OnLine Journal of Biological Sciences

Original Research Paper

Visual-Spatial Attention Abilities Among School Children Exposed to Low Environmental Lead Level

[1]Sana Maidoumi, [1]Mariam Ouisselsat, [1]Charif Radouan Ouaziz, [1,2]Nadia Abbassi, [3]Mohamed Loukid, [4]Ahmed Ahami, [5]Alain Pineau and [1]Azeddine Sedki

[1]*Laboratory of Water, Biodiversity and Climate Change, Department of Biology, Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakech, Morocco*
[2]*CarMeN Laboratory, INSERM, INRAE, INSA Lyon, Université Claude-Bernard Lyon 1, Lyon, France*
[3]*Laboratory of Pharmacology, Neurobiology, Anthropobiology, Environment, and Behaviour, Department of Biology, Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakech, Morocco*
[4]*Laboratory of Biology and Health, Unit of Neuroscience and Nutrition, Department of Biology, Faculty of Science, Ibn Tofail University, Kenitra, Morocco*
[5]*Laboratory of Toxicology, Mineral Element Dosing Centre, UFR of Pharmaceutical and Biological Sciences, University of Nantes, Nantes, France*

Article history
Received: 28-04-2022
Revised: 14-07-2022
Accepted: 17-08-2022

Corresponding Author:
Sana Maidoumi
Laboratory of Water, Biodiversity and Climate Change, Department of Biology, Faculty of Sciences Semlalia, Cadi Ayyad University, Marrakech, Morocco
Email: smaidoumi@gmail.com

Abstract: Lead (Pb) is an intrusive toxic matter which harms the neuro-cognitive and behavioral development of children even with doses considered normal. The present paper aims at evaluating the visual-spatial attention function among 142 schoolchildren living in a mining area (cases) in comparison to 177 living in the Chouiter area (control group) in Marrakech. We used the Bell Dam Test (BDT) for the assessment of their visual attentional abilities and unilateral spatial neglect. Interviews with parents were conducted to identify co-variables related to Pb exposure. Agricultural soil, drinking, and groundwater were collected from the surrounding area of the children's school. The determination of Pb content in the environment was performed by ICP-MS. The results demonstrated that cases' scores in the test of visual attentional abilities and in scanning procedures were significantly worse in comparison to the control group ($p = 0.05$ and $p = 0.002$, respectively). In cases, soil Pb level was higher (67.14±10.13 g/g) than in controls (41.73±13.6 g/g). Pb levels in groundwater and drinking water were low with a significant difference between the two areas in groundwater. The mean scores of visual attentions were significantly lower in children exposed to environmental Pb contamination compared to those who are not exposed ($p = 0.008$). These findings suggest that Pb is probably incriminated in the genesis of visual attention deficit.

Keywords: Lead, Soil Pollution, Water, Attention, Children, Morocco

Introduction

Trace Elements are essential to the state of trace for numerous cellular processes (low proportion) but can become toxic when the concentration exceeds a certain threshold like Copper (Cu), Nickel (Ni), Iron (Fe), Zinc (Zn), etc. The non-essential trace elements have no beneficial effect on the cell. By contrast, they have a polluting character with toxic effects on the live bodies even in low concentrations, such as lead (Pb), Aluminum (Al), Cadmium (Cd), mercury (Hg), and so forth. These micropollutants cause nuisances, even when they are rejected in very low quantities. Their toxicity is developed by bioaccumulation along the food chain (Tchounwou *et al*., 2012). The inorganic form of Pb which is the oldest and most widely used by humanity is neurotoxic even at rates met in the environment. Children are most vulnerable and most exposed to Pb (NTP, 2012). Moreover, it was reported that, compared to other pollutants, Pb is a more significant predictor of cognitive impairment (Clay *et al*., 2019).

Surface soil contamination has long been acknowledged to be a major lead exposure in humans and is currently a global health concern (Mielke and Reagan, 1998; Rabinowitz *et al*., 1991). Additionally, high soil lead concentrations will likely last for centuries and re-suspension of Pb-contaminated soil can increase atmospheric Pb levels and spread lead to nearby places (Laidlaw and Filippelli, 2008).

Exposure to Pb levels during development, even if they are weak, could have adverse effects on the neurobehavioral and cognitive performance of children (Finkelstein *et al*., 1998). Manifest distraction, low frustration tolerance, impulsivity, and organizational inabilities have all been identified as symptoms of attention behavior dose-dependent impairment (Bellinger *et al*., 1984). The U.S. National

Toxicology Program (NTP, 2012) concluded that, in children, blood Pb levels below 5 g/dL are associated with an increase in the diagnosis of behavioral problems related to attention and a decline in cognitive function. In this context, the presence of a heavy metals mine (copper, cadmium, and lead) in Marrakech city suggests targeting this sector. Compared to Lekouch (2004), the average blood lead level decreased from 12 to 3.14 µg/dL (Bouhouch *et al*., 2016), nevertheless, the risk of lead exposure still exists due to the environmental load in Pb (Barkouch, 2007; Zaida, 2007; El-Fadeli *et al*., 2014).

