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RESEARCH ARTICLE

Neurotoxins in the Human Brain in the Anthropocene; Tipping Points

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Abstract

We measured neurotoxic metal content in 16 human mummified brains collected from sites in New Mexico, USA and locations in Belgium, Chile and Peru. We modeled statistically the tipping points in terms of the accumulation of Hg or of other metals known to cause clinical harm.

We find that neurotoxins are present in human nervous tissues and have consequences for human health and well being in the Anthropocene. In Belgium, North and South America the levels of these neurotoxins show that tipping points have been reached though these vary by region. Thus when modeled statistically, tipping points may reach critical levels in the Anthropocene and predict human clinical effects.

Key words: Neurotoxic metals; mummified brains; regional variations; tipping points; statistical modeling; critical levels; human clinical effects.

Introduction

The Anthropocene is the geological period we now live in. Although the exact start of this period continues to be debated there is no doubt that the human impact on the environment is widely felt and frequently induces tipping points on oscillating systems such that the normal oscillations of the systems no longer occur **[1]**

We report on an examination of the toxic metal content of pre Anthropocene mummified brains from Belgium, Peru and Northern Chile and on induced tipping points in patients with a childhood neuropathy from a highly polluted region of the USA **[2].**

This disease was first described in 1976 under the name of *Acromutilating paralyzing neuropathy with corneal ulceration in Navajo children* **[2].** The etiology of this devastating childhood disease, confined to Navajo children, remained unknown until 2006 when a mutation in the MPV17 gene in the patients was discovered which is caused by a single missense mutation in exon 2 in the *MPV17* gene **[3]**. This disease, however, is not confined to the Four Corner Region of the South-Western United states; it also occurs in other highly polluted areas of the world such as Iraq and Morocco **[4].**

Our results are consistent with the hypothesis that patients with this disease had reached the tipping point with Hg and Cd

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but that many without the mutation in the MPV-17 gene and living in the Four Corner Region, USA and other parts of the world could have reached tipping points with other neurotoxic metals.

Tipping points are statistically modeled values which in human biology are influenced by numerous intrinsic and extrinsic factors, such as genetic influences **[5]** food intake, age, environmental toxins, place of residence and many more. Thus their actual clinical manifestation are not predictable by statistical modeling alone, nevertheless our analyses of human nervous tissues suggests that the Anthropocene may soon affect the levels of toxic metals with discernible biological effects.

Materials and Methods

Definition of Tipping Point

Here we define biological tipping point