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Metal mixtures, industrial proximity, and child IQ: A cross-sectional biomarkers and longitudinal tooth analysis in schoolchildren from Taranto, Italy

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Highlights

- Residence within 500 m captured the strongest manganese and mercury gradients.
- Cadmium and manganese were independently associated with lower child IQ.
- BKMR identified cadmium as the dominant contributor to the metal mixture.
- Tooth-based models found no robust metal-specific critical exposure windows.
- Near-source residence was consistently associated with lower child IQ.

Abstract

Children living near industrial sources may experience simultaneous exposure to multiple neurotoxic metals, with risks shaped by proximity, socioeconomic conditions, and developmental timing. We investigated associations among metal exposures, residential proximity to industrial sites and intelligence quotient (IQ) in 630 schoolchildren aged 6–15 years from Taranto, Italy. Child cognition was assessed using the Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) and parental cognitive ability using Raven's Standard Progressive Matrices (SPM). Blood, hair, and urine biomarkers of cadmium, mercury, arsenic, lead, and manganese were analyzed cross-sectionally (n = 437), while deciduous tooth trends reconstructed exposure across 22 time points (n = 173). Analyses included regression, Spearman correlations, BKMR, BKMR-DLM, and TDLMM, adjusting for age, sex, SES, parental SPM, and proximity. Residence within 500 m captured the strongest spatial signal for manganese and mercury. Urine cadmium (β=−3.12, p < 0.001) and hair manganese (β=−0.0055, p = 0.001) were inversely associated with IQ, and BKMR ranked cadmium as the dominant mixture component (PIP=0.98). Time-resolved models identified no robust metal-specific critical windows, while residence within 500 m was consistently associated with lower IQ. Parental SPM was associated with child IQ and SES, while lower SES was associated with shorter residential distance from the industrial site. Near-source residence captured proximity-related metal elevations and cognitive disadvantage, while cadmium showed an IQ association without a clear spatial footprint. These findings highlight the sensitivity of metal–IQ associations to spatial selection and covariate adjustment and underscore the importance of accounting for socioeconomic and residential factors when evaluating environmental metal exposures.

Key words

Metal mixtures; Deciduous teeth; Manganese; Cadmium; Child cognition; Industrial emissions

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Introduction

Child cognitive development is influenced by biological inheritance, early-life environment, and socioeconomic context (Tucker-Drob et al., 2013, Figlio et al., 2017). Exposure to neurotoxic metals, including lead (Pb), mercury (Hg), arsenic (As), cadmium (Cd), and manganese (Mn), has been consistently associated with impaired neurodevelopment, even at low concentrations (Lanphear et al., 2005, Kippler et al., 2012, Grandjean and Landrigan, 2006, Tchounwou et al., 2012). Children are especially susceptible due to rapid brain growth, higher intake per body mass, and behaviors that increase exposure, such as hand-to-mouth activity (Rauh and Margolis, 2016, Bellinger, 2012). Metal exposure has been linked to lower IQ, reduced executive function, attention deficits, and learning difficulties across diverse settings (Bakulski et al., 2020, Tanvir Hasan et al., 2025, Liu et al., 2018, Neal and Guilarte, 2011).

Most studies have looked at single metals on their own, but in reality, people are exposed to several metals at once through air, soil, food, and water (Tanvir Hasan et al., 2025, Tucker-Drob and Briley, 2014, Ibrahimou et al., 2024a). Studying mixtures is challenging because metals can have nonlinear effects and may interact in ways that change their impact on health (Anon, 2021, Cai et al., 2010, CORRIGENDUM, 2012). These issues are even more complex because the effects of exposure can vary depending on the stage of development, with prenatal and early childhood periods possibly being times of greater sensitivity.