In addition, with those low average concentrations of lead measured within the children, chelator therapy didn't change significantly their scores on neuropsychological tests (Bouhouch *et al*., 2016). Recently, we have found a significant association ($p<0.031$) between the visual attentional function of schoolchildren living in the mining area and Pb content on their nails (Maidoumi *et al*., 2017). Whereas, it's interesting to assess at last how environmental Pb content may affect their superior brain functions to understand the Pb exposition pathways and suggest eventual solutions. Therefore, this study aims at evaluating visual attentional function and unilateral spatial neglect among lead-exposed Moroccan children in comparison with the control group.

Materials and Methods

Study Location

The research was carried out in Marrakech, which is approximately located in the center of Morocco. This study was interested in two suburban areas; one on the West of Marrakesh called «Sâada» and the other the 20 km on the Eastern part of Marrakesh called «Chouiter» far from any sources of contamination (Fig. 1). "Drâa Lesfer" which is a mining area is located in the Saada region, 13 kilometers west of Marrakech. This mine extracts Pb, Cd, and, Cu. Zn is naturally associated with these metals in the rock.

Participants

Data were obtained through a cross-sectional study, which includes 319 children aged 6 to 10 years living in Marrakech. Participants were drawn from four schools chosen to represent the two suburban areas "Sâada" and "Chouiter" and enrolled in the study from September 27th, 2019, to February 5th, 2020.

Socio-Demographic Variables

Parents filled out a questionnaire on their children's sex, age, parental educational level, father's occupation, and their children eating habits. This information was obtained at the time when the children's cognitive functions were assessed. Anthropometric measurements of children were also noted to understand their nutritional status (BMI).

Cognitive Performance Assessment

We used the bell test, designed by Gauthier *et al*. (1989), for the evaluation of Visual Attention (VA) and unilateral spatial neglect. The total number of surrounding bells was noted along with the time it took for the patient to run. The maximum score is 35. Forgetting 6 or more bells, at the right or left of the page indicates unilateral spatial neglect. The spatial distribution of omitted bells allows the examiner to assess the severity of visual neglect as well as the laterality of this negligence (right or left). The sequence by which the children completed this task can be figured by connecting the bells surrounded by the following order he performed.

Environmental Assessment

To understand the effect of environmental contamination on the attention performance of these children, measurements of Pb on soil and water were performed in both areas. Since painting, interior dust, and exterior soil or dust are three routes to which children can be exposed directly or indirectly and which contain significant amounts of lead, we then studied the spread of lead in soil. Tap water, being a weak source of lead exposure, was also analyzed.

Soil Sampling

Forty-eight soil samples were collected from the school garden. Soil samples were taken randomly from the upper layer (0-10 cm) and homogenized to form a composite sample. Then, the soil was dried in ambient air and sieved through a mesh whose diameter is less than 2 mm. The soil was sealed in paper envelopes for later analysis.

Mineralization: From each sample, three powder samples were taken and accurately weighed (0.5 g). The soil samples were then placed in crucibles to be gradually heated to 450°C. After cooling, bi-digestion with Hydrofluoric acid (HF) and perchloric acid ($HClO_4$) was performed on a hot plate. Subsequently and to complete the dissolution, Hydrochloric acid (HCl) was added. Finally, distilled water was used to reach a volume of 50 mL (AFNOR, 1997).

Samples analysis: The metal analyses (Pb) of samples were carried out by using Thermo Fisher ICP-MS of the characterization center of the Faculty of Science Semlalia of Marrakesh. Standard solutions (HNO_3 1M: 500 ng/mL) made it possible to draw up the calibration curve (10, 100, 500 µL). Then, 100 mL of 1 m nitric acid was added to a volume of 0.5 mL of the mineralized soil solution.

Water Analysis

Water sampling: Two water samples were taken from each school. One was taken from the drinking water and the other from the groundwater next to the target school. Polyethylene bottles pre-washed with nitric acid (1%) were used to preserve the samples. These latter were maintained at 4°C until they were sent to the mineral dosing center at the pharmaceutical UFR in Nantes, France.

