Low Blood Lead Levels and educational achievement in 7-8 year old children in the Community of Madrid (Spain)

Bajos niveles de plomo en sangre y rendimiento escolar en niños de 7-8 años en la Comunidad de Madrid (España)

Baixos níveis de chumbo no sangue e sucesso escolar nas crianças entre os 7-8 anos na Comunidade de Madrid (Espanha)

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Cita: Ordóñez-Iriarte JM, Aparicio-Madre MI, Guillén Pérez JJ, Martínez García MJ. Low Blood Lead Levels and educational achievement in 7-8 year old children in the Community of Madrid (Spain). Rev salud ambient. 2013;13(1):12-21.

Recibido: 18 de octubre de 2012. **Aceptado:** 20 de marzo de 2013. **Publicado:** 28 de junio de 2013.

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Financiación: Este trabajo fue financiado mediante beca 93/908 del Fondo de Investigaciones Sanitarias.

Declaración de conflicto de intereses: Los autores declaran que no existen conflictos de intereses que hayan influido en la realización y la preparación de este trabajo.

Abstract

Background: Lead affects the behavioral and cognitive functions of children. The current lead safety level for avoiding these adverse effects is still controversial.
Methods of study: A cross-sectional study included 511 children from 23 primary schools within the *Comunidad de Madrid* (the Madrid Region –including the city of Madrid and the large urban-industrial conurbation of satellite towns surrounding it), Spain. The children's blood lead levels were determined by atomic absorption spectrophotometry. In addition, the teachers completed an eight-item questionnaire about the children's behavior and academic achievement. Parents filled in a self-completion survey about the sociodemographic variables of the children and the family.
Results: The mean Blood Lead Level (BLL) of the children was 4.1 µg/dL SD 1.6 µg/dL (log transformed 3.8 µg/dL SD 0.2 µg/dL). Multivariate analysis controlling for relevant sociodemographic cofactors (among others, sex, age and educational level of the parents) showed a negative association, but this was not statistically significant.
Conclusions: Despite the low blood lead levels found in the children of the *Comunidad de Madrid* (Spain) and the design limitations of the study, the results obtained suggest the existence of a harmful, but not statistically significant, effect of blood lead on the behavior and academic achievement of children.

Keywords: Blood lead levels; children; alteration of cognitive functions

Resumen

Objetivos: El plomo en sangre provoca en los niños efectos sobre las funciones cognitivas y sobre el comportamiento. No existe acuerdo sobre los niveles en sangre que evitarían esos efectos.
Métodos: Estudio transversal en el que participaron 511 niños pertenecientes a 23 colegios de la Comunidad de Madrid (la ciudad de

Madrid y su Corona Metropolitana), España, a los que se les determinaron los niveles de plomo en sangre por espectrofotometría de absorción atómica. Además, los profesores cumplimentaron un cuestionario de ocho preguntas sobre aspectos conductuales y de rendimiento académico de los niños. Los padres rellenaron a su vez una encuesta relativa a las variables sociodemográficas de los niños y su familia.
Resultados: El nivel medio de plomo en sangre fue de 4,1 µg/dL DE 1,6 µg/dL (log transformado 3,8 µg/dL, DE 0,2 µg/dL). El análisis multivariado controlando por cofactores sociodemográficos relevantes (entre otros, sexo, edad y nivel de educación de los padres) mostró una asociación negativa, pero sin significación estadística.
Conclusiones: A pesar de las bajas concentraciones de plomo encontradas en la sangre de los niños de la Comunidad de Madrid y de las limitaciones del diseño, los resultados obtenidos sugieren la existencia de un efecto nocivo del plomo en sangre sobre la conducta y el rendimiento académico de los niños, no significativo.

