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Faculty of Medicine and Life Sciences

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Master of Biomedical Sciences

Master's thesis

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Adriana Soza Torrico

Thesis presented in fulfillment of the requirements for the degree of Master of Biomedical Sciences, specialization Environmental Health Sciences

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Association between black carbon exposure and neurocognitive outcomes in 4- to 6-year-old children from a peri-urban area of Cochabamba, Bolivia

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*Running title: *Black carbon and cognition in Bolivian children*

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ABSTRACT

Black Carbon (BC), a combustion-derived pollutant, has been linked to neurodegeneration and cognitive decline. Although 58% of Latin America's population lives in areas exceeding WHO air quality guidelines, the impact of BC on child cognition remains underexplored. In Bolivia, $PM_{2.5}$ is unregulated, and concentrations in Cochabamba range from 50 to 120 µg/m³, suggesting significant BC exposure. This study assessed the association between urinary BC levels and cognitive performance in children aged 4–6 years in Cochabamba. Participants (n = 55; 30 boys, 25 girls; mean age = 5.27 ± 1.01 years) were recruited via door-to-door health surveys and a mobile unit. Most were Quechua (74.5%) and lived in poverty (72.73%); 13 had no formal education. Lifestyle, socioeconomic factors, and behavior were recorded via questionnaire. Cognition was assessed using a culturally adapted Rapid Assessment of Cognitive Impairment and eye-tracking. Time viewed (Tv%) on correct answers served as a proxy for cognitive load across six domains. Urinary BC (particles/ml) was measured via inverted laser-scanning microscopy (mean = 106,971,136; SD = 168,163,890). Linear regression showed no significant association with total Tv% (β = -0.0066, p = 0.773). However, quantile-based g-computation revealed significant negative associations in memory (B = -0.182, p = 0.04) and visuospatial function I (B = -0.134, p = 0.03), for the combined effect of BC and Unmet Basic Needs index NBI. . These results suggest that the neurotoxic effect of BC is amplified by structural conditions of inequality, characteristic of many peri-urban areas of Latin America.

INTRODUCTION

Air pollution is one of the principal threats to public health due to its widespread presence, which is increased by the accelerated pace of economic and industrial development. Each year, over 8.8 million deaths are linked to air pollution, primarily through its contribution to respiratory and cardiovascular diseases(1). Furthermore, air pollution has also been associated with cognitive impairment and with pathologies characteristic of neurodegeneration (2). Its effects in early childhood, a crucial time, of rapid growth, neurodevelopment, and poor protective mechanisms are especially concerning (3–6).

Between air pollutants, Black Carbon (BC), a combustion-derived particle matter with a size range between 10 to 50 nanometers, is especially harmful due to its ability to translocate into the central nervous system (CNS) through the nasal olfactory bulb and by crossing the blood-brain barrier (7,8). BC may trigger an immunological reaction, leading to oxidative stress and inflammation, damaging neurons, and resulting in neurodegeneration(9–12). Studies on BC exposure and cognitive functioning in children have varied results, but often reported associations between BC and worse cognitive outcomes(4,13–21). Evidence suggests a negative association between BC and attention, working memory, and executive function (13,15,16,19,21). Nonetheless, some studies reported a negative association only for boys or not at all (14,17,18,20). The variety in findings may, in part, be explained by individual variability, diversity of tests used, or/and different exposure levels between studies. This inconsistency may also reflect the difficulty of detecting subtle cognitive changes through conventional performance-based tests, particularly in populations with relatively low exposure levels.

Cognitive function depends on the synchrony of different parts of the brain. An effect on cognitive function is the end of a cascade of different processes that went wrong. Moreover, children with different experiences and abilities can handle the same task in different ways (22). Cognitive workload (CW) is described as a quantitative measure of the amount of mental effort necessary to perform a task and can be interpreted as a step before cognitive decline(23). CW offers a window into the cognitive processes leading up to conventional cognitive function tests, revealing subtle or early impairments that might otherwise go unnoticed. CW has recently gained more attention due to its practicality. Using eye tracking to measure task-evoked pupillary responses related to CW offers a more sensitive and dynamic measure of early cognitive strain(24). In this study, CW will be assessed

Despite the growing evidence linking black carbon (BC) to cognitive function, there is a critical lack of studies conducted in the Global South, where air pollution levels are often higher(25,26). In Latin America, approximately 172 million people, or 58% of the population, live in areas with air pollution levels exceeding the WHO Air Quality Guidelines (AQG) of 10 µg/m³ annual average. Among this population, about 12 million are children under five years (27). In Bolivia, $PM^{2.5}$ is still not monitored or regulated(28), and in Cochabamba, PM^{10} concentrations from road traffic ranged from 50 to 120 µg/m³(29). La Maica is a pre-urban region located in Cochabamba, Bolivia, with 1,420 inhabitants, characterized by mixed land use, low-income households, and limited environmental monitoring. Children from this area may be exposed to high concentrations of BC, as indicated by elevated PM^{10} levels in the region.

This study evaluates the association between BC and cognitive functions in 4 to 6-year-old children from La Maica, Bolivia. Furthermore, generating evidence in this underrepresented region is essential to fill a critical research gap (25,26), improve the external validity of environmental neurotoxicity findings, and clarify the impact of BC. At the local level, the findings will help drive local and national initiatives, such as the monitoring of $PM^{2.5}$ particles, and support improvements in the quality of life for people in the area by enabling decision-making based on scientific evidence. Additionally, conventional cognitive tests may not detect early, subtle alterations. The use of eye-tracking to measure cognitive workload offers a sensitive and innovative method that remains unexplored in environmental health research regarding vulnerable populations.

EXPERIMENTAL PROCEDURES

Participant recruitment and eligibility criteria

The study was presented to local authorities in the communities of Maica Norte, Maica Kaspichaca, Asociación Bolivia, Maica Central, and Maica Chica. Upon approval, informative videos and images were distributed through each community's internal communication channels to build trust and encourage participation.

Initially a door-to-door health survey was conducted by trained volunteers covering the entire area and reaching 500 families. Based on the collected data, 75 families that met the inclusion criteria were identified and contacted via phone calls and WhatsApp messages and were invited to the hospital Elizabeth Seton. To further increase engagement, a Christmas event was held. Despite the efforts only 10 families agreed to participate, consequently a mobile unit was deployed to continue with the recruitment and conduct a home base evaluation. A total of 68 children aged 4 to 6 years at the moment of assessment (between December 2024 – March 2025) were recruited. Only children with good health, and sufficient cooperation and language skills (Spanish) to complete the assessments were considered. At least one of the parents were also required to be able to read, write and speak Spanish. Children with cognitive and physical impairments were excluded (Figure 1).

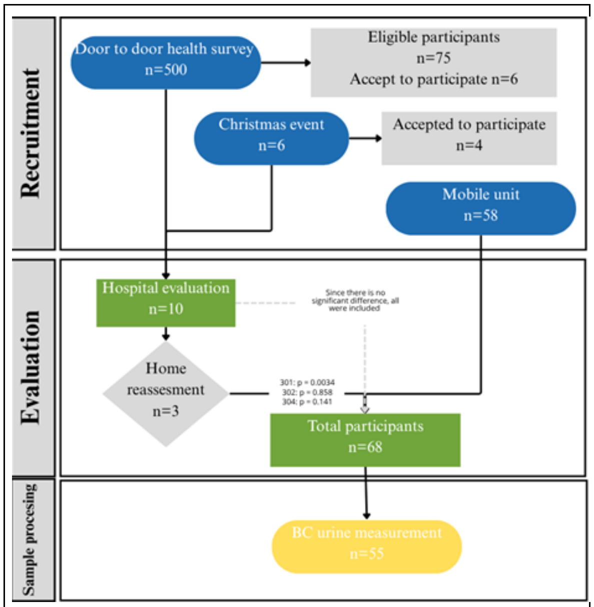


Figure 1. Flowchart of the selection process and recruited participants.

Data collection

Assessment setting

Children recruited through the initial strategies were evaluated in Elizabeth Seton Hospital. Those enrolled via the mobile unit were evaluated in their homes using a portable setup SUP 1. To evaluate data consistency across settings, three hospital-assed children were reevaluated in their homes to determine the inclusion validity of hospital-based data.

Questionnaire data

A general questionnaire was used to gather information on lifestyle, dietary habits, socioeconomic status and children behaviour. It includes date of birth, sex, weight, height, ethnicity (quechua, aymara, mestizo, other), exposure to second hand smoking (y/n), previous medical diagnoses of mental illness (y/n), screen time (1,3a5 8). Parental education level was classified according to the International Standard Classification of Education (ISCED) levels (ISCED 0-8) and grouped as low, medium or high (30,31). Socio economic status was calculated using the Unmet Basic Needs Index (NBI) (32–35). Additionally children behavior was asses by applying the Conners Rating Scale for Parents (Conners CBRS) (36). Vital signs and anthropometric measurements were recorded, including five blood pressure readings, heart rate, respiratory rate, weight, and height. BMI was calculated by dividing the weight (kilograms) by the square of height in meters and categorize in underweight, healthy weight, and overweight (37).