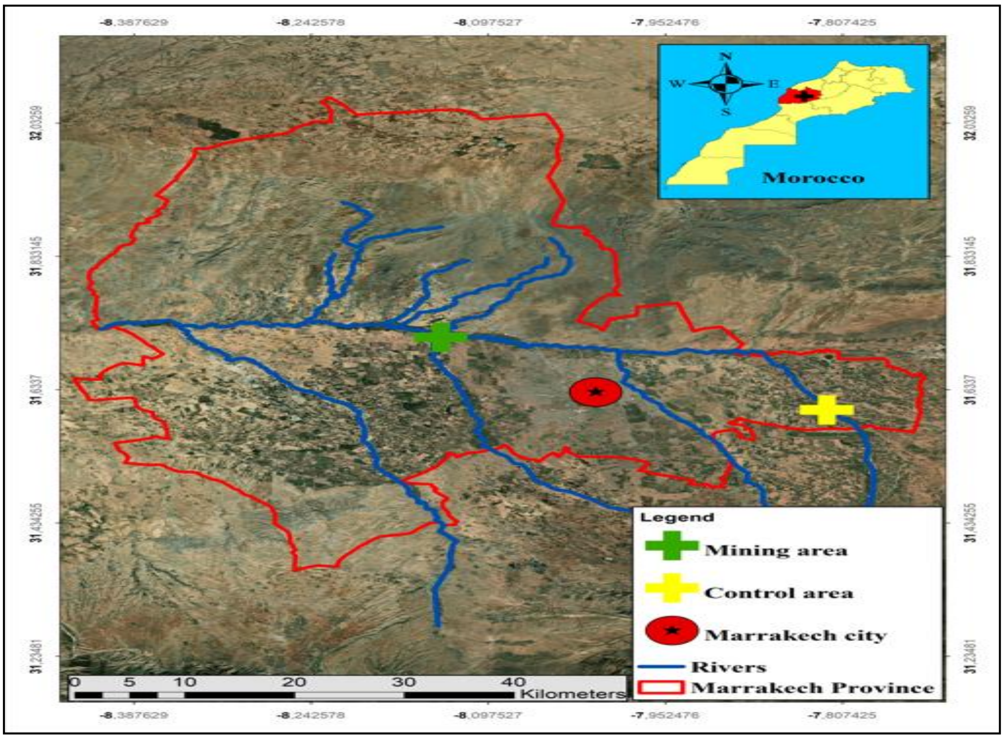

Fig. 1: A map showing where the setting of both areas of study is located (Sâada in Mining area and Chouiter in control area)

Lead content in water: Perkin-Elmer Inductively Coupled Plasma Mass Spectrometry (ICP-MS) model NexION 300 X was used to measure Pb concentrations. Doses are expressed in µg/L. Two water-based Nist-certified controls were employed to confirm the analytical procedure's accuracy (SRM 1643f and SRM 1640a). The controls are analyzed at each assay run and are run regularly every 10 samples and at the end of the essay. The calibration standards were made using a stock solution containing 1 g/L of lead. The stock solution was purchased from Carl ROTH. Starting from the 1 g/L solutions, a stock solution S1 (Pb: 500 µg/L) is made by successive dissolutions. The calibration range is created based on the anticipated Pb detection thresholds for water and the S1 stock solution. The element has been calibrated as follows: Pb: 6.25-12.5-25 µg/L. Millipore Direct Q UV3 instrument's Milli-Q ultrapure water was the water used to perform the standards. This is an ultrapure water system coming directly from the tap. The internal standard is Rh (100µg/L). The isotope used is Pb: 207.977. The acidified water samples are directly analyzed and the results are read in µg/L.

Ethical Considerations

The Mohammed VI University Hospital Center's ethics committee approved the study protocol on October 29, 2019. The parents of the children submitted written consent in advance concerning their children's privacy rights and protection of their data. The Ministry of Health and Social Protection provided support for the study. The Ministry of the Interior and the Ministry of Education both approved of it as well.

Statistical Analysis

SPSS (20th edition) was used to analyze the collected data. For a univariate study, centrality and dispersion parameters were assessed (mean, minimum, maximum, and standard deviation). Compliance analyses were performed using kurtosis, Kolmogorov-Smirnov, and skewness. Variances' homogeneity was analyzed using Levene's test. After that, bivariate analysis was conducted using parametric tests (student test, Anova). The significance level is retained for a $p<0.05$.

Results and Discussion

Population-Related Variables

The demographic characteristics are detailed below (Table 1) and show that the two groups of children have roughly the same average age. The sex ratio was 0.77 for both populations. The participants were matched by gender and age. We find that each educational level (CE1 and CE2) is almost half of the population of children whether for cases or control. Approximately half of the mothers breastfed their children and the average breastfeeding between both groups showed that there was no significant variance in duration (t = -1.575; p = 0.116). Furthermore, 37.4% and 29.2% of children do not eat their breakfast regularly (always and often) for the cases and controls respectively. The Body Weight index (BWI) was 14.84±1.25 (Kg.m-2) in children from mining areas compared to the control 22.9±4.41. This disparity is statistically significant (t = -6.075; p = 0.001).

