians and then shared with study staff.

Dental histories were extracted from the records of 408 children. Among them, 205 children who never received dental amalgam treatment were enrolled as referents. Details for each treatment (date, number of amalgam fillings, number of visible amalgam surfaces) for the 203 children who had amalgam treatment histories were reviewed by a dentist. Five children were excluded because of incomplete amalgam data, leaving 198 children who were included in the amalgam group. One parent of each child signed a written informed consent form. The protocol was approved by Office of Research, Fudan University; the analyses in this paper were designated exempt from any further clearance by the Office of Human Subjects Research at the U.S. National Institutes of Health. The student and parents were asked to complete a questionnaire about the child's demographics, lifestyle (frequency of consuming fish or eating hot food, and gum-chewing habits), and general health status.

2.2. Exposure Index

In addition to the urinary biomarker (described below), four approaches were used to evaluate exposure: time since first amalgam treatment, total number of amalgam fillings at the time of participation, total number of amalgam surfaces at the time of participation, and a cumulative exposure index. The cumulative exposure index was calculated as follows:

$$\text{Cumulative exposure index}=\sum Ni \times Ti$$

Where, N_i is the number of amalgam surfaces for *i* th amalgam filling and T_i is the number of months the *i* th filling was in place.

2.3. Laboratory Analysis

On the morning the questionnaire was administered, each child was asked to provide a spot urine sample (10 mL). Three hundred and sixty-two (90%) students (180 in the amalgam group and 182 in the referent group) provided a urine sample. The urine samples were sent to the laboratory on ice and frozen at −20°C until analysis. Total mercury concentration was measured using cold-vapor atomic absorption spectrophotometry (Ministry of Health, 1996). The limit of detection (LOD) was 0.5 μg/L. In 67 children (16.7%), the level was less than the LOD. When the level of urinary mercury was below the LOD, a value was imputed as the LOD divided by the square root of two. The recovery ranged from 80.0% to 111.3% and the intra-assay precision ranged from 2.7% to 5.1%.

Two biomarkers of renal function, albumin (ALB) and N-acetyl-β-D-glucosaminidase (NAG) activity (Price, 2000), were measured with enzyme-linked immunosorbent assay kits provided by Shanghai Debo Biotechnology Co. Ltd. Urinary creatinine concentrations were measured according to the method of Larsen et al. (Larsen, 1972). All urinary biomarker levels were adjusted for creatinine.

2.4. Neurobehavioral and Neuropsychological Assessment

2.4.1. Child Behavior Checklist (CBCL)—The Child Behavior Checklist (CBCL) is one of the most widely-used scales for assessing behavioral and emotional problems in children (Achenbach and Ruffle, 2000). Parents of all subjects completed the standardized form at home. The CBCL consists of 112 items which are scored on a 3-point scale ranging from not true (score=0) to often true (score=2). The CBCL includes measures of eight domains (subscales): anxiety/depression, withdrawal, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior. The CBCL also allows the examination of two broad groups of syndromes: internalizing problems (anxiety/depression, withdrawal, and somatic complaints) and externalizing problems (rule-breaking behavior and aggressive behavior). The Chinese version of the CBCL has been validated by Jin et al. (Jin et al., 1992) and has been used successfully in research and clinical settings in China. Standardized scores were calculated from raw scores for each subscale, the two syndromes, and for the total problems overall.

2.4.2. Eysenck Personality Questionnaire (EPQ)—The Eysenck Personality Questionnaire (EPQ) is a classic personality assessment tool (Eysenck and Eysenck, 1975; Barrett et al., 1998). The EPQ has 85 items, and measures four traits of personality: psychoticism, extraversion, neuroticism, and lying. The Chinese version of EPQ was previously validated (Gong, 1984). The EPQ was administered by trained interviewers to 400 students (197 students in the amalgam group and 203 students in the referent group). The raw scores for each subscale were standardized.