Cognitive outcomes

Cognitive workload was assed using an adapted version of the Rapid Assessment of Cognitive Impairment (38) designed for Gazepoint GP3 HD eye tracker (60Hz) (39). The adaptation includes language and cultural considerations for the study population. Children sat in front of the monitor and followed spoken and written instructions on the screen. An eye position calibration (9-points) was used to ensure accuracy. Fourteen tasks were displayed to target seven cognitive domains SUP 2. Two versions of the test were used:

1. *Attention and calculation*

Fruits and Vegetables (apples, bananas, corn or tomatoes) were displayed in the screen. Children were asked to count the items and fixate on the correct number displayed afterwards. on the monitor. This task evaluated visual attention, basic numeracy, and sustained focus.

2. *Memory*

Five animals are displayed on the screen. A red cube moves over each one and stops randomly. Later children are asked to remember the animal chosen at the beginning. This task assessed encoding, retention, and retrieval of visual information.

3. *Deductive reasoning*

Six objects are displayed on the screen. Children are instructed to focus on the object that does not belong categorically (e.g. five bottles and one cup). This task evaluated categorical reasoning and logical inference.

4. *Visual working memory*

An intersecting double geometric figure (pentagon or square) is displayed on the monitor; children are instructed to locate the pair matching the initial figure from a set of distinct intersecting orientation figures. This task targeted visual discrimination and short-term memory updating.

5. *Visuospatial function I-Figure search*

A Rhomb and a red L were displayed in the monitor. Children were instructed to locate and focus on the target shape among distractor shapes. This task assessed spatial orientation, visual scanning, and target identification within cluttered environments

6. *Visuospatial function II-Color discrimination*

Several colored squares are displayed in the monitor; the children are asked to memorize the colors and focus on the identified color that changes. This task evaluated visual memory, color discrimination, and attentional control.
A Region of interest (ROI) was set for the correct answer (target image) for each task. The average percentage viewed was calculated. The results from 7 tasks were averaged and used as an eye tracking-based cognitive score.

BC exposure analysis

A urine sample was collected in a 50ml sterile containers at the time of children evaluation. Samples were kept at room temperature until transported to a clinical laboratory at the end of the day. Samples were shake for 10min and under a laminal flow transferred to Eppendorf tube, labelled and stored at room temperature until shipment to Belgium.
Upon arrival in Belgium, the samples were mounted on imaging chamber (40,41). Imaging was performed at room temperature using an inverted laser-scanning microscope (Zeiss Axiovert 200XM; Carl Zeiss) equipped with the EC Plan Neofluar 20×per 0.5 objective (Carl Zeiss). For each sample tile scan, 9 images (1,536×1,536-pixel) were recorded with a 1,60μs pixel dwell time at five different locations in the imaging chamber. Images were taken 5um above the coverslip using two emission channels: SHG (450–650 nm) and TPAF(400-410 nm). A peak-finding algorithm in MATLAB (MATLAB 2010; MathWorks, Inc.) detected BC particles by counting pixels above a defined threshold: 0.5% and 45% below the maximum intensity in both channels, respectively. The pixels exceeding the threshold in both channels were classified as BC particles. The mean particle count across the 9 images was used to calculate particle concentration per ml of urine. Urine concentration variability was not taken intoaccount, since the semi-micro osmometer was broken(41).

Stadistics

Linear model

To investigate the association between BC and cognitive workload, we selected covariates a priori and complemented with a directed acyclic_graph (DAG), built with dagitty 3.0 (42) SUP 6. Based on the DAG, two models with different sets of covariates were build. model 1 includes minimal sufficient adjustment for age, sex and socioeconomic status (NBI). model 2. that corrects age, sex maternal education and school attendance and siblings SUP 8._All analysis were performed software R (version 4.0.5 (2021.09.2+382)). Assumptions for model linearity (normality, homoscedasticity, linearity and independence) were verified for urine BC load and per cognitive task. Statistical significance was set at $p < 0.05$. To reduce kurtosis and skewness of the distribution values, BC was log transformed and the % time view per task was log plus1 transformed. Based on DAG two linear regression models with different set of covariates were constructed for each cognitive outcome. Furthermore, sensitivity analyses were performed SUP 7. This models illustrated BC associates with each cognitive outcome when no accounting for other co-exposures.

Individual effects

To further investigate the association between BC exposure and cognitive outcomes in children from La maica, Bolivia a LASSO regression model was conducted using R R package glmnet to determine which mixture component most contributes to BC urinary load (log) effect SUP 4. LASSO regression is a type of supervised regression analysis that identifies the variables that most significantly impact the outcome while reducing the effect estimates for those variables that have little influence on the outcome (43,44). This technique carries out variable selection while taking into account co-exposures and confounding factors.(45) Cross-validation was used to determine the best value of λ , therefore chosen penalization level for the modes was λ (s =60). To better visualization the shrinkage path was plotted using a standardized λ (s = 30), which effectively highlighted the behavior of the coefficients under moderate penalization.
The most strongly associated variable was chosen for the rest of statistical analysis.

Effect modification by NBI

Quantile-based G-computation allows estimation of the joint effects of the mixture as a whole (46). With a one quantile rise across all components at once, this technique uses G-computation to evaluate the overall impact of the combination on the result. Moreover, in the mix effect estimate, it determines the weight of each exposure, hence producing the proportion of the partial effect caused SUP 5 by a particular exposure(46). The qgcomp package in R (ver. 3.6.1) was used for all investigations.

RESULTS

Study population characteristics,

55 children, 30 boys and 25 girls with a mean age (SD) of 5.27 (1.01) years were included in this study. Most of the children belonged to an indigenous group, Quechua (74.5%) and Aymara (1.8%). According to IOTF, 25 children were normal weight, 22 were overweight or obese (obese n=3, and severely obese n=7, overweight n=12). In the other hand, 8 children were underweight (thinness 1 n=3, thinness 2 n=3, thinness 3 n=2). 13 children did receive any type of school education at the time of evaluation. Furthermore, 6 children had at least one sibling also participating in the study.20 mothers (36.4%) had a medium education level, 19 (34.5%) low, and 16 (29.1%) high. NBI index showed that only 4 households (7.3%) had their basic needs met, while the majority were living in poverty (moderate poverty n= 26, severe poverty n= 26, and extreme poverty n= 26)(Table1).

Neurobehavioral performances and BC load–

All of the cognitive tasks evaluated in this study showed a high degree of variability in the time viewed (%) toward the correct ROI. In the attention and calculation task, the average was 4.82% (SD = 3.86), with values ranging from 0% to 15.03%. The interquartile range (IQR) between 1.62% and 7.49%. The Memory task had an average of 9.04% (SD = 11.38). Over the 25th percentile have a 0% time viewed while other children saw 46.56%. For the Deductive Reasoning task, the average was 12.03% (SD = 10.88), with an interquartile range of 2.83% to 18.63%. The Visual Memory task had a mean of 10.99% (SD = 12.29), but it also showed great variation, with a maximum of 64.81% and a lower quartile of 1.58%. For visuospatial function task I and II the 25th percentile was 0% indicating that a quarter of the children never saw to the correct ROI during these tasks. Visuospatial Function test I showed the lowest average 2.63% (SD = 5.50). Visuospatial Function task II, on the other hand, had a mean of 8.88% (SD = 11.92) and a maximum of 44.08. With an IQR of 2.49% to 9.48%, the total mean view % across all activities was 6.53% (SD = 5.27)(Table 2).

BC urinary load in vulnerable population

The mean concentration of BC particles per ml was 106,971,136 (SD=168,163,890) (Figure2A). The minimum number of particles measured was 20,775, whereas the maximum observed is 758,837,669 The IQR extended from 2,721,561 (Q1) to 138,321,776 (Q3), and the median (Q2) was 21,654,328, which is considerably lower than the mean. This further confirms a positive, right skew distribution. After logarithmic transformation the distribution becomes more symmetric. The mean of the transformed value was 16.58, closely aligned with the median of 16.89, indicating reduced skewness. The values ranged from 9.94 to 20.45, and the interquartile range (IQR) spanned from 14.82 (Q1) to 18.75 (Q3) (Figure 2B).