Compared to the control group, the proportion of children with two educated parents is much lower in the cases (21.5% versus 48.7%) (X^2 = 22.687; p = 0.000***).

Visual Attentional Scores and Unilateral Spatial Neglect

The mean score of exposed children (cases) on the VA test was 16.63±7.07 out of 35 for the CE1 and was significantly lower (t = -2.999, p = 0.003) compared to the controls (19.85±5.3 out of 35). In the same way, a significant difference in mean VA scores was elucidated (t = -2.562, p = 0.011) between the two groups enrolled in CE2 (Cases: 21.23±6.36; Control: 23.57±5.36), Fig. 2. Moreover, the mean score, for both population and the two levels (CE1, CE2), was significantly lower compared to the reference standard ODEDYS (T-test/ p = 0.000). The reference means the score is 28 out of 35 for the CE1 and 29out of 35 for the CE2 (Berthelot *et al*., 2005).

As a result, we found that both groups of children have low visual attentional skills. When these scores were compared to those from another research, Aboussaleh *et al*. (2011) reported a mean score of 30.54 and Maidoumi *et al*. (2017) discovered a mean score of 19.75±7.72. This gap might be explained by the children's ages and grade levels in these studies.

Regarding the distribution of omissions, we concluded that the majority of children omitted 6 or more bells independently (X^2 = 6.039, p = 0,110) from their living site (Fig. 3). In fact, the omission of 6 or more bells indicates unilateral spatial neglect (Gauthier *et al*., 1989).

The second step is to investigate the severity of this neglect by identifying the laterality of the distribution of omitted bells. Indeed, the majority of omitted bells are located on right and left of the paper for cases and controls. For the exposed children (cases), about 3.5% of them have right visual-spatial neglect compared to only 2.3% in control (Fig. 4).

However, 3.4% of control children had central neglect. Since omissions in more centered columns of the sheet suggest greater neglect (Gauthier *et al*., 1989), this could have an impact on their learning quality.

The way by which the children encircled the bells indicates that the majority of children didn't use the same scanning strategy (Table 2).

The scanning method chosen is disorganized in 47.7% of the exposed children and significantly different (p = 0.002) from those of non-exposed ones (35%). This result corroborates the findings of Gauthier *et al*. (1989) which demonstrated that the strategy of scanning left hemiplegic is disorganized compared to that of normal. Subjects with VA deficiency exhibit a disorganized scanning strategy and remission of visual neglect syndrome may lead, in brain-damaged subjects, to a reorganization of the scanning strategy.

The DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4^{th} edition, 1994) classification describes this attention deficit as relating to a young child with a lack of attention to detail. Indeed, the child has difficulty maintaining his attention on a particular task or game, has difficulty in organizing tasks, and has frequent forgetfulness during daily activities with easy distraction to external stimuli. The bells test requires maintaining attention (selective attention) while performing a conflicting task, as well as visual processing (visual-spatial scanning) (Azzano *et al*., 2011). Therefore, a deficiency in VA may be associated with a dysfunction in the parietal and temporal lobes, especially the posterior associative cortex. Indeed, the Inferotemporal cortex contains a whole region dedicated to visual object recognition and the temporal lobe regions are crucial for understanding the spatial relationships among objects in a visual field (Purves *et al*., 2004).

At molecular level, it is known that cognition, attention, memory, mood, and reward behaviors are mediated by monoaminergic neurotransmitters such as serotonin and dopamine. Pb suppresses neurotransmitter levels at lower concentrations, whereas, during prolonged exposure or at higher concentrations, Pb mimics Ca and thus promotes the release of neurotransmitters, which increases their concentration in the synaptic cleft (Malavika *et al*., 2021). By altering synaptosome production, release, uptake, receptors, and transporters, as well as the quantities of second and third messengers like PKC, Ca, transcription factors, etc., it is also considered that Pb affects the availability of neurotransmitters (Sadiq *et al*., 2012).

Based on these results that describe visual attentional disorders in schoolchildren from the mining area, we observed that visual attention was affected. Although, the laterality of spatial neglect didn't show any differences between the two groups or the two sides of spatial neglect, the scanning strategy organization was disturbed. The results corroborate those of El Azmy *et al*. (2014) on children in the Mrirt area (Middle Atlas, Morocco) which showed that 64% of children, especially those with VA issues, do not adopt an organized scanning method to look for bells.