2.4.3. Intelligence test—We used the Chinese version of the self-test instrument "Test Your IQ" (Jin and Li, 1988). This test has 60 multiple-choice questions about language, figures, and numbers. These questions were designed to measure the general intelligence level of children. This test has been shown to have good validity (correlation coefficients >0.7 using the Wechsler scale as a gold standard), and good reliability (the intraclass correlation coefficients of two repeated measures of test components were 0.6-0.89) among Chinese students (Jin and Li, 1988). Thirteen children (3%) declined to take this test.

The latest test scores for two courses, Chinese and mathematics, were provided by school teachers to evaluate school academic performance.

2.5. Statistical Analysis

Children with dental amalgam were divided into low and high exposure groups using various exposure assessment approaches: the total number of amalgam fillings at the time of participation in this study (<=2 *vs.* >2), the total number of visible amalgam surfaces at the time of participation (<=2 *vs.* >2), time since first amalgam treatment (<=30 months *vs.* >30 months), and cumulative exposure index (<=60 visible surface-months *vs.* >60 visible surface-months). Because log 10 transformed urinary mercury concentrations were normally distributed, transformed levels were compared between children with and without amalgam fillings using a t-test. One-way analysis of variance was used to compare transformed levels among subsets of the amalgam group and the referent group. Multiple regression models of transformed urinary mercury level were fit to test each exposure index, controlling for age (continuous), sex, family income (3 categories: <1500, 1500-3000, >=3000 Chinese Yuan per month), consumption of fish (4 categories: <1, 1, 2-3,>=4 meals/week), hot food habit (yes vs. no), and gum chewing habit (yes vs. no). Potential confounders were selected according to prior knowledge about relationships between these factors and urinary mercury level, amalgam filling exposure, and the outcomes.

Creatinine-adjusted NAG activity and ALB concentration were compared between children with and without amalgam. Multiple regression models of log10 transformed levels of NAG and ALB were fit among all subjects, using amalgam filling status (yes vs. no) as an independent variable. Separate models were also fit among all subjects and children with amalgam respectively, using one of five continuous measures (urinary mercury level, time since first amalgam treatment, total number of amalgam fillings at the time of participation, total number of visible amalgam surfaces at the time of participation, and cumulative exposure index) as an independent variable. Children with ALB>30 mg/g Cr were considered as having microalbuminuria (Fingerhut, 2007). For NAG, activity of 20 U/g Cr (the 95th percentile of reference group) was used to define a higher level. The prevalence of microalbuminuria and high NAG activity was compared between the amalgam and the referent groups (Chi-square test). Logistic models were fit for microalbuminuria and high NAG activity using each exposure indicator as an independent variable. A priori, age (continuous), sex, family income (3 categories: <1500, 1500-3000, >=3000 Chinese Yuan per month), and fish consumption (4 categories: <1, 1, 2-3,>=4 meals/week) were adjusted in all linear and logistic regression models.

For neurobehavioral and neuropsychological outcomes (CBCL, EPQ, and IQ), standardized scores were compared between children with and without amalgam, controlling sex, age, grade (2 categories: grade 3 or grade 4), fish consumption (4 categories: <1, 1, 2-3,>=4 meals/week), parental education (3 categories: less than high school, high school, college), family income. School test scores were similarly analyzed. Multiple regression models for all these outcomes were fit among all subjects, using amalgam filling status (yes vs. no) as an independent variable. Separate models were also fit among all subjects and children with amalgam respectively, using one of five continuous measures (as above) as the independent variable. The interaction of amalgam exposure and socioeconomic level (family income) was tested in all models. All analyses were done using SPSS 15.0 (SPSS Inc., Chicago, IL).