Palabras clave: Plomo en sangre; niños; alteraciones de las funciones cognitivas

Resumo

Enquadramento: O chumbo afeta as funções comportamentais e cognitivas das crianças. Não há consenso acerca do atual nível de segurança do chumbo que visa evitar estes efeitos adversos.
Métodos: Estudo transversal com 511 crianças de 23 escolas primárias da Comunidade de Madrid, Espanha (Região de Madrid - incluindo a cidade de Madrid e a aglomeração urbano-industrial das cidades satélites que a rodeiam). O nível de chumbo no sangue das crianças foi determinado por espectrofotometria de absorção atómica. Além disso, os professores responderam a um questionário de oito itens sobre o comportamento das crianças e desempenho escolar. Os pais preencheram um questionário sobre as variáveis sociodemográficas das crianças e da família.
Resultados: O nível médio de chumbo no sangue das crianças foi de 4,1 µg/dL SD 1,6 µg/dL (log transformado 3,8 µg/dL SD 0,2 µg/dL). A análise multivariada controlada pelas variáveis sociodemográficas (idade, sexo e nível de escolaridade dos pais, entre outros) mostrou uma associação negativa, mas esta não foi estatisticamente significativa.
Conclusões: Apesar dos baixos níveis de chumbo encontrados no sangue das crianças da Comunidade de Madrid (Espanha) e das limitações do desenho do estudo os resultados obtidos, embora não estatisticamente significativos, sugerem a existência de efeitos nocivos do chumbo no sangue das crianças sobre o seu comportamento e desempenho escolar.

Palavras-chave: Níveis de chumbo no sangue; crianças; alteração das funções cognitivas.

INTRODUCTION

Lead is a toxic element for humans. According to the US Agency for Toxic Substances and Diseases Registry[1], this toxicity presents several clinical manifestations that are expressed even at very low BLLs, traditionally considered to be safe[2]. One of the most severe effects is neurological disturbance[3]. It has recently been shown that lead-induced neurological effects include not only clear alterations in brain functions, but also physical brain alterations[4]; both have been demonstrated in studies in animals[5] and in humans[6]. Therefore, it can be assumed that lead produces cognitive and behavioral alterations in children, which could be reflected by a reduction of several points in the intellectual coefficient, as well as by an increase in the frequency of hyperactivity and violent behavior of the children[7-9].

The importance of the effects of lead at increasingly low levels, caused the World Health Organization[7] and the US Centers for Diseases Control and Prevention (CDC)[8] to progressively reduce the BLLs considered safe for children from 60 µg/dL in the 1960s to 10 µg/dL in 1991, which is still the accepted level, despite critical reservations[9,10].

Several research studies[11-14] have called into question the protective capacity of this threshold level in relation to specific neurotoxic effects and their repercussion on intelligence and behavior, as adverse effects have been seen at lead levels below this threshold. The lack of studies and, therefore, of a well-defined lead dose-response curve for below 10 µg/dL, as well as the analytical problems in detecting lead levels below this threshold, have meant that the CDC has not yet modified this blood lead threshold value[15].

The Madrid Region is located in central Spain and has a current population of 6 100 000 inhabitants. There is a large urban-industrial conurbation around the city of Madrid with numerous satellite towns forming the *Corona Metropolitana*. These circumstances could produce a considerable potential for lead exposure among the population, which makes it necessary to find out the extent of the problem, to determine the real level of effect as well as the main factors involved.

Our study aims to find out the assessable specific toxic effects of low-level lead exposure on the cognitive-behavioral development in children of the Madrid Region.

METHODOLOGY

a. Type of study

A cross-sectional study was used and carried out between March and December 1995. The general methodology of this study has been described previously[16].

b. Study population

In 1995, the population of children of 7 and 8 years of age in the Comunidad de Madrid (Madrid Region) was 103 377 (Institute of Statistics of the Comunidad de Madrid), with most of them enrolled in the second year of Primary Education; 48 975 (47.4 %) lived in the city of Madrid, 43 492 (42.1 %) in the municipalities within the Corona Metropolitana and 10 910 (10.6 %) in the remaining municipalities within the region. These children attended a total of 1345 primary schools, with the sample selection limited to those primary schools in the city of Madrid and the Corona Metropolitana.

c. Sample

A simple conglomerate type of sample was used, selecting the classes of a predetermined level. Twenty-three educational centers were chosen randomly, 13 in the city of Madrid and 10 in the *Corona Metropolitana.*

d. Recruitment of children and the biological tests

Members of the research team met with the parents in the primary schools and distributed self-completion questionnaires that gathered information about various sociodemographic and environmental aspects of the family, based on a limited number of questions. On the selected day, the children with written authorization were transferred by school bus to the collaborating hospital "Gregorio Marañón", where specialized nursing staff undertook blood collection (10 mL). A basic clinical examination was carried out for each child.

e. Studied outcomes

To find out the repercussion of lead on behavior and educational achievement, the teachers completed a questionnaire about all the children in the selected class, before blood collection was carried out. The questions were based on previously applied methods[17].