Environmental Assessment

In Table 3 we have shown the concentrations of Pb in soil and water in the two areas. We sum up by saying that the average Pb levels in the soil were lower than the limit values for soil (100 µg/g) in France (MATF, 1998) but higher than the normal levels in uncontaminated soil (35 µg/g) (Bowen, 1979). Additionally, a highly significant difference was elucidated between the mining area and the control one ($t = 1.563$; $p = 0.000$). This disparity can be explained by the exposure of 35.9% of children from the mining area to Pb through their father's occupational clothing.

Table 1: Demographic characteristics

	% or Mean ± SD		
Characteristics	Cases (N = 142)	Control (N = 177)	Test value
Gender			
-Male	41.5%	58.5%	42.9%
-Female	57.1%	$X^2 = 0.077$	
Age	7.51±0.88	7.52 ± 0.86	t = 0.037
Basic education levels:			
-First level (CE1)	41.5%	53.7%	$X^2 = 1.518$
-Second level (CE2)	58.5%	46.3%	
Type of breastfeeding:			
-Maternal exclusive	58.6%	49.9%	$X^2 = 5.903$
-Mixed	12.9%	28.5%	
-Artificial	10.3%	39.8%	
Breastfeeding duration (/month)	13.77±8.73	15.39±7.98	t = -1.575
Breakfast intake:			
-Regularly	62.6%	70.8%	$X^2 = 0.844$
-Irregularly	37.4%	29.2%	
BMI(Kg.m-2)	14.84±1.25	22.9±4.41	t = -.075**
Parent's educational level:			
-Both illiterate	23.2%	12.1%	X^2= 22.687***
-One of the two illiterate	55.3%	39.2%	
-The two educated	21.5%	48.7%	
Pb exposure in children via their father's work outfits:			
-Yes	35.9%	0%	X^2 = 74.476***
-No	64.1%	100%	

**significant correlation is at p<0.005
***significant correlation is at p<0.001

Table 2: The way through which the children encircled the bells

	Scanning strategy	Cases (%)	Control (%)
Organized strategies	From right to left high (A)	10.6	12.8
	Left to right high (B)	30.9	30.3
	Right to left low (C)	0.0	5.0
	Left to right low (D)	1.7	2.7
	From top to bottom right (E)	4.0	6.5
	From top to bottom left (F)	3.4	4.2
	Bottom to top right (G)	1.7	3.5
	Disorganization strategy (I)	47.7	35.0
	Test Value	X^2 = 23.083**	

**The correlation is significant at p<0.005

Table 3: The content of Pb's distribution in soil and water in the two study areas

	Mining area		Chouiter area			
Pb content	N	Mean ± SD	N	Mean ± SD	Test value	RV
Soil (µg/g)	24	67.140±10.130	24	41.73±13.600	t = 1.563***	100
Drinking water (µg/L)	10	0.120±00.050	10	0.13±00.110	t = -0.203	10
Groundwater (µg/L)	5	0.065±00.017	5	-0.01±00.007	t = 4.840***	50

*** The correlation is significant at p<0.001. RV: Reference Value according to WHO (1993) experiment in µg/g for soil and µg/l for water)

Table 4: Association between VA scores and lead contamination of soil

Lead contamination of soil	Group	N	VA Mean ± SD	Test value
Uncontaminated soil	Cases	0	22.75±6.41	t = 2.737**
(< = 35 µg/g)	Control	59		
Contaminated soil	Cases	146	20.22±6.32	
(>35 µg/g)	Control	117		

**The correlation is significant at p<0.005

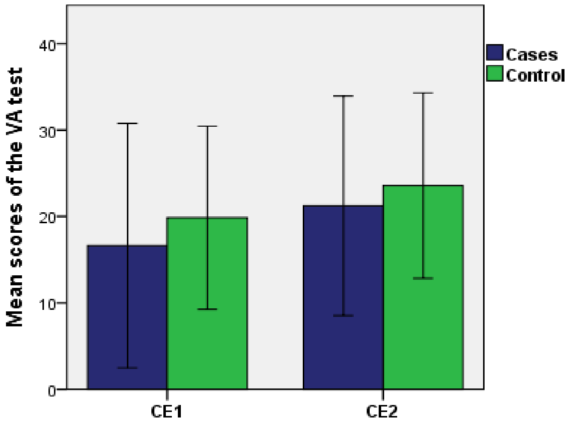

Fig. 2: Comparison of the VA test's mean scores for the two groups (*<0.05, **<0.005)