3. Results

The characteristics of children with and without amalgam fillings were similar and there were no statistically significant differences (Table 1). Children in the amalgam group had, on average, 2 amalgam fillings (range=1-7) and 2 visible amalgam surfaces (range=0-12). The duration of amalgam exposure (time since first amalgam treatment) ranged from 1 to 96 months, with a median of 31 months. The median cumulative exposure index was 56 visible surface-months (range=0-514 visible surface-months).

The geometric mean level of urinary mercury was about 15% higher in the amalgam group (1.6 μg/g Cr) than in the referent group (1.4 μg/g Cr), but this difference was not statistically significant (p=0.11), as shown in Table 2. Amalgam filling status was not associated with urinary mercury levels in the multiple linear regression model, controlling for fish consumption and other covariates. The urinary mercury level in children who had amalgam treatment longer than 30 months (1.8 μg/g Cr) was higher than that in children who had shorter duration of amalgam treatment (1.3 μg/g Cr). When a multiple linear model was fit, exposure duration (time since first treatment) was also associated with log 10 transformed mercury level in urine (coefficient=0.003 log 10 μg/g Cr per month, p=0.01). Other exposure indices did not show any statistically significant associations.

Children with and without amalgam fillings had similar adjusted levels of NAG activity and ALB in multiple regression models (Table 3). NAG activity (creatinine adjusted) was related to urinary mercury level (coefficient=-0.037 log10 U/g Cr per 1 ug/g Cr mercury, p=0.03). However, when a creatinine unadjusted NAG activity model was fit including creatinine as a covariate, there was no association between urinary mercury level and NAG activity. The prevalence of high NAG activity (>20 U/g Cr) was 4.4% for the amalgam group and 6.0% for the reference group. The prevalence of microalbuminuria (ALB>30 mg/g Cr) was 5.0% for the amalgam group and 6.0% for the referent group. Logistic regression analysis showed no associations between amalgam exposure and risk of microalbuminuria or high NAG activity after controlling potential confounders (data not shown). None of the other four exposure indices was associated with NAG activity or ALB concentration. Similar results were found when these analyses were restricted to children with amalgam.

Children with and without amalgam fillings had similar adjusted scores on neurobehavioral and neuropsychological tests (Table 4). Likewise, no difference in IQ or school performance (Table 5) was found between the two groups. Parent education and family income were positively associated with children's IQ. The total number of amalgam filling at the time of participation was associated with the mathematics score (coefficient=0.62 point per amalgam, p=0.02) but not the Chinese score. There was no notable interaction between amalgam exposure and family income for any outcome. When fitting the models of IQ and school performance using urinary mercury level as an independent variable and controlling for potential confounders, associations were found neither among all children nor among children with amalgam (data not shown). Among children with amalgams, associations between the outcomes and the other continuous exposure indicators were also not present.

4. Discussion

After amalgam placement, the Hg^0 released is absorbed and then oxidized to inorganic divalent mercury (Hg^{++}) *in vivo* (International Program on Chemical Safety, 2003; Counter and Buchanan, 2004). The main route of excretion of elemental or inorganic mercury compounds is via the urine. Therefore, urine samples provide the best marker of body burden of mercury from low-level long-term exposure to elemental and inorganic mercury (International Program on Chemical Safety, 2003).

For children with and without amalgam fillings, urinary mercury concentrations were not statistically significantly different in the present study. The levels of mercury in urine in the present population were similar to those reported by DeRouen et al. (2006) but higher than those in the Bellinger et al. study (2006). Why levels were higher than in the Bellinger et al. study remains unclear. Urinary mercury levels in all three studies, however, were in the range of general background levels (<5 μg/g Cr) in unexposed populations (International Program on Chemical Safety, 2003). Previous studies in children have shown that urinary mercury concentrations were correlated with the number of amalgam fillings (Woods et al., 2007; Dunn et al., 2008). This association was not found in the present study or another study (Khordi-Mood et al., 2001). The null results may be because the number of amalgam surfaces in the mouth of children in the present study (median=2) was much less than that in the US (median=13) and Portugal (median=16) studies. But we did find that urinary mercury levels were positively related to time since first amalgam treatment. This finding is consistent with that in one of the two recent clinical trials (Woods et al., 2007). The mechanism of this association is unclear and may be related to cumulative deposition of inorganic mercury in the kidney and its excretion in urine.