Socioeconomic predictors of BC exposure

BC levels in children were significantly associated with living in extreme poverty were significantly higher (β = 2.33, p = 0.032) and while those in moderate or severe poverty showed non-significant trends (β = 1.28, p > 0.20). Lower maternal education was also associated with increased BC concentrations, although the associations did not reach significance for medium (β = 1.69 , p = 0.102) or low education (β = 1.24, p =0.150). The interaction model revealed that maternal education modified the association between poverty and BC exposure. Notably, children with medium maternal education living Notably, children with medium maternal education living in moderately poor households showed a strong negative interaction effect (β = –12.51, p = 0.004) (Figure 2D)

Association between BC load and cognitive outcomes

Linear regression models showed no statistically significant association between BC urinary load and the six cognitive areas. Negative trends were observed in visual memory (β = –0.021, *p* = 0.434), visuospatial function I (β = –0.015, *p* = 0.492).Other tasks presented coefficients near zero and not statistically significant association, deductive reasoning (β = 0.006, *p* = 0.832), memory (β = 0.024, *p* = 0.442), attention and calculation (β = 0.003, *p* = 0.890), and visuospatial function II (β = 0.001, *p* = 0.970) (Figure 3).

BC, Basic needs index and their association with cognitive outcomes in children

LASSO regression models were employed to assess the relationships between urinary black carbon (BC) load, the unmet basic needs index (NBI), maternal education, and the six task and a total cognitive outcome. Across the models, urinary BC load coefficients showed coefficients near zero or slightly negative across all cognitive domains, including Attention (β = -0.00019), Deductive Reasoning (β = -0.00075), Visual Memory (β = -0.01405), Visuospatial Function Task I (β = -0.02582), and Total cognitive score (β = -0.00446), indicating no significant impact on cognitive outcomes. NBI showed negative coefficients suggesting that poorer households is linked to worse cognitive performance. This was observed on memory (β = -1.87), attention and calculation (β = -0.03), deductive reasoning (β = -0.29), visual memory (β = -0.27), and visuospatial function tasks (β = -0.20 and β = -0.14), as well as on the total cognitive score (β = -0.39). Maternal education produced small positive or near-zero coefficients (β range: -0.03 to 0.06), indicating a weak protective effect on cognitive outcomes. These findings suggest that socioeconomic factors, as indicated by the NBI, are the primary predictors of cognitive performance within this cohort, while the urinary BC load did not demonstrate meaningful predictive value in the LASSO models. (Figure 4A).

Quantile-based G-computation showed that higher BC and low basic needs meet index is associated with poorer cognitive performance in children. Significant negative associations were found in the memory task (B = -0.182, p = 0.04) and visuospatial function I (B = -0.134, p = 0.03). Additionally, there was a marginal effect observed in deductive reasoning (B = -0.129, p = 0.08) and total cognition (B = -0.106, p = 0.09) (Figure 4B).. Across various cognitive domains, BC exposure exhibited the highest positive weight (weight = 1.00), positioning it as a primary driver of adverse effects, while the NBI consistently showed negative weights with relatively lower contributions. suggesting that poorer households is linked to worse cognitive performance. (Figure 4C).

Table 1 – Baseline characteristics of included participants (N = 55)

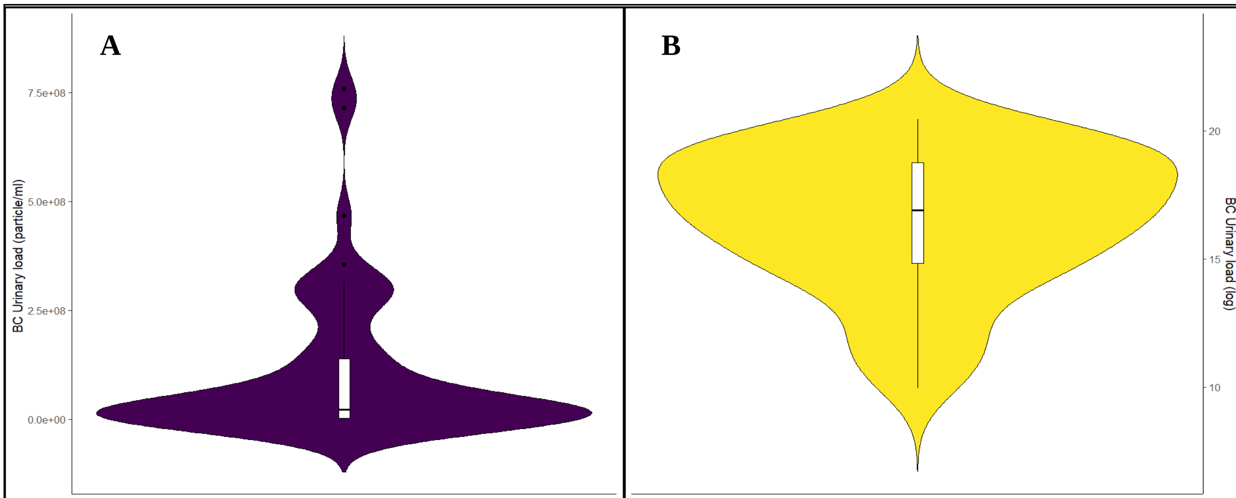
Characteristics	Study population	
Age[1]	5.27	
Sex		
Boys	30.00	54.55%
Girls	25.00	45.45%
Ethnicity		
Aymara	1.00	1.82%
Quechua	41.00	74.55%
IOFT[2]		
Thinness grade 3	2.00	3.64%
Thinness grade 2	3.00	5.45%
Thinness grade 1	3.00	5.45%
Normal weight	25.00	45.45%
Obesity	3.00	5.45%
Severe obesity	7.00	12.73%
Overweight	12.00	21.82%
Maternal education		
High education	17.00	30.91%
Medium education	12.00	47.27%
Low education	12.00	21.82%
NBI[3]		
Basic needs met	15.00	27.27%
Moderate poverty	13.00	23.64%
Severe poverty	13.00	23.64%
Extreme poverty	14.00	25.45%
Do not attend to school	13.00	23.64%
Other member of the in the study	13.00	23.64%

[1]Mean age in years.[2]International Obesity Task Force classification [3] Unmet Basic Need index (NBI)

Table 2. Cognitive score (% time view) across six cognitive areas

Cognitive area	n	Mean	StdDev	Min	Pctl25	Pctl75	Max
Attention and calculation	55	4.82	3.86	0.00	1.62	7.49	15.03
Memory	55	9.04	11.38	0.00	0.00	13.39	46.56
Deductive reasoning	55	12.03	10.88	0.00	2.83	18.63	40.16
Visual memory	55	10.99	12.29	0.00	1.58	15.03	64.81
Visuospatial function	55	2.63	5.50	0.00	0.00	1.86	27.41
Visuospatial function II	55	8.88	11.92	0.00	0.00	14.85	44.08
Total	55	6.53	5.27	0.00	2.49	9.48	20.59

Percentage of time across six cognitive areas, as well as the overall cognitive score. expressed as mean, standard deviation (StdDev), minimum (Min), 25th percentile (Pctl25), 75th percentile (Pctl75), and maximum (Max).



	Min	Q1	Median	Q3
BC (particle/ml)	20,775	2,721,561	21,654,328	138,321,776

	Min	Q1	Median	Q3	Máximo
BC log (particle/ml)	9.942	14.817	16.891	18.745	20.447

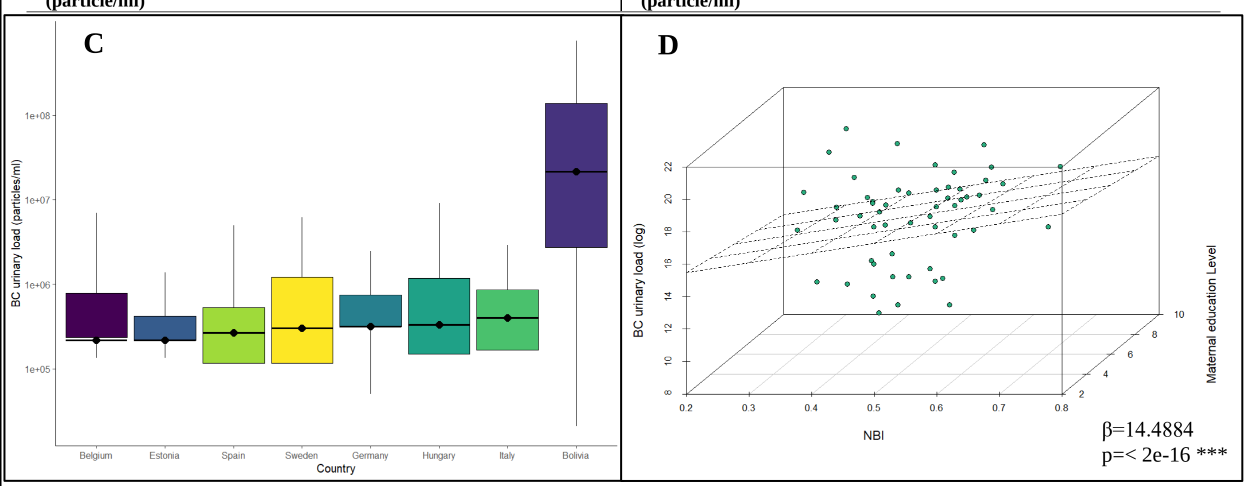
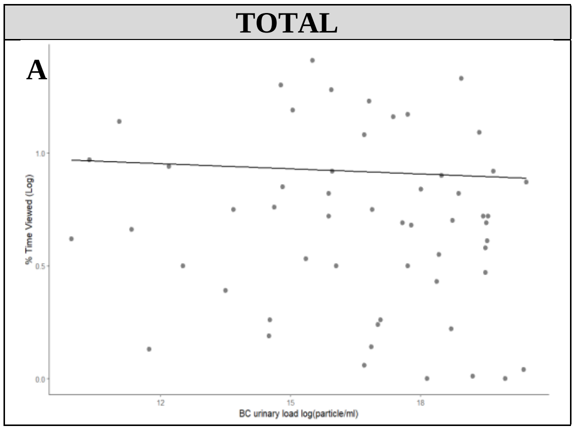