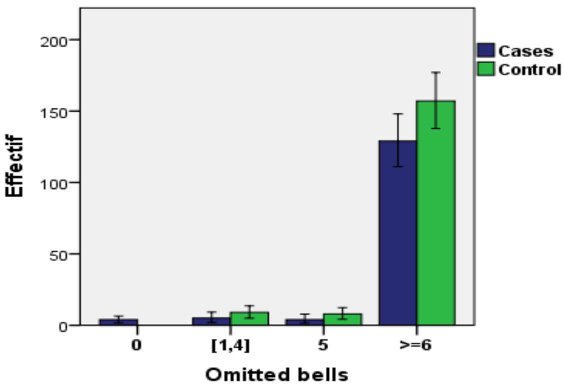

Fig. 3: Distribution of omitted bells in cases and controls

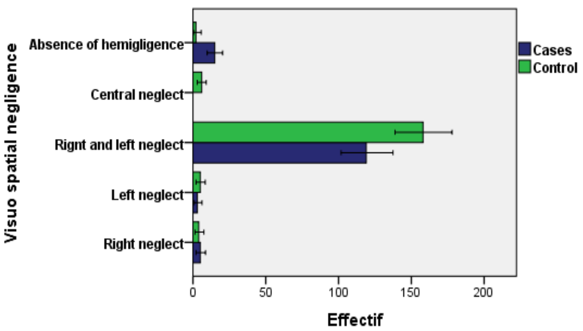

Fig. 4: Spatial distribution of omitted bells among cases and controls

The Pb content in water was very low in both areas and remains far from the Moroccan limit value (10 µg/L) determined by the standard 03.7.001 (OMS, 2017). However, the groundwater content of Pb in the mining area showed a very significant difference from that of the control (p = 0.000). Nevertheless, the water of both zones is far from being declared contaminated. This result contradicts that of Zaida *et al.* (2007) indicating lead contamination of the water of the mining area. The installation of a drinking water distribution network about ten years ago could be an explanation for the drop in lead levels in the water in this area.

Association of Environmental Pb Content and Visual Attention Function

The significant difference in mean scores between children exposed to lead contamination and those who are not (p = 0.008) suggests that lead is probably incriminated in the genesis of this cognitive deficit (Table 4). The study of (Ruebner *et al.*, 2019) corroborates this finding.

Indeed, the risk of attention deficit disorder (sustained attention and attention regulation) has been raised by environmental lead exposure. The results of Bellinger *et al*. (1994) state that, early exposure to lead in children and adolescents resulted in difficulties focusing and shifting attention, which most likely contributed to overall cognitive impairments.

Learning problems can be expected and could hinder their academic success. This conclusion was confirmed by several studies that reported a link between visual processing and academic success (Dhingra *et al*., 2010; Goldstand *et al*., 2005).

Thus, early detection of lead exposure and associated neurocognitive developmental issues may allow for the adoption of certain interventions, such as remediation, to inhance cognitive trajectories.

Finally, to minimize early contamination, precautionary measures should be taken to prevent environmental lead exposure. Lifestyle changes are advised, including washing hands before meals, decreasing the frequency of eating roadside food, reducing the use of kohl-based cosmetics, streamlining the use of conventional medicine, and the choice of accommodation away from heavy traffic.

Conclusion

Despite the existence of a proven association in this study between children's visual attention abilities and the risk of environmental lead exposure, however, it is not yet clear whether this is a causal association or not. Other factors could likely affect the children's academic achievement as well as the deterioration of their cognition.

Validation of these results could be considered using impregnation data such as blood lead. Thus, a comparison could be established with children from municipalities with similar population density and socio-economic parameters. In addition, other environmental factors should be investigated, such as children's diet and parents' occupation. This would strengthen the study conclusions and would allow the establishment of Pb exposure reduction strategies targeted at young children.

Acknowledgment

This study would not have been possible without the collaboration of the Mineral Element Dosing center of the Pharmaceutical Science University of Nantes and the Characterization Center of the Faculty of Science Semlalia of Marrakesh. Hence, the authors recognize the effort of all the work teams for their assistance during the analysis.

Funding Information

The resources made available to us by the Mineral Elements Dosing Center at the Pharmaceutical department of the University of Nantes (France) were used to support this work.

Author's Contributions

Sana Maidoumi and Nadia Abbassi: Conceptualization, writing- original draft preparation, Methodology, investigation, resources, data processing, and curation and funding acquisition.

Mariam Ouisselsat: Conceptualization, writing-original draft preparation, Methodology, investigation, resources, data processing, and curation.

Charif Radouan Ouaziz: Conceptualization, writing-original draft preparation, Methodology, validation, formal analysis, resources, data processing, and curation.

Mohamed Loukid: Conceptualization, Methodology, software, validation, formal analysis, resources, data processing and curation, writing-review and editing, visualization, supervision.