Metals can harm brain development by causing oxidative stress, inflammation, and changes in how nerve cells communicate (Anon, 2020). Lead affects synaptic transmission and calcium signaling, leading to lower IQ, attention problems, and weaker working memory (Lanphear et al., 2005, Kippler et al., 2012, Grandjean and Landrigan, 2006). Mercury interferes with how neurons move and develop, which can cause language and motor skill delays (Grandjean and Landrigan, 2006, Anon, 2018). Arsenic changes oestrogen stress and neurotransmitter function, which can impair learning and thinking abilities (Tian et al., 2025, Rosado et al., 2007). Cadmium affects dopamine and acetylcholine systems, leading to memory and learning problems (Bakulski et al., 2020, Sanders et al., 2009). Manganese is needed in small amounts but becomes harmful at higher levels, especially in polluted areas, and can cause cognitive and behavioral issues.

Being exposed to more than one metal at a time can lead to additive, greater than additive (synergistic), or less than additive (antagonistic) effects on each other. (Anon, 2021, Cai et al., 2010, CORRIGENDUM, 2012) but research results are mixed. This is partly because it is difficult to detect these interactions due to limited available statistical methods and because exposure sources and social conditions vary between groups. People in industrial areas, especially those with lower socioeconomic status, are more likely to live near pollution sources, which increases their exposure and adds stress and other risks. Because of this, environmental toxins and social factors should be studied together.

Traditional methods like multiple linear regression or generalized additive models can estimate average effects, but they often miss important features of environmental mixtures, such as related exposures, nonlinear effects, interactions, and changes over time (Tanvir Hasan et al., 2025, Ibrahimou et al., 2024, Bobb et al., 2014, Duan et al., 2024). Bayesian Kernel Machine Regression (BKMR) addresses these issues by modeling complex exposure–response relationships and showing which variables matter most, using measures like posterior inclusion probabilities (Tanvir Hasan et al., 2025, Ibrahimou et al., 2024, Bobb et al., 2014, Duan et al., 2024, Mercier et al., 2021). Newer versions, such as BKMR distributed lag models (BKMR-DLM) (Wilson et al., 2022) help study exposures over time and find sensitive periods in development. Tree-based models like the Tree Distributed Lag Mixture Model (TDLMM) (Mork and Wilson, 2021) can also track complex patterns over time with fewer assumptions.

Measuring exposure is also challenging. Common samples like blood, urine, and hair show exposure over different periods, but they often do not give enough detail for prenatal and early postnatal times. Baby teeth offer a special way to track exposure throughout development by using the neonatal line as a time marker, which helps researchers study possible sensitive periods (Hare et al., 2011, Lee et al., 1998).

This study utilizes a community-based cohort of Italian schoolchildren from Taranto, an industrial area with a history of pollution. Taranto represents one of the most emblematic environmental health crises in Europe. The city hosts one of the largest steel plants in Europe, active since the 1960s, together with other major industrial sources, and for decades this industrial complex has generated substantial emissions affecting a wide surrounding area, including densely populated neighborhoods. This long-standing contamination burden led Taranto to be included among Italy's National Priority Contaminated Sites and has made it a paradigmatic setting for environmental epidemiology and environmental justice research. Beyond well-documented concerns for adverse respiratory, cardiovascular, and neurodevelopmental outcomes, the area has also been associated with excess cancer burden, including evidence linking residential proximity to industrial sources with increased cancer incidence and mortality in nearby communities (Anon., 2023). Therefore, the public-health relevance of Taranto has also been recognized internationally: the United Nations Special Rapporteur on human rights and the environment identified Taranto among the world's "sacrifice zones," namely areas where economic interests have been prioritized over health, human rights, and environmental protection. In this sense, Taranto is not only a local case of industrial pollution, but also a symbolic example of how prolonged environmental contamination can intersect with social vulnerability and produce enduring health inequities, especially for children living near major emission sources (Anon, 2022).