Figure 2. A. BC Urinary load particle/ml B. Log transformed Urinary Load particle/ml C. Mean BC urinary load per country D. 3D scatter plot of the association of BC, NBI and maternal education



B

Test	β	P value	Significant Covariates (β / p-value)
T1	0.003	0.89	Maternal education: Low (-0.053 / 0.800)
T2	0.024	0.44	Maternal education: Low (-0.133 / 0.343) Sex (Girls: -0.291 / 0.036) * School attendance (0.364 / 0.026) *
T3	0.006	0.83	Maternal education: Low (-0.078 / 0.680) Sex (Girls: -0.266 / 0.099) † School attendance (0.386 / 0.043) * Other family member in the study (-0.505 / 0.015) *
T4	-0.021	0.04	Maternal education: Low (-0.133 / 0.343) Sex (Girls: -0.291 / 0.036) * School attendance (0.364 / 0.026) *
T5	-0.015	0.49	Maternal education: Low (-0.056 / 0.707) Age (0.154 / 0.024) * School attendance (0.297 / 0.067) †
T6	0.001	0.97	Maternal education: Low (-0.193 / 0.151) † School attendance (0.245 / 0.065) † Other family member in the study (-0.236 / 0.099) †

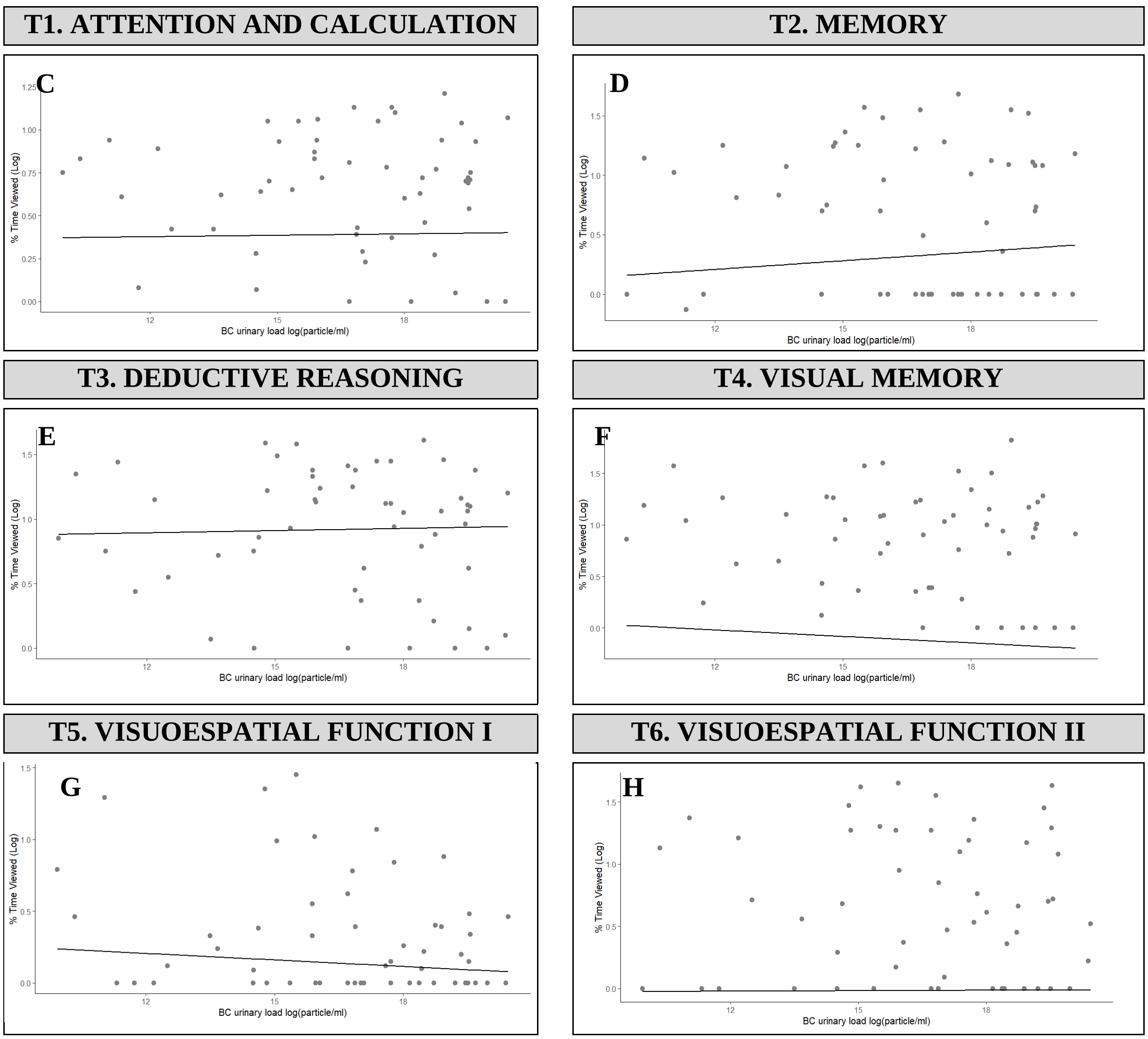


Figure 3 Scatter plot of the association of BC and cognitive outcomes adjusted for Age, Sex Maternal.education, School.attendance and another sibling in the study for A.,C-H 6 cognitive outcomes. B. Beta and P values of each model and the most influential variables

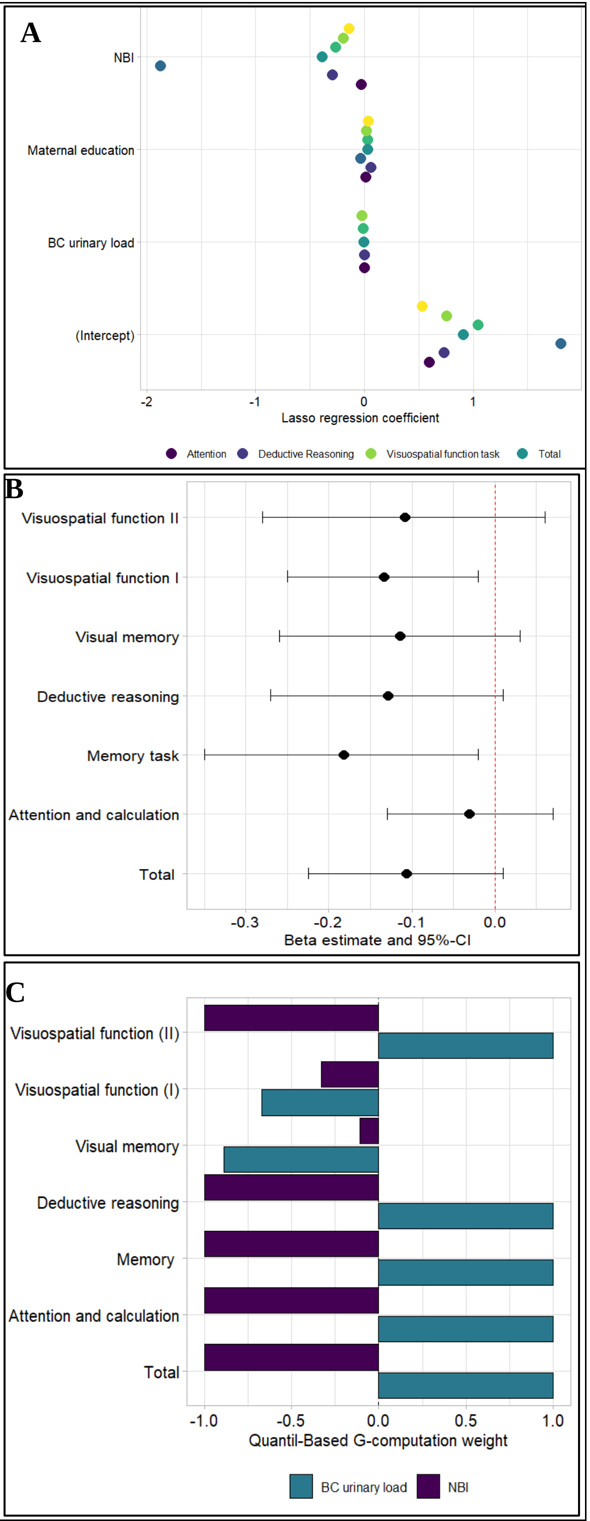


Figure 4. Effect of interquartile range (IQR) increases in BC urinary load and NBI on time view(log)(A) LASSO regression coefficients (βLASSO) (B) Linear models adjusted for NBI (C) Quantile g-computation weights indicating the relative contribution of each exposure BC