Fish consumption, a primary source of methylmercury exposure, and other factors including sex, gum chewing, bruxism, and consumption of very hot food have been associated with urinary mercury levels (International Program on Chemical Safety, 1990, 2003; Woods et al., 2007; Dunn et al., 2008). We did not find effects of fish consumption or the other factors on urinary mercury concentrations in the present study. The null results on fish consumption may be due to the difference in fish species consumed across populations. Mercury levels in fish vary also in different areas (International Program on Chemical Safety, 1990).

The kidneys are sensitive to mercury because, as noted above, mercury bioaccumulates in them (Agency for Toxic Substances and Disease Registry, 1999). NAG is frequently used as a renal tubular function biomarker and ALB as a glomerular function biomarker (Price, 2000). Renal effects have been most often found among populations (mainly workers) with urinary mercury level greater than 30 μg/g Cr (International Program on Chemical Safety, 2003). But the renal effects of background level exposure among children are unclear. De Burbure et al. (2003) found no association between urinary mercury levels (with a mean of about 1μg/g Cr) and renal glomerular and tubular functional biomarkers including ALB and NAG among 400 French Children. This group then expanded their study to Poland and the Czech Republic where children had much lower mercury exposure levels and found urinary mercury was correlated with levels of renal tubular biomarkers in urine (NAG, retinol-binding protein, and Clara cell protein), controlling for lead and cadmium exposure (De Burbure et al., 2006). The latter report from De Burbure et al. (2006) was the first indicating effects of background-level mercury on NAG activity, suggesting that there may be no threshold level for an effect on NAG activity. Higher prevalence of microalbuminuria was observed among children in the amalgam group in one of the two trials noted above (Barregard et al., 2008). However, we did not find associations between any exposure indicator and either of the biomarkers of renal function. This might be due to the small number of amalgam fillings among children in the present study. Daily total mercury intake from amalgam generally is less than 5 μg, ranging from 1 to 27 μg (International Program on Chemical Safety, 2003). For children weighting 30 kg (mean weight of children in Shanghai), the corresponding daily intake per body weight is 0.17 μg/kg, much lower than the recommended minimum risk levels of chronic exposure (2 μg/kg/day) for renal effects of inorganic mercury .

In the present study, amalgam fillings were not associated with any adverse neurodevelopmental effects among children. Hg^0 is highly lipophilic and can readily cross blood-brain barrier; once it crosses, it is oxidized to Hg^{++} and can not cross back out. Due to mercury's neurotoxicity, the biggest concern is neurodevelopmental effects after placement of amalgam. Our findings of no association were consistent with two recent clinical trials. In the first study (DeRouen et al., 2006) conducted in Lisbon, Portugal, 507 children were randomly assigned to receive either amalgam (n=254) or mercury free composite (n=253) and were followed for 7 years (1997 to 2005). No statistically significant differences in neurobehavioral assessment (memory, attention, motor development, nerve conduction velocities) or intelligence were found between the two groups. The second study (Bellinger et al., 2006, 2007, 2008) conducted in two U.S. cities followed 534 children (267 for amalgam and 267 for resin composite) for 5 years. Likewise, there were no statistically significant differences in full-scale IQ scores, memory, or visuomotor ability between children with and without amalgam.

School performance was not associated with urinary mercury levels or amalgam filling status. The only observed association, between the total number of amalgam fillings and mathematics performance, was in the direction opposite of what was hypothesized and might be a random finding or due to multiple comparisons.