The responses had to be completed taking into account the average score for children of that age. The survey had two different sections; the first assessed the attention and attitude of the children, with the following questions: a1.- Does the child finish tasks he/she has started?; a2.- Is the child easily distracted?; a3.- Does the child have problems keeping still when seated?; and a4.- Does the child exhibit restless and anxious behavior? The responses were: "never", "seldom", "average", "often" and "always". A consecutive number from 1 to 5 was assigned to these responses, to allow numerical handling and to be able to present the results in a synthetic way (e.g.: means).

The second section had questions about academic achievement, with values from 1 (minimum) to 5 (maximum), with 3 being "average". It included the following areas of assessment: b1.-Reading comprehension; b2.-Oral expression; b3.-Writing ability and b4.-Mathematics. Given that the test was undertaken prior to the hospital visit, any selection bias could be measured between the children who participated and those that did not.

f. Laboratory analysis

The blood samples for the lead analysis were collected in vacuum tubes (Venoject Terumo®, of 5 mL -VT-050SHL- with 75 USP units of lithium heparin), and were refrigerated until their analysis by atomic absorption spectrophotometry in a graphite oven with correction for the Zeeman effect (Perkin-Elmer Zeeman/3030). The average precision of the method for the 0.2-1.6 µg/dL interval was 10 µg/dL. The detection limit was set at 1.5 µg/dL. Samples with figures below detection were assigned a value of 1.0 µg/dL. The analytical laboratory was taking part in several international quality control programs.

- Statistical analysis. Data were stored and cleaned in standard databases and processed using the SPSS 14.0 and EpiInfo V6 statistical packages. To describe the variables, means and 95 % confidence intervals for the means, were calculated. Log-transformed lead data were used, except for multilinear regressions, when untransformed data were used. Multiple regression analyses were carried out to study the repercussions of blood lead levels on the assessments of behavior and academic achievement, controlling for various cofactors. In these regressions, the numerical academic assessment scores were treat as a dependent variable; for assessment of aspects of behavior, their numerical correlates were used.

Synthetic indices were prepared to assess both behavior and academic achievement in an overall numerical way. The overall assessment of behavior was constructed by subtracting the sum of the other behavioral variables ('ease of distraction' + 'restlessness in class' + 'restless behavior') from the value for 'finishing tasks' (with values ranging from -14 to 2); the overall index for assessing academic achievement was calculated by the simple sum of the scores obtained for each one of the categories (with values ranging from 4 to 20).

RESULTS

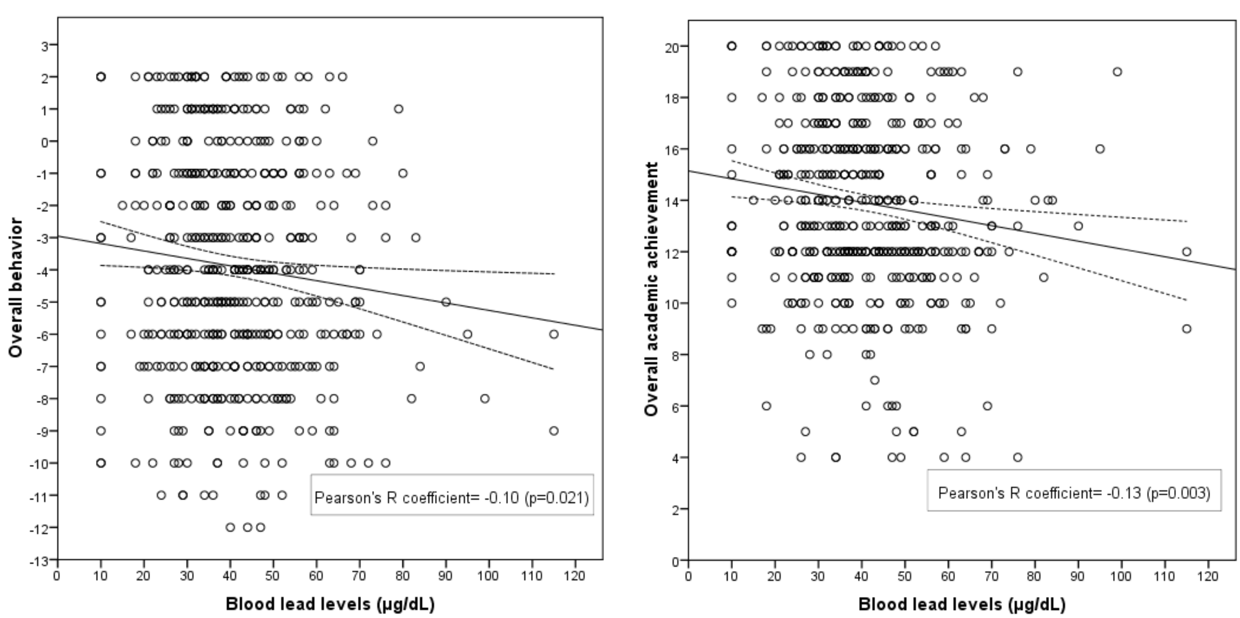
The 23 sampled primary schools had 834 children at the school age for the study, of which 525 (62.9 %) were authorized to participate. Blood samples and completed questionnaires on academic assessment were obtained for a final number (n) of 511 participating children. Some 58.3 % of the children (n=298) lived in the city of Madrid; the remaining children (n=213) were from the *Corona Metropolitana*. In terms of gender, boys predominated (62.7 %), not because of a higher response rate, but because of a majority in the primary school classes studied (61.3 % of males overall, *p*=n.s.). Average age was around 92.0 months (SD 4.8 months), without significant gender differences.