DISCUSSION

The primary objective of this study was to investigate the association of BC exposure and cognitive outcomes in children from a high polluted and vulnerable population. The main findings revealed that BC concentrations ranged between 20,775 and 758,837,669.particle/ml of urine. Children with less Basic needs meet are exposed to significantly higher levels of BC. The interaction exposure model revealed that maternal education modified the association between poverty and BC exposure, it mitigates the adverse effects of socioeconomic disadvantage on children's BC burden, highlighting the importance of maternal knowledge in shaping early-life environmental health risks. Linear regression models showed a negative trend between BC exposure and cognitive performance, although these associations did not have a pronounced effect. However, when using a quintile-based G computation model approach with particular attention to the interaction between urinary BC and NBI we were able to estimate a significant decrease in memory, visuospatial function and deductive reasoning per BC urine load.

BC urinary load in vulnerable population

Urinary BC load in Bolivian children revels alarming high levels compared to the reported in international studies (47). The mean value is 463-855 times higher than those found in European studies. 463 times more than Italy, 617 times higher than Sweden and up to 855 times higher than Estonia and Belgium (47). This extreme variability not only evidence a critical local concern but also highlights air pollution exposure concentrations variability around the world. Historically, countries in the Global South have faced higher environmental pollution concentrations than other countries due to weak environmental regulations and governmental corruption. (48). Communities with low incomes often face disproportionate burden of environmental externalities (49). This is known as environmental injustice and is explained by the triple jeopardy hypothesis where lower SES is associated with both higher environmental exposure greater health vulnerability (48).
The interaction model between unmet basic needs (NBI) and maternal education level showed a significant effect on BC urinary load, suggesting

that individuals from poorer households in the Maica zone, especially those with lower education levels, exhibit higher urinary BC levels. In the other hand, maternal education not only correlates with children's BC exposure, but significantly modulates the impact of poverty. Specifically, among low-income families, having a mother with a medium education was associated with a significant reduction in children's BC exposure. This finding suggests that maternal education may function as a resilience factor against environmental vulnerability, potentially by influencing behaviors, mobility patterns, or home-based protective strategies. In the Bolivian context, where women often play central roles not only in domestic labor but also in household decision-making and economic activities, this result is particularly meaningful. Our findings are consistent with other international studies which also report that subpopulations with lower education and income levels or low SES experience high air pollution exposure (48–53). In France air quality improvements are not equally distributed across social groups or geographic areas(49). A study in Flanders, Belgium report that neighborhood income significantly influenced exposure to air pollution, while parental education alone did not. However, the interaction between low income and low education did predict higher levels of pollution exposure(53). Despite local characteristics the pattern is clear, poorer populations are more exposed to pollution(52).

The variability on air pollution exposure around the globe can be influence by distinct social dynamics shaped by housing policies(49), historical urban development(50), and patterns of mobility (52) and environmental injustice(48,51). Thus, we must consider local social and spatial factors when assessing how pollution affects vulnerable communities to inform equitable public health interventions.

Association between BC load and cognitive outcomes

Regarding the association between air pollution and cognitive outcomes, several epidemiological studies have documented links between air pollution and cognitive functions such as working memory, sustained attention, and processing speed(15–19,21,41). Therefore, given the high concentrations of urinary BC load in the Bolivian children, it would be expected to find statistically significant associations between exposure and poorer cognitive outcomes. However, our results did not find statistically significant associations after controlling for socioeconomic, maternal education, school attendance, sex and age. Consistent negative trends were observed in tasks related to visual memory and visuospatial function. This pattern supports previous findings that link air pollution to the development of visuospatial abilities from early stages of life. For example, a study of children aged 1 to 2 in rural India revealed that poor air quality was associated with impairments in visual working memory as early as the first year(54). Additionally, the SALIA cohort demonstrated that long-term exposure to air pollution over a span of 22 years was inversely related to visuospatial abilities in older women(55). Visuospatial function, involves identifying and locating stimuli in space, relies on a broad network of brain regions (56). These skills develop early in childhood and are essential for academic achievement (57). One possible interpretation of these findings is that visuospatial and visual memory functions, which depend on neural circuits that are still maturing in early childhood, may be more sensitive to the neurotoxic effects of environmental exposures such as BC. This vulnerability may explain why the observed effects are pronounced in these specific domains while remaining undetected in others.

Research shows that the effects of black carbon (BC) exposure on cognitive development can vary widely, and they can have less pronounced effect than $PM^{2.5}$. A study in Boston found a weak link between high BC exposure and attention problems in Hispanic school-age children from low-income families. (17). In Spain, the BREATHE study found that children exposed to BC in schools faced more behavioural problems and lower working memory scores (19). A separate study from the same cohort also indicated that exposure to particulate matter (PM) harmed children's cognitive performance, though the effects of BC were less clear due BC exposure was estimated using a spatial model (16).A study on different exposure times and its effect on cognitive outcomes on children report exposure to PM was negatively associated with children's cognitive performance. However, the observed effects for BC were stratified by sex and

marginally significant, because BC exposure was estimated using a spatial model (14).
Overall, these findings emphasize that the relationship between air pollution and negative cognitive outcomes can have different results. It is also highlight that this relationship seems to be non-linear and depends on various factors such as the sensibility of exposure measurements, time of exposure, sex, and socioeconomic factors (socioeconomic status, violence exposure, parental education).

BC, Basic needs index and their association with cognitive outcomes in La maica children
As we could not identify any significant associations with the linear model, we explore the joint effect of BC exposure and Sociodemographic variables (NBI, maternal education level) on cognition in Bolivian children. These factors are particularly relevant in vulnerable contexts such as La Maica, Bolivia, where urban pollution, socioeconomic disparities may elevate the risk of adverse neurocognitive outcomes. To gain a better understanding of the overlapping vulnerabilities and their impact on cognition, we utilized urinary BC load, NBI, and maternal education level to construct a lasso regression model. This result reaffirmed the importance of NBI as the strongest and most constant factor with pronounced negative coefficients; urinary BC load had a lower coefficient compared to NBI. Although it has an adverse effect on five of the seven cognitive outcomes, the NBI effect is larger and overlaps with it. While maternal education shows small positive coefficients in all models suggesting a protective role in this social context. Since its coefficient was small, as shown in the LASSO regression model, we decided to exclude it from subsequent analyses to maintain parsimony in the models.
Beta values showed that the total cognitive score decreased marginally significantly with increases in urinary BC load across quintiles. Additionally, memory and visuospatial tasks were significantly and inversely associated with increased urinary BC quintiles. Other tasks such as attention and calculation, visual memory, visuospatial function II also showed a negative, less pronounced negative effect.
These results are consistent with other studies that have shown that SES not only has a confounding role but also a modifying effect in the relationship between air pollution and cognitive outcomes (CO_x, NO_x, $PM^{2.5}$)(58). A stronger association exists between air pollution and cognitive impairment has been reported in older adults who live in disadvantaged neighborhoods in Atlanta(59). The Americans Changing Lives study reported similar results, where $PM^{2.5}$ and cognitive outcomes had a stronger association among participants from neighborhoods with higher stress levels(60). The German Heinz Nixdorf Recall cohort study also identified associations between distinct combinations of intercorrelated air pollution, road traffic noise, and nSEP disadvantages with poorer cognitive function(61). These studies support the environmental injustice and the triple jeopardy hypothesis, showing that beyond the independent effects of air pollution and socioeconomic factors(48). Socioeconomic status (including income, education, and disadvantaged neighborhoods) may be a critical moderator of the impact of air pollution on cognitive outcomes. Wight, 2006 hypothesized that late life cognition results from the combination of environmental factors and individual traits(62). Our study contributes to this framework by suggesting that such vulnerabilities may begin shaping cognitive development as early as childhood.
This relationship is not only evident in cognitive outcomes among older adults but also in brain morphological changes in adolescents, as observed in participants from the ABCD study(63). The primary effect of neighborhood disadvantage was associated with reductions in brain structure, although this was not statistically significant. The greater the neighborhood disadvantage, the smaller the cortical surface areas in frontal, temporal, parietal, and occipital regions, as well as reduced volumes in key subcortical structures, such as the amygdala, hippocampus, and basal ganglia, alongside decreased cerebral white matter and cerebellar volumes. It stood out that several of these regions, including the prefrontal cortex, hippocampus, thalamus, amygdala, and superior temporal gyrus, have also been identified in postmortem studies as accumulating high concentrations of black carbon particles(64). It is essential to note that the ABCD cohort has not identified associations between exposure to total $PM^{2.5}$ mass and behavioral outcomes in large children and adolescent cohorts. Although no associations have yet been found, this does not rule

out future cognitive or behavioral effects. Given the brain's plasticity at younger ages, it is possible that regulatory mechanisms delay the manifestation of these outcomes until later in life, as seen in elderly populations. Certain brain regions that exhibit volume reductions and BC particle accumulation, are functionally related to visuospatial memory, spatial information processing and working memory processes.

