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Association of serum metals/metalloids levels with migraine and non-migraine headache types in a 4-year follow-up analysis with 2,662 participants in the ELSA-Brasil study

Arão Belitardo de Oliveira[1], Fernando Barbosa Jr[2], Itamar S. Santos[1,3], Mario Fernando Prieto Peres[4,5], Paulo A. Lotufo [1,3], Isabela M. Benseñor[1,3], Alessandra C. Goulart[1,6]

[1]Center for Clinical and Epidemiological Research, Hospital Universitario, Universidade de Sao Paulo, Brazil
[2]Laboratório de Toxicologia Analítica e de Sistemas (ASTOx). Departamento de Análises Clínicas, Toxicológicas e Bromatológicas, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil
[3]Department of Internal Medicine, School of Medicine, Universidade de Sao Paulo, Sao Paulo, Brazil
[4]Instituto do Cérebro, Hospital Israelita Albert Einstein, Sao Paulo, Brazil
[5]Instituto de Psiquiatria, Hospital das Clínicas, Universidade de São Paulo, São Paulo, Brazil
[6]School of Public Health, Department of Epidemiology, University of Sao Paulo, Sao Paulo, Brazil

Background
Migraine disorders are thought to be influenced by a myriad of endogenous and environmental factors, including its association with metals/metalloid levels. However, this intricate relationship has never been comprehensively studied. Objective: We aimed to examine the risk of migraine disorders associated with serum levels of 16 metals/metalloids in the ELSA-Brasil study.

Methods
This is a prospective analysis based on the serum levels of metals/metalloids in the baseline wave (2008-2010) and the migraine diagnosis in the inter-wave (2012-2014). Metals quantification was performed by Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and migraine diagnosis was based on ICHD-3, grouped as migraine without aura (MWO), migraine with aura (MWA), and non-migraine headache (NO). Modified Poisson regression models estimated the risk ratios (RR) with [95% confidence interval] for migraine diagnosis, according to metals concentration quintiles (Q), with the median as reference and 1st and 5th quintiles representing the lowest and highest metal levels, respectively. The adjusted models controlled for sex. age, education, race, smoking, alcohol intake, migraine prophylactic medication, and cardiometabolic risk factors.

Results
The study included 2,662 adults, with a median (IQR) age: of 51 (45, 58) years and 52.7.0% (n = 1,403) female. In the adjusted models, 5th Q of Cu (RR: .79 [.64, .97]) and 3rd Q of Ba (RR: .86 [.76, .96]) were associated with a lower risk of NO, while 5th Q of Pb (RR: 1.16 [1.00, 1.34]) were associated with a higher risk of NO. The 1st Q of Fe (RR: 1.31 [1.01, 1.69]), 3rd Q of Ba (RR: 1.39 [1.14, 1.70]), and the 5th Q of Cd (RR: 1.35 [1.05, 1.74]) were associated with higher risk of MWO, while 5th Q of Se (RR: .70 [.50, .99]) and 3rd Q of Zn (RR: .78 [.63, .97]) were associated with lower risk of MWO. The extreme levels of Cd and Sr (5th Q and 1st Q) were associated with increased risk of MWA (RR: 1.48 [1.04, 2.10] and RR: 1.41 [1.01, 1.97], respectively). Finally, the 1st Q of Cu was associated with a lower risk of MWA (RR: .65 [.44, .97]).

Conclusion
In the ELSA-Brasil, a diverse relationship was observed between metals and headaches with a higher magnitude of associations noticed with higher levels of Cd and both migraine subtypes.