As an overall assessment of all the children in the classes was available, bias could be controlled. There was a greater but non-significant female presence among those not participating. The children not participating in the study had worse assessments in all categories, which were not significant in the behavioral parameters, but were significant in the academic assessments ($p < 0.01$).

Table 1 shows the sociodemographic characteristics of the sample and their relationship with BLLs. The mean BLL of the children was 4.1 µg/dL (SD 1.6 µg/dL), and the log-transformed BLL was 3.8 µg/dL (SD 0.2 µg/dL). The main factors influencing the variation of this BLL were the age of the children, with a significant decrease for each month of life, and their home address, with higher levels for those living in the city of Madrid and lower levels for those who had a cat as a pet.

Figure 1 describes the relationship between the indices for behavior and academic achievement. The girls had better scores than the boys in all categories; although in reading comprehension and mathematics these differences did not reach statistical significance. The children of the city of Madrid had worse assessments from their teachers in all categories ($p<0.01$), as compared to the children of the *Corona Metropolitana*. Age has a strong direct association with the parameters of behavior and academic achievement. Yet, nursery or preschool attendance was associated with worse results for behavior in boys, but had little repercussion on the assessment of academic achievement.

Figure 1. Relationship of the blood lead levels of 7-8 year old children in the Madrid Region with the teachers' overall assessment parameters for behavior and academic achievement. Straight-line adjustment with 95% CI and correlation coefficients



Left-hand figure, Overall assessment of behavior = Value for finishing tasks – Ease of distraction – Difficulties in keeping still – Restless behavior.
Right-hand figure, Overall assessment of academic achievement = Reading comprehension + Oral expression + Writing ability + Mathematics.
Correlation coefficients: p value in brackets. Straight-line regression with 95%

Table 1. Main sociodemographic characteristics of parents and children and their relationship with blood lead levels