Amalgam is cheap, durable, and requires only basic dental technology. Banning amalgam would cause an increase in cost of dental care. According to estimates by Beazoglou et al. (2007), expenditures in the U.S. would increase $1.1 billion for children and $8.2 billion for the entire population in the first year of such a ban. A national survey in China showed that 29% of children between 5-15 years of age had dental caries, and 11% of them received treatment (Ministry of Health, 2007). Why the rate of receiving treatment is low is unclear, but economic burden and lack of dental service are believed to be the major reasons in undeveloped areas.

The present study is the first in China to evaluate health impact of dental amalgam among children. Several approaches were used to evaluate external and internal exposure levels, taking duration of exposure into account. We evaluated nephrotoxicity using sensitive renal function biomarkers, and neurobehavioral and neuropsychological performance using validated instruments. The self-administrated IQ test used in the study, however, may not have been as sensitive as traditional IQ tests. However, the validation study among Chinese students showed that the validity and the reliability was reasonably good (Jin and Li, 1988). To minimize exposure misclassification, each record was reviewed by a dentist and parents were asked to confirm the dental history. However, this study had several limitations. First, this is a cross sectional study. Thus, we cannot be certain that mercury exposure preceded any suboptimal status in the outcomes. This may cause a problem in causal inference, but it is unlikely that the outcomes studied affect amalgam treatment, especially because the results were adjusted for family income. Another issue is that some children in this study had had amalgam treatment for only a short time. Thus, any nephrotoxicy and neurotoxicity owing to low level mercury exposure might not have yet been manifest among those children. The second weakness is that the variation of urinary mercury levels from day to day will result in some misclassification due to using one sample as a measure of exposure. Third, this study may have had insufficient statistical power to detect subtle effects, due to the small sample size and the limited number of amalgam fillings. Fourth, in the statistical analyses, we controlled for potential confounders that were selected according to priori knowledge. However, because the subjects were not randomized to a treatment group, we can not exclude the possibility that residual confounding related to factors which were not measured might have masked a true association. Finally, the generalization of results of this study was limited due to: younger children (<8 years) who may be more vulnerable to mercury toxicity were not included; and the participants were children in Shanghai which is one of the most developed cities in China and may not represent the whole population.

In conclusion, although urinary mercury concentration was slightly elevated among children with amalgam fillings, we found no evidence of adverse effects on the outcomes evaluated. These results agree with those from recent trials in developed countries.

Acknowledgments

This study was funded by Xuhui Department of Health, Shanghai (02123 to X.Y.). This study was supported in part by the Intramural Research Program, National Institute of Environmental Health Sciences, National Institutes of Health.

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Table 1
Characteristics of children with and without amalgam fillings

	Amalgam Group (N=198)	Referent Group (N=205)
Age, mean± SD (year)	9.9±0.7	9.8±0.8
Gender, %		
Male	44.9	54.6
Female	55.1	45.4
Ethnicity, %		
Han	97.0	97.6
Others	3.0	2.4
Father's education, %		
Less than high school	14.3	20.6
High school	33.2	31.9
College	52.6	47.5
Mother 's education, %		
Less than high school	23.2	22.2
High school	33.3	36.0
College	43.4	41.9
Family income, %		
<1500 CNY/person/month [a]	27.6	29.1
1500-CNY/person/month	40.2	36.9
>=3000 CNY/person/month	32.2	34.0
Hot food consumption habit [b], %		
Yes	78.8	74.1
No	21.2	25.9
Gum chewing habit [c], %		
Yes	20.7	18.2
No	79.3	81.8
Bruxism habit, %		
Yes	5.0	6.0
No	94.5	94.6
Fish consumption, %		
<=1 meal/week	17.8	16.3
1 meal/week	23.8	23.6
2-3 meals/week	53.5	48.3
>=4 meals/week	5.0	11.8
Total number of amalgam fillings at the time of participation, median (range)	2 (1-7)	
Total number of visible amalgam surfaces at the time of participation, median (range)	2 (0-12)	
Time (months) since first amalgam treatment, median (range)	31 (1-96)	
Cumulative exposure index (visible surface-months), median (range)	56 (0-514)	

Percentages were calculated based on the numbers of subjects with data on this item

[a]CNY: Chinese Yuan

[b]Hot food consumption habit: answered “usually” to the question “How often do you eat foods, soups, and drinks when they are still hot?”.