To the best of our knowledge, this study represents the first evaluation of the combined effects of air pollution and socioeconomic status on such a vulnerable population in Latin America. Our findings indicate that memory and visuospatial function are the most significantly impacted cognitive domains. Across all these studies, the interconnected effects of environmental exposures and socioeconomic factors have been consistently documented. This interaction appears to be especially critical in contexts of environmental injustice, where children from low socioeconomic backgrounds are not only more exposed to pollutants like black carbon but also less protected by supportive environments and are more prone to long term consequences. This pattern reinforce the Developmental Origins of Health and Disease (DOHaD) theory(65). and makes a call for urgent public health targeted interventions that reduce pollution exposure in vulnerable communities and incorporate social protection strategies, especially during early childhood.

Strengths and limitations

The key strength of this study is the integral approach, which actively incorporates community involvement in the project's development. It also benefits from collaborations with experts across all evaluation fields, ensuring the technical quality of the processes involved. Medical professionals for the children evaluation, volunteers for the recruitment strategies and finally experts on BC measurements. A significant advantage is the development of culturally adapted cognitive tests, which is particularly important when working with children, as it allows for the detection of subtle cognitive effects through eye-tracking technology, being the first in the continent(39). Additionally, measuring black carbon (BC) in urine provides a methodological advantage by offering a more sensitive indicator compared to other methodologies(41). However, the study does have its limitations. The most notable issue is the small sample size of only 55 participants, which resulted from challenging logistical and contextual circumstances during sampling, leading to low statistical power. Nevertheless, this research offers a valuable benchmark for future investigations in similar contexts. Due to the limited sample size and the high variability in the data, there are constraints on the ability to account for covariates or apply multiple comparison corrections from a statistical perspective. Furthermore, while urinary BC levels were assessed, normalization is still required, as equipment malfunction prevented the measurement of urine osmolality.

CONCLUSION

Our findings show high levels of urinary BC load in children from La Maica Bolivia. BC load was negatively associated with worse cognitive performance on memory and visuospatial task. This association was particularly strong in children from precarious homes and with mothers with low education levels. These results suggest that the neurotoxic effect of BC is amplified by structural conditions of inequality, characteristic of many peri-urban areas of Latin America.

From an environmental health and social justice perspective, this study highlights the urgent need for integrated public policies that reduce exposure to pollutants, improve living conditions, and strengthen education on vulnerable communities.

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Author contributions – **Who did what**? AST, MP, KV, PdA conceived and designed the research. Ast performed experiments and data analysis. KV provided assistance with BC measurements. MP and BR provided assistance with statistics. AST wrote the paper.Kv and PdA carefully review the paper.
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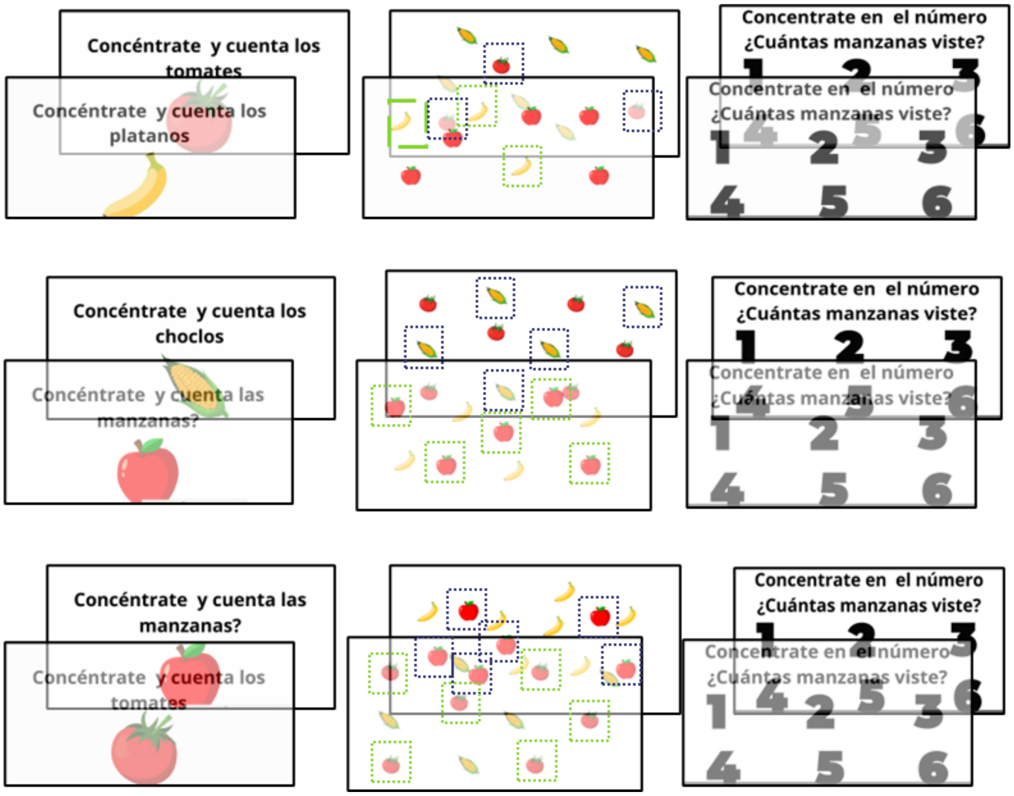
SUPPLEMENTARY INFORMATION

S1: Mobile unit set up

S2Task movies and pictures for the cognitive assessment–Pictures of each task are shown below. Video with oral instructions and the images were produced as part of the thesis.

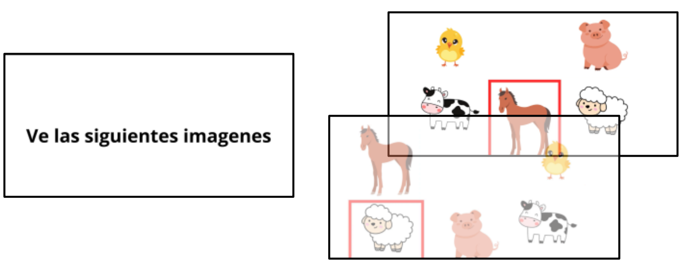
Task1. Attention and calculation task (count objects) Stimuli T1,T2,T3

11 (s)	13 (s)	13 (s)



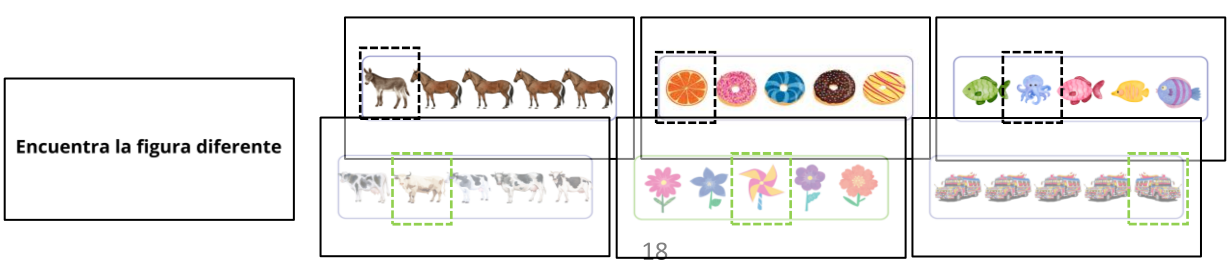
Task 2. Memory task (follow the red cube and remember the animal) Stimuli T4a

10 (s)	6 (s)