Sociademographic characteristics of the children, parents and their surroundings		Number[*]/ Mean	Blood lead level (μg/dL) [**]	p
- Global BLL:	• Arithmetic mean • Geometric mean	511 511	4,1 (1,6) 3,8 (0,2)	
- Gender (*n*):	• Boys • Girls	297 214	3.9 (0.2) 3.7 (0.2)	0.087
- Age (*months, SD*[***]):		92.0 (4.8)	-0.09	0.003
- Home address:	• City of Madrid • *Corona Metropolitana*	298 213	4.0 (0.1) 3.5 (0.2)	0.000
- Nursery/preschool attendance (*n*):	• Yes • No	458 52	3.8 (0.2) 3.7 (0.2)	n.s.
- Nursery/preschool attendance (*years*, SD):		2.4 (1.3)	0.04	n.s.
- Use of School Cafeteria (*n*):	• Yes • No	126 215	4.0 (0.2) 3.9 (0.2)	n.s.
- Age (*years*, SD):	• Fathers • Mothers	42.8 (16.8) 37.8 (12.4)	0.04 0.00	n.s. n.s.
- Educational level (*n*):				
• Fathers:	• Illiterate/ Primary Ed. or Incomplete Sec. Ed. • Equiv. Junior High School/Vocational Training Level 1 • Equiv. High School Graduate/ VT Level 2 • University Graduate	74 218 80 86	3.9 (0.1) 3.8 (0.2) 3.5 (0.1) 3.9 (0.1)	n.s.
• Mothers:	• Illiterate/ Primary Ed. or Incomplete Sec. Ed. • Equiv. Junior High School/Vocational Training Level 1 • Equiv. High School Graduate/ VT Level 2. • University Graduate	93 244 93 56	4.1 (0.1) 3.7 (0.2) 3.8 (0.1) 3.7 (0.1)	n.s.
- Employment situation (*n*):				
• Fathers:	• Actively employed • Unemployed/ retired/ disability pension/ housework	438 30	3.8 (0.1) 3.9 (0.1)	n.s.
• Mothers:	• Actively employed • Unemployed/ retired/ disability pension/ housework	179 313	3.8 (0.1) 3.8 (0.1)	n.s.
- Tobacco Smoking (*n*):				
• Fathers:	• Non-smoker (including ex-smokers) • Smokers	192 278	3.9 (0.1) 3.6 (0.1)	0.089
• Mothers:	• Non-smoker (including ex-smokers) • Smokers	241 251	3.9 (0.1) 3.7 (0.1)	0.081
- Pets:				
• Dogs:	• Yes • No	59 442	3.8 (0.2) 3.8 (0.1)	n.s.
• Cats:	• Yes • No	32 468	3.2 (0.2) 3.8 (0.1)	0.010
• Others:	• Yes • No	218 286	3.7 (0.1) 3.9 (0.1)	n.s.

[*] = In the numerical breakdowns, up to n=511 belong to the category "unknown". [**] = All means are geometric, except for the global arithmetic mean. [***] = Standard deviation.

The educational level of the parents resulted in a direct correlation with the teachers' assessment, often in a statistically significant way. Moreover, there are negative associations with tobacco smoking by the parents; these assessments were made significant in differentiated ways; smoking by the father seems to have greater repercussion on the academic data, while smoking by the mother had more effect on the behavioral assessment. The presence of pets was found to be negatively associated with behavior as well as the academic results of the children.

Table 2 shows the results of the multiple regression analysis of BLLs and the teachers' assessments, controlling for various sociodemographic factors. In these results, the strength of the negative correlation between BLL and the teachers' assessments was directional, but weak. Only reading comprehension and mathematics are close to statistical significance (p=0.069 and p=0.082, respectively). Among the variables that are most strongly associated to the teachers' assessments, the greatest determinant is home address, which shows worse scores for the children living in the city of Madrid; followed by gender of the children, especially for behavioral variables, the presence of some pets and, to a lesser extent, the educational level of the parents.

Table 2. Blood lead levels (BLL) in children and the teachers' assessments of behavior and academic achievement: regression coefficients of BLL and sociodemographic variables in multivariate analysis