Ahmed Ahami and Alain Pineau: Conceptualization, Methodology, software, validation, formal analysis, resources, data curation, writing-review and editing, visualization, supervision.

Azeddine Sedki: Conceptualization, Methodology, software, validation, formal analysis, resources, data curation, writing-review and editing, visualization, supervision, project administration.

References

Aboussaleh, Y., Sbaibi, R., El Hioui, M., & Ahami, A. (2011). La carence en fer et le développement cognitif. *Antropo*, *25*, 91-96. http://www.didac.ehu.es/antropo/25/25-8/Aboussaleh.pdf

AFNOR. (1997). *Frame work of standardization programme "soil quality". AFNOR [Association francaise pour la normalisation] and ISO developments, connections with AFES [Association francaise pour l'etudes du sol]*. https://agris.fao.org/agris-search/search.do?recordID=FR9608191

Azzano, V., Jacquier-Roux, M., Lepaul, D., Lequette, C., Pouget, G., & Zorman, M. (2011). BSEDS 5-6 Bilan de Santé Évaluation du Développement pour la Scolarité 5 à 6 ans.

Barkouch, Y. (2007). *Etude du transfert des éléments traces métalliques (Al, Cd, Cu, Pb, Se et Zn) dans une chaîne alimentaire d'une zone minière de la région de Marrakech–Maroc* (Doctoral dissertation, Nantes). https://www.theses.fr/2007NANT33VS

Bellinger, D., Hu, H., Titlebaum, L., & Needleman, H. L. (1994). Attentional correlates of dentin and bone lead levels in adolescents. *Archives of Environmental Health: An International Journal*, *49*(2), 98-105. https://doi.org/10.1080/00039896.1994.9937461

Bellinger, D., Needleman, H. L., Bromfield, R., & Mintz, M. (1984). A followup study of the academic attainment and classroom behavior of children with elevated dentine lead levels. *Biological Trace Element Research*, *6*(3), 207-223. https://doi.org/10.1007/BF02917507

Berthelot, M., Cnrs, N., Mend, P., & Bp, A. C. (2005). Outil de DÉpistage des DYSlexies Septembre 2005. *1-Dyslexie*, *vers 2*, 1–71.

Bouhouch, R. R., El-Fadeli, S. andersson, M., Aboussad, A., Chabaa, L., Zeder, C., ... & Zimmermann, M. B. (2016). Effects of wheat-flour biscuits fortified with iron and EDTA, alone and in combination, on blood lead concentration, iron status, and cognition in children: A double-blind randomized controlled trial. *The American Journal of Clinical Nutrition*, *104*(5), 1318-1326. https://doi.org/10.3945/ajcn.115.129346.1318

Bowen, H. J. M. (1979). *Environmental chemistry of the elements*. Academic Press. https://doi.org/10.1080/00346767800000037

Clay, K., Portnykh, M., & Severnini, E. (2019). The legacy lead deposition in soils and its impact on cognitive function in preschool-aged children in the United States. *Economics & Human Biology*, *33*, 181-192. https://doi.org/10.1016/j.ehb.2019.03.001

Dhingra, R., Manhas, S., & Kohli, N. (2010). Relationship of perceptual abilities with academic performance of children. *Journal of Social Sciences*, *23*(2), 143-147. https://doi.org/10.1080/09718923.2010.11892823

El Azmy, J., Ahami, A. O., Badda, B., Aboussaleh, Y., El Hessni, A., & Rusinek, S. (2014). Etude des troubles d'attention (négligence spatiale unilatérale) au sein d'un échantillon de collégiens à M'rirt (Moyen Atlas, Maroc)[Screening for attention deficit disorder (unilatéral spatial neglect) in a sample of junior high school students of M'rirt (Middle Atlas-Morocco)]. *International Journal of Innovation and Applied Studies*, *9*(2), 937. https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.684.6044&rep=rep1&type=pdf

El-Fadeli, S., Bouhouch, R. R., El-Abbassi, A., Chaik, M., Aboussad, A., Chabaa, L., ... & Sedki, A. (2014). Health risk assessment of lead contamination in soil, drinking water and plants from Marrakech urban area, Morocco. *Journal of Materials and Environmental Science*, *5*(1), 225-230. https://www.research-collection.ethz.ch/handle/20.500.11850/76217

Finkelstein, Y., Markowitz, M. E., & Rosen, J. F. (1998). Low-level lead-induced neurotoxicity in children: An update on central nervous system effects. *Brain Research Reviews*, *27*(2), 168-176. https://doi.org/10.1016/S0165-0173(98)00011-3

Gauthier, L., Dehaut, F., & Joanette, Y. (1989). The bells test: A quantitative and qualitative test for visual neglect. *International Journal of Clinical Neuropsychology*, *11*(2), 49-54.