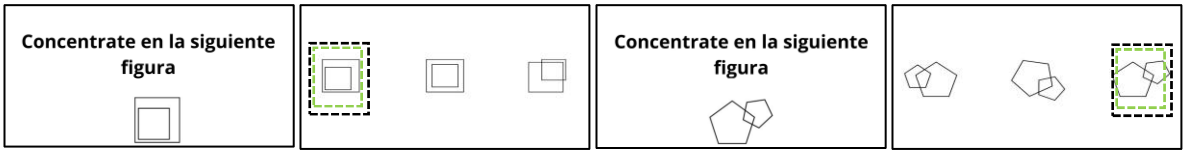
Task 3. Deductive reasoning (Odd one out) Stimuli T5, T6, T7

10 (s)	10 (s)	10 (s)	10 (s)



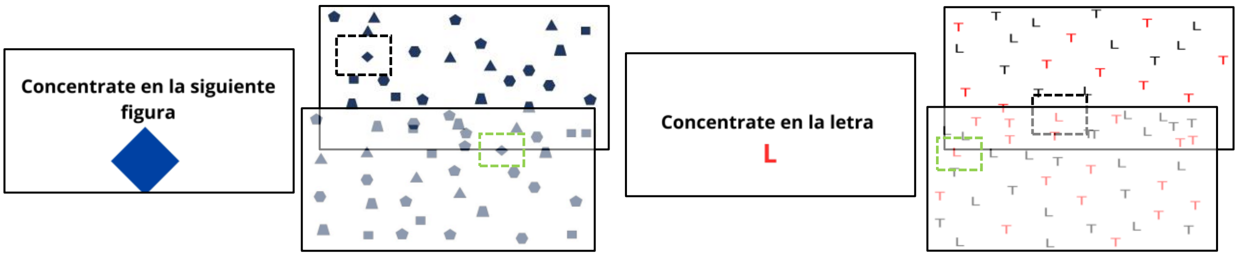
Task 4. Visual memory task Stimuli T8, T9

10 (s)	10 (s)	10 (s)	10 (s)



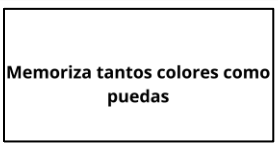
Task 5. Visuospatial function task T11, T12

10 (s)	10 (s)	10 (s)	10 (s)

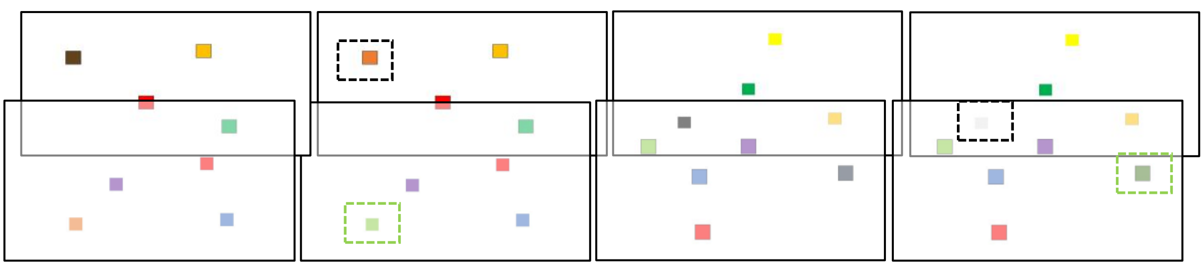


Task 6. Visuospatial function task II T13, T14

10 (s)

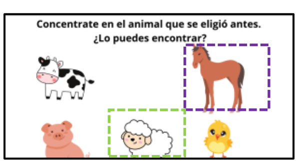


15 (s)	15 (s)	15 (s)	15 (s)



Task 2. Memory task T4b

10 (s)



S3 Comparison of the Two Test Versions: Shapiro-Wilk Normality Test and Wilcoxon Test Results

Table 1.

Task	Shapiro-Wilk (V1)	Shapiro-Wilk (V2)	Wilcoxon W	Wilcoxon p-value
T1	W = 0.81, $p < 2.2\text{x}10^{-16}$	W = 0.84, $p < 2.2\ \text{x}10^{-16}$	123012	0.07
T2	W = 0.85, p = 0.00013	W = 0.84, p = 0.00022	573.5	0.53
T3	W = 0.89, $p = 1.7\text{x}10^{-07}$	W = 0.91, $p = 3.7\ \text{x}10^{-06}$	5472.5	0.70
T4	W = 0.91, $p = 7.9\text{x}10^{-05}$	W = 0.94, p = 0.00189	2653	0.55
T5	W = 0.74, $p = 2.8\text{x}10^{-10}$	W = 0.62, $p = 7.8\ \text{x}10^{-12}$	2774.5	0.21
T6	W = 0.85, $p = 4.2\text{x}10^{-07}$	W = 0.82, $p = 5.8\ \text{x}10^{-07}$	2397	0.41
Total	W = 0.85, $p < 2.2\text{x}10^{-16}$	W = 0.85, $p < 2.2\text{x}10^{-16}$	493162	0.485

*V1 Version 1 of the test *V2 version 2 of the test

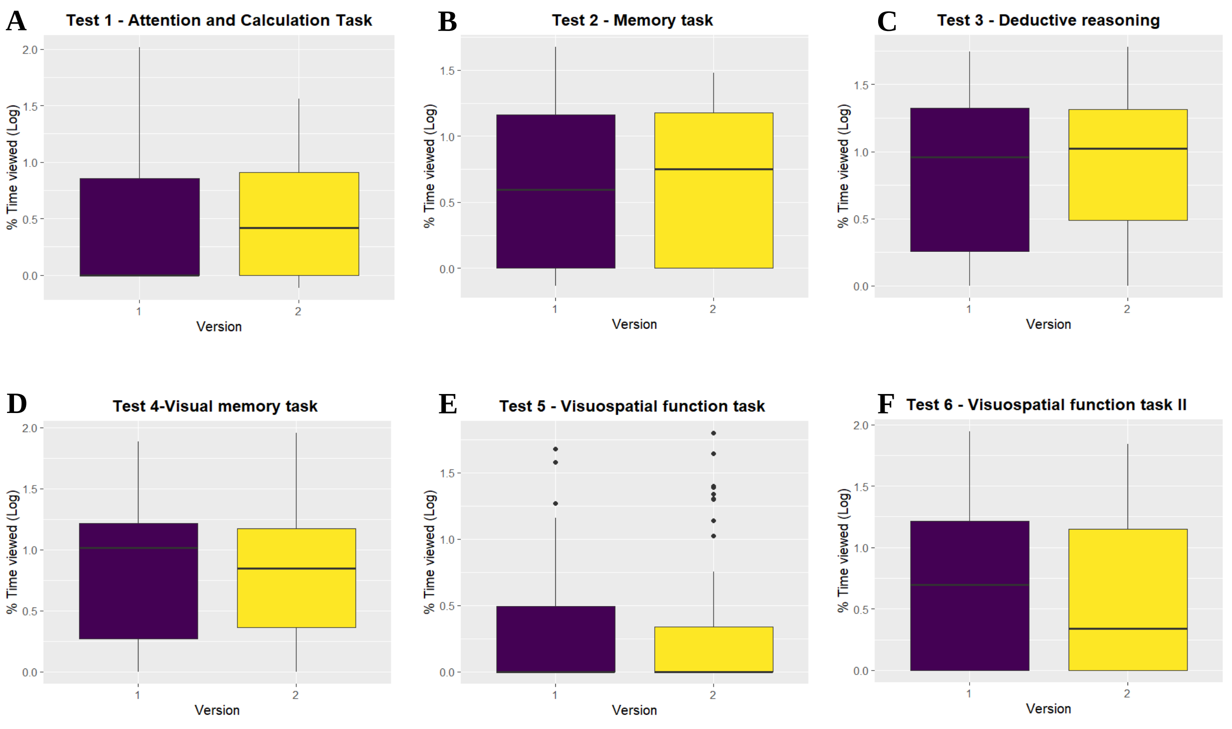


Figure 5

S3 Comparison of the Two Test Versions: Shapiro-Wilk Normality Test and Wilcoxon Test Results

Table 2.