	Regression coefficients									
	Behavioral assessment					Assessment of academic achievement				
	Finishing of tasks	Ease of distraction	Difficulties keeping still when seated	Restless behavior	Overall behavior	Reading compre-hension	Oral expression	Writing ability	Mathematics	Overall academic achieve-ment
- Blood lead level	-0.032	0.024	0.020	0.036	-0.112	-0.058*	-0.001	-0.044	-0.054*	-0.158
- Age (in months):	0.027**	-0.013	-0.007	-0.019*	0.052	0.011	0.007	0.018*	0.007	0.044
- Gender	-0.218**	0.256***	0.300***	0.357***	-1.131***	-0.083	-0.160*	-0.410***	0.048	-0.605*
- Residence (City of Madrid and Corona Metropolitana)	-0.210*	0.376***	0.503***	0.375***	-1.464***	-0.566***	-0.559***	-0.485***	-0.495***	-2.104***
- Nursery/preschool attendance (yes/no):	0.024	0.144	0.125	0.007	-0.252	-0.054	0.039	0.008	-0.108	-0.115
- Nursery/preschool attendance (years)	-0.108*	0.038	0.073**	0.122**	-0.340**	-0.018	0.019	0.004	0.065	0.064
- Age of parents (years):										
• Fathers	0.008	-0.018	0.000	-0.020	0.046	0.036**	0.027**	0.012	0.028**	0.103**
• Mothers	-0.006	0.009	-0.017	-0.009	0.011	-0.034**	-0.025*	-0.007	-0.023	-0.088
- Educational level (4-level scale):										
• Fathers	0.178**	-0.105	-0.120*	-0.110*	0.514**	0.015	0.045	0.143**	0.150**	0.353
• Mothers	0.048	-0.095	-0.038	-0.053	0.234	0.108	0.133*	0.106	0.113	0.460*
- Employment situation (actively employed/ unemployed):										
• Fathers:	0.103	0.056	-0.122	-0.119	0.288	-0.214	-0.098	0.050	-0.004	-0.265
• Mothers:	-0.019	0.009	0.140	0.068	-0.236	-0.037	0.098	0.028	0.062	0.150
- Tobacco smoking (yes/no):										
• Fathers:	-0.045	0.053	0.119	0.128	-0.346	-0.046	-0.075	-0.078	-0.101	-0.301
• Mothers:	-0.024	0.018	-0.042	-0.054	-0.054	-0.024	0.019	-0.027	-0.020	-0.013
- Pets (yes/no):										
• Dogs:	-0.336*	0.352**	0.375**	0.228	-1.290**	-0.463***	-0.426***	-0.472***	-0.391***	-1.752***
• Cats:	-0.194	-0.034	0.205	0.084	-0.450	-0.083	-0.011	0.038	-0.090	-0.116
• Other pets:	-0.330***	0.171*	0.180*	0.253***	-0.935***	-0.255***	-0.163*	-0.273***	-0.243**	-0.934***

n=430; * = p≤0.10; ** = p≤0.05; *** = p≤0.01

DISCUSSION

The results of this study show that BLLs, much lower than those considered safe by the CDC, are associated with negative effects on the behavior and academic achievement of 7-8 year old children, but this association is not statistically significant.

This relationship occurs with low BLLs in the children of the Madrid Region (a log mean of 3.8 µg/dL), which are comparable in size to those of other western countries[18,19], and that are the result of the banning of leaded gasoline among other factors. The developing countries are still far from achieving such low figures, their population problem is even more important[20-23], and there is much more evidence of these effects on intellectual impairment and behavioral problems.

The negative associations found between BLLs and the parameters for behavior and educational achievement concur with the results of both recent follow-up studies[12,14,13] and cross-sectional studies like ours[24,25], which show that the onset of this effect is at levels considerably below the 10 µg/dL threshold established by the CDC. When possible neurocognitive damage is extrapolated to the population level, the number of children who could possibly be affected is very high[26].

Prenatal[27,28] and postnatal[14,12] studies suggest that low BLLs can be the most damaging. Our study finds this correlation for academic assessment, but not for behavioral problems, with higher BLLs causing worse behavior. This perhaps could be explained because there are fewer figures for BLLs higher than 8 µg/dL that condition a greater damage in the range above 5 µg/dL.

Adjustment of the relationship between BLLs and neurocognitive damage should take into consideration a substantial number of cofactors, but as these cofactors are added, the strength of the relationship is increasingly affected[29]. In our study, one of the most important cofactors is the home address of the children: city of Madrid vs. the *Corona Metropolitana*. This important cofactor appears to be an indicator of a large number of other factors associated to it, which reflect the difference in socioeconomic level between the two environmental areas. Even the teachers' assessments have drastic differences, which negatively affects the children of the city of Madrid.

Moreover, this important factor could also act as an overmatching effect, as it involves other factors such as older housing (and, consequently, with a greater risk of having lead piping), higher exposure to traffic[30], etc., which are direct factors in the causal relationship between blood lead and intellectual damage and, therefore, data should be handled with care[31].

Measurement of lead was undertaken for children of 7-8 years of age, and it is known[32,9] that maximum BLLs are reached around two years of age, followed by a continuous decline. Therefore, the children of this study could have reached average BLLs of around 6-7 µg/dL at two years of age. At such levels, a fair percentage of them could have had previous levels higher than 10 µg/dL. Here again is the old dilemma, are the effects of the lead from current exposure or are they derived from the maximum exposure to the metal that occurred in early infancy? The studies of Chen et al[33] indicated that, even though the neurological damage could be an old one, the effects are continuous and more noticeable with time. However, the production of negative effects at very low lead levels appears to have its origin in the womb, during pregnancy[34,28], although other studies[35] have not found this association. It seems that cognitive impairment not only affects children, but also adults at various levels[36], even very low ones[37]. As with other aspects of the neuropathology of lead, there are insufficient studies to evaluate the timing of its effects[9].