[c]Gum chewing habit: Those answered “usually” to the question “How often do you chew gum?”.

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Table 2

Urinary mercury levels (μg/g Cr) among children with and without amalgam fillings

Group	N	Geometric Mean	Median	Range
Referent	182	1.4	1.2	0.3-16.6
Amalgam (total)	180	1.6	1.4	0.2-26.3
By total number of amalgams at the time of participation (N)				
<=2	116	1.7	1.5	0.2-26.3
>2	64	1.4	1.2	0.3-17.5
By total number of visible amalgam surfaces at the time of participation (N)				
<=2	90	1.7	1.7	0.2-26.3
>2	90	1.3	1.3	0.3-17.5
By time since first filling (months)				
<=30	84	1.3	1.1	0.2-26.3
>30	96	1 8[†, ‡]	1.7	0.3-16.6
By cumulative exposure dose (visible surface-months)				
<=60	91	1.5	1.3	0.2-26.3
>60	89	1.6	1.5	0.3-17.5

Note: Controlling for age, sex, family income, hot-food consumption, gum chewing, and fish consumption.

[†] P<0.05, compared to referents;

[‡] P<0.05 compared to <= 30 months group

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Table 3

Urinary ALB concentrations and NAG activity among children with and without amalgam fillings

Group	N	Urinary ALB concentration (mg/g Cr)			Urinary NAG activity (U/g Cr)		
		GM	**Median**	**Range**	**GM**	**Median**	**Range**
Amalgam	180	6.8	6.7	0.6-52.4	5.5	5.7	0.3-74.3
Reference	182	6.0	6.5	0.2-62.3	5.8	5.9	0.6-58.9

Abbreviations: GM, geometric mean; ALB, albumin; NAG, N-acetyl-β-D-glucosaminidase

Note: means shown are adjusted for age, sex, family income, and fish consumption.

Table 4

Neurobehavioral and neuropsychological test scores (standardized) in children with and without amalgam fillings*

Test	Group	
	Amalgam	Reference
Child Behavior Checklist (N)	198	205
Anxiety/Depression	49.8±9.5	50.5±9.7
Withdrawal	50.1±8.9	50.6±9.5
Somatic Complaints	50.7±9.1	50.1±8.9
Social Problems	49.4±8.7	51.1±9.5
Thought Problems	50.4±8.1	50.7±9.0
Attention Problems	50.1±9.5	49.9±9.6
Rule-breaking Behavior	50.8±8.1	50.6±8.2
Aggressive Behavior	49.9±9.5	50.2±10.2
Internalizing Problems	49.7±9.7	50.3±9.9
Externalizing Problems	50.0±9.4	50.3±10.1
Total Problems	49.8±9.7	50.3±10.1
Eysenck Personality Questionnaire (N)	197	203
Psychoticism	44.2±8.9	45.0±9.7
Extraversion	48.5±12.9	47.1±12.2
Neuroticism	45.6±10.4	46.8±9.8
Lying	55.2±9.2	54.1±8.1

*Controlling for age, sex, family income, fish consumption, parent education, and grade. None of the differences was statistically significant.

N: number of children

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Table 5

Adjusted intelligence and school performance of children with and without amalgam fillings*

Parameter	Amalgam	Reference
IQ	109±17 (191)‡	107±17 (197)
School performance		
Chinese	83±8 (169)	83±8 (167)
Mathematics	88±12 (168)	88±10 (167)

*No statistically significant differences were present, controlling for age, sex, family income, fish consumption, parent education, and grade.

‡Numbers in parentheses are sample sizes