Task	Shapiro-Wilk (Hospital)	Shapiro-Wilk (Home reassesment)	Wilcoxon W	Wilcoxon p-value
301	W = 0.947, p = 0.195	W = 0.841, p = 0.00096	502.5	0.0024
302	W = 0.859, p = 0.00174	W = 0.900, p = 0.0116	389	0.858
304	W = 0.852, p = 0.00156	W = 0.846, p = 0.00120	417	0.141

*V1 Version 1 of the test *V2 version 2 of the test

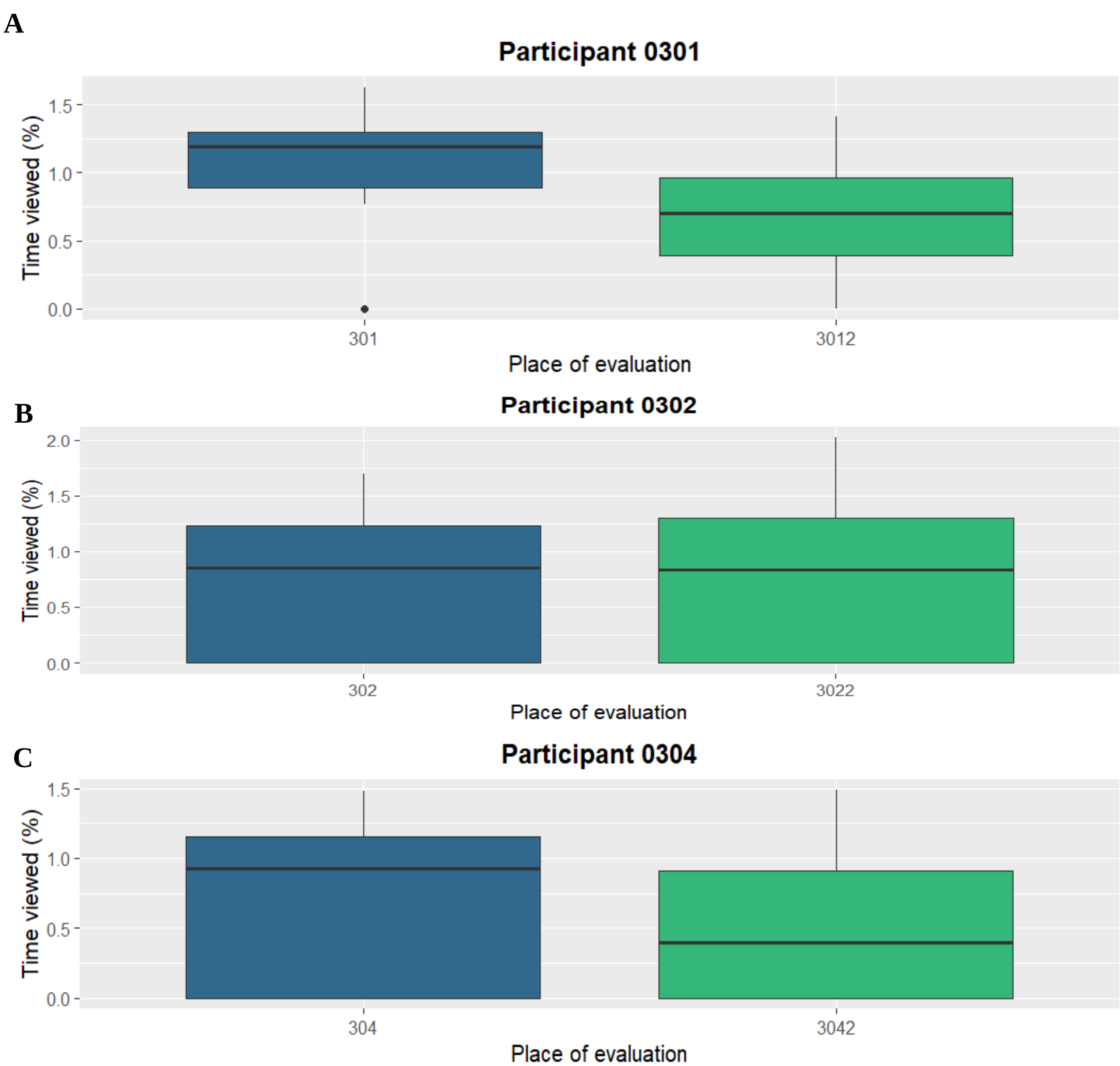


Figure 6

S4 LASSO regression results

Table 3. Lasso regression coefficients

variable	coefficient	model
Intercept	0.59712	Attention
BC urinary load (log)	-0.00019	Attention
NBI	-0.03127	Attention
Maternal education	0.01307	Attention
Intercept	1.80658	Memory
NBI	-1.87332	Memory
Maternal education	-0.03411	Memory
Intercept	0.73354	Deductive Reasoning
BC urinary load (log)	-0.00075	Deductive Reasoning
NBI	-0.29215	Deductive Reasoning
Maternal education	0.05875	Deductive Reasoning
Intercept	1.04529	Visual memory
BC urinary load (log)	-0.01405	Visual memory
NBI	-0.26588	Visual memory
Maternal education	0.03087	Visual memory
Intercept	0.75208	Visuospatial function task
BC urinary load (log)	-0.02582	Visuospatial function task
NBI	-0.19734	Visuospatial function task
Maternal education	0.01600	Visuospatial function task
Intercept	0.53222	Visuospatial function task II
NBI	-0.14186	Visuospatial function task II
Maternal education	0.03449	Visuospatial function task II
Intercept	0.90961	Total
BC urinary load (log)	-0.00446	Total
NBI	-0.38772	Total
Maternal education	0.02743	Total

S5 Quantile g-computation results

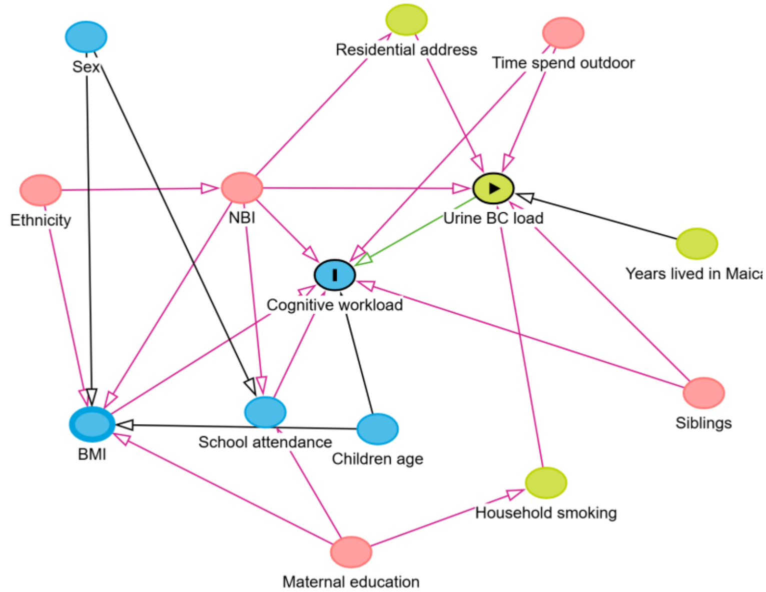
Table 7. B values for the linear models adjusted for NBI

Test	B	StdError	pvalue	Lower 95% CI	Upper 95% CI
Total	-0.106	0.06	0.09	-0.225	0.01
Attention and calculation	-0.031	0.05	0.55	-0.13	0.07
Memory task	-0.182	0.08	0.04	-0.35	-0.02
Deductive reasoning	-0.129	0.07	0.08	-0.27	0.01
Visual memory	-0.114	0.07	0.13	-0.26	0.03
Visuospatial function I	-0.134	0.06	0.03	-0.25	-0.02
Visuospatial function II	-0.108	0.09	0.21	-0.28	0.06

Table 8. Quantile g-computation weights

Test	**Variable**	**Weight**	**Type**
Total	BC urinary load log (particleml)	1.00	Positive
Total	NBI	1.00	Negative
Attention and calculation	BC urinary load log(particleml)	1.00	Positive
Attention and calculation	NBI	1.00	Negative
Memory task	BC urinary load log(particleml)	1.00	Positive
Memory task	NBI	1.00	Negative
Deductive reasoning	BC urinary load log(particleml)	1.00	Positive
Deductive reasoning	NBI	1.00	Negative
Visual memory	BC urinary load log(particleml)	0.89	Negative
Visual memory	NBI	0.11	Negative
Visuospatial function (I)	BC urinary load log(particleml)	0.67	Negative
Visuospatial function (I)	NBI	0.33	Negative
Visuospatial function (II)	BC urinary load log(particleml)	1.00	Positive
Visuospatial function (II)	NBI	1.00	Negative

S6 DAG



S7 Sensitivity analysis

Sensitivity analisi	Minimal adjusted	Extensive adjustment	Interaction(Sex)	Sens 1	Sens 2	Sens 3	Sens 4	Sens 5	Sens 6	Sens 7	Sensibility 8 only 85 por	Interaccion
Age	X	X	X	X	X	X	X	X	X	X	X	X
Sex	X	X		X	X	X	X	Girls	boys	X	X	X
NBI	X	X			X	X	X	X	X	X	X	
BMI		X					X					
Ethnicity		X				X						
Maternal education		X		X								
School attendance		X		X	X	X	X	X	X	only yes	X	
Siblings in the study		X										
ylim					X							

S8. Linear regression model for the two sets of covariates