An unexpected result was the role played by pets. Usually, the toxic levels in pets will be interpreted as markers of the same levels for their owners[38]. There has been little research into the association between pets and the teachers' assessments of normal children, but in our study dogs and other pets (excluding cats) have been shown to be excellent markers of worse results.

The techniques normally used in the study of the neurological damage due to lead include the use of specific fairly sophisticated tools, such as intelligence tests, which are given to the parents and main educational staff, as well as to the children in the study[39,40,13], as a compulsory control of one of the most relevant cofactors. Moreover, when measurement of the effect of lead is not undertaken in a direct way, but by teachers' assessments, the Rutter test or Conners Rating Scales have been used[33]. Both of these methods have a larger number of questions and, consequently, need more time to be completed, and have mainly been used to assess behavioral impairment[41,33,17].

The tool used in our study is very rapid and extremely simple, but still demonstrated its usefulness for highlighting complex sociodemographic data, such as a clear difference between the assessments of the children of the city of Madrid and those of the *Corona Metropolitana*. This difference was reflected by several variables, which were mainly manifested by effects on the behavioral assessments of the children, with those for the children of the city of Madrid being much worse.

These studies have found associations between lead levels and behavioral parameters using a relatively simple tool like teachers' assessment[42]. However, the tool has numerous and varied limitations. For example, in the assessment of the behavior scale, the results for finishing school tasks were clearly asymmetric, so that the scale could be fairly inadequate. Nevertheless, in the adjusted statistical analyses, the results have shown that the relationship between lead levels with the behavior and academic achievement of the children is negative, but is unable to achieve significant associations, although the trends of the coefficients indicate toxic effects at low lead levels.

Another drawback is the cross-sectional type of study, which can have important limitations on the cause-effect analysis of lead at very low levels[43].

The sample design of the study, for obtaining the blood lead levels of children, had several identifiable biases, some of which had possible repercussions on the teachers' assessments of behavior and academic achievement. The first bias was that caused by the absence of children from more rural areas, and were excluded because of their greater geographical distance. However, this rural population was not very important in numerical terms. The second bias was the absence of children from private primary schools, with children from the upper social classes, who in our analytical parameters would have had to be included with the children living in the center of Madrid, and were the children of parents with a very high educational level. This profile did not seem to have had repercussions in the evaluation of BLL, as no differences were seen on the basis of the sociocultural level of both parents. The third bias to be taken into account was that of the children not-authorized to take part in the study by their parents, which tended to act as a protection of those children with worse academic scores. If an a priori assumption was made of an association between high BLLs and worse teachers' assessments, possibly the children with the highest BLLs would have been excluded from the study. However, given the low BLLs found, the bias regarding population evaluation should be considered as of little importance, with the differences not reaching 1 µg/dL. Nevertheless, these biases could have acted in a more relevant way that was detrimental to the strength of the association of BLLs with behavior and academic achievement, as the presence of these non-authorized children, with possible BLL values in the range of 5-10 µg/dL, would have been of considerable interest when establishing the strength of the associations.

Another bias could be the time of year when the study was undertaken. It was carried out at the end of the school year for the children in the *Corona Metropolitana*, who were therefore older within the age range, versus the children of the city of Madrid, who were tested at the beginning of the same school year, and were, consequently somewhat younger within the age range. This could have slightly increased the evaluation of the BLLs in the population of the *Corona Metropolitana*.

In the controversial debate about the safety threshold for BLLs, our study suggests that even fairly unsophisticated tools appear to show the damaging effects at very low lead doses, further reinforcing the need to undertake research about the adverse effects of low lead levels and to reduce the lead levels considered to be safe.

ACKNOWLEDGEMENTS

The authors wish to thank all the children who took part in the study, as well as their parents and the directors and teachers of the primary schools involved. We especially wish to thank to the health professionals of the Pediatrics Department of Gregorio Marañón University Teaching Hospital, led by Dr I. Villa Elízaga and Dr Vicente Climent and the nursing staff who collaborated in the study.

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