Goldstand, S., Koslowe, K. C., & Parush, S. (2005). Vision, visual-information processing and academic performance among seventh-grade schoolchildren: A more significant relationship than we thought? *The American Journal of Occupational Therapy*, *59*(4), 377-389. https://research.aota.org/ajot/article-abstract/59/4/377/4945

Laidlaw, M. A., & Filippelli, G. M. (2008). Resuspension of urban soils as a persistent source of lead poisoning in children: A review and new directions. *Applied Geochemistry*, *23*(8), 2021-2039. https://doi.org/10.1016/j.apgeochem.2008.05.009

Lekouch, N. (2004). *Evaluation de l'exposition de la population humaine aux éléments traces métalliques dans la région de Marrakech: Etude du risque saturnin* (Doctoral dissertation, Thèse de doctorat, University Cadi Ayyad, Faculté des sciences Semlalia Marrakech, Maroc).

Maidoumi, S., Belcaid, HA, Sebban, H., Ahami, AOT, Lekouch, N., & Sedki, A. (2017). Study of the effect of metallic trace elements on the neurocognitive functions of schoolchildren in the region of Marrakech: Case of lead. *Antropo*, (37), 91-103. https://dialnet.unirioja.es/servlet/articulo?codigo=6118287

Malavika, L., Mitra, P., Goyal, T., Sharma, S., Purohit, P., & Sharma, P. (2021). Association of blood lead level with neurobehavior and neurotransmitter expressions in Indian children. *Toxicology reports*, *8*, 971-976. https://doi.org/10.1016/j.toxrep.2021.05.002

MATF. (1998). *Ministère de l'Aménagement du Territoire français. Teneurs limites de concentration en ETM dans le sol. Arrêté du 8 janvier 1998. Journal Officiel de la République Française du 31 janvier 1998.*

Mielke, H. W., & Reagan, P. L. (1998). Soil is an important pathway of human lead exposure. *Environmental Health Perspectives*, *106*(suppl 1), 217-229. https://doi.org/10.1289/ehp.98106s1217

Organisation Mondiale de la Santé (OMS) (2017). *Directives De Qualité Pour L'Eau De Boisson Quatrième Édition Intégrant Le Premier Additif* (Issue Guidelines for drinking-water quality: 4th ed. incorporating first addendum). https://doi.org/10.1080/02626669609491505

NTP. (2012). NTP monograph on health effects of low-level lead. National Toxicology Program U.S. Department of Health and Human Services. [accessed: Jun. 14 2012] Available at: http://ntp.niehs.nih.gov/?objectid=4F04B8EA-B187- 9EF2-9F9413C68E76458E.

Purves, D., Augustine, G. J., Fitzpatrick, D., Hall, W. C., LaMantia, A. S., McNamara, J. O. and williams, S. M. (2004). Neuroscience. In *Sunderland, Massachusetts U.S.A. Third Edition.* https://doi.org/10.1016/B978-0-12-801238-3.62132-3

Rabinowitz, M. B., Wang, J. D., & Soong, W. T. (1991). Dentine lead and child intelligence in Taiwan. *Archives of Environmental Health: An International Journal*, *46*(6), 351-360. https://doi.org/10.1080/00039896.1991.9934402

Ruebner, R. L., Hooper, S. R., Parrish, C., Furth, S. L., & Fadrowski, J. J. (2019). Environmental lead exposure is associated with neurocognitive dysfunction in children with chronic kidney disease. *Pediatric Nephrology*, *34*(11), 2371-2379. https://doi.org/10.1007/s00467-019-04306-7

Sadiq, S., Ghazala, Z., Chowdhury, A., & Büsselberg, D. (2012). Metal toxicity at the synapse: Presynaptic, postsynaptic and long-term effects. *Journal of Toxicology*, *2012*. https://doi.org/10.1155/2012/132671

Tchounwou, P. B., Yedjou, C. G., Patlolla, A. K., & Sutton, D. J. (2012). Heavy metal toxicity and the environment. *Molecular, Clinical and Environmental Toxicology*, 133-164. https://doi.org/10.1007/978-3-7643-8340-4_6

World Health Organization (WHO). (1993). Guidelines for drinking-water quality: Volume 1: Recommendations, 2nd ed. World Health.

Zaida, F., Chadrame, S., Sedki, A., Lekouch, N., Bureau, F., Arhan, P., & Bouglé, D. (2007). Lead and aluminum levels in infants' hair, diet, and the local environment in the Moroccan city of Marrakech. *Science of the Total Environment*, *377*(2-3), 152-158. https://doi.org/10.1016/j.scitotenv.2006.10.017