Previous studies from this group focused on exposure-related neurodevelopmental impacts showed a marked cognitive decline related to the industrial proximity and metal biomarkers, with relevant interactions between blood lead and SES, (Lucchini et al., 2019, Renzetti et al., 2021) and between blood lead and urinary arsenic. Environmental soil measurements further supported a coherent contribution of environmental and social inequality gradients jointly affecting the IQ levels (Lucchini et al., 2019). Here, environmental inequality refers to unequal distribution of potential pollution related exposure across residential and socioeconomic groups, rather than a causal effect established by this analysis.

This new analysis combines novel mixture modeling, detailed exposure tracking over time, and social and family context to answer four main research questions:

1. Does proximity to the industrial site predict elevated metal concentrations?
2. Which metals are most strongly associated with child IQ when considered jointly as a mixture?
3. Do metal–IQ associations vary across developmental timing, indicating potential time-varying exposure–IQ associations?
4. How do parental cognitive ability and socioeconomic position structure exposure and cognition, and what is the role of the "missing SES" category in interpretation?

Previous studies have used both metal mixtures and deciduous teeth to characterize early life exposures. The contribution of the present study is the combined application of these methods to a Taranto sample. This research moves the field of environmental neurodevelopment forward in three main ways. First, it looks at metals as a group instead of one by one, which better matches real-life exposures. Second, it uses tooth biomarkers to test ideas about when children are most sensitive to exposure, something that is hard to do with regular samples. Third, models take family and socioeconomic factors into account, recognizing that location where people live and their environmental exposure often follow social patterns, meaning household socioeconomic circumstances may influence residential location through differences in housing affordability and access to residential opportunities. Consequently, children from socioeconomically disadvantaged households may be more likely to live near sources of industrial pollution and experience greater environmental exposure. By improving how we measure the effects of mixtures and timing in a population exposed to industrial pollution, this study aims to guide public health actions, environmental rules, and screening for children at higher risk.

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Study setting and population

Details about the study area, sampling frame, and recruitment can be found in earlier publications (Lucchini et al., 2019, Renzetti et al., 2021, Bansal et al., 2019, Bansal et al., 2023). The research took place in Taranto, a city in southern Italy with a large industrial complex that includes one of Europe's biggest steel plants. These industrial activities have led to ongoing emissions of metals and other pollutants, which may spread over a wide area. The present study combined data from two ...

Cohort and analytic subsets

The study included 630 children. To answer questions about both the importance of cross-sectional mixtures and the timing of exposure, we used two overlapping data sets. The first included 437 children with complete blood, hair, and urine biomarker data for cross-sectional analyses. The second included 173 children with tooth biomarker profiles measured at 22 time points, allowing us to see if effects changed during different developmental periods. This two-part approach let us study spatial ...

Integrated interpretation: overall summary of findings

In all analyses, cadmium and manganese were the most important metals for child cognition, but they seem to reach children in different ways. Cadmium was the top metal in cross-sectional mixture models (highest BKMR PIP) and was strongly linked to lower IQ, but it was not related to how close children lived to the industrial site. This suggests that cadmium exposure in this group likely comes from sources other than proximity, such as food, household items, or general environmental pollution. ...

Conclusion

This study used both cross-sectional mixture modeling and time-resolved tooth biomarker analysis to better understand how living near industry, metal exposure, and family and social factors together affect children's cognitive development. Cadmium and manganese were the metals most strongly linked to IQ, but they showed different patterns. Cadmium had the biggest impact in the cross-sectional analyses and was linked to lower IQ, but its levels did not match how close children lived to the ...

CRediT authorship contribution statement

Kazi Tanvir Hasan: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Gabriel Odom:** Writing – review & editing, Methodology, Formal analysis. **Boubakari Ibrahimou:** Writing – review & editing. **Zoran Bursac:** Writing – review & editing. **Roberto Lucchini:** Writing – review & editing, Supervision, Resources, Investigation, Funding acquisition, Conceptualization. ...

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Declaration of Competing Interest

No potential conflict of interest was reported by the author(s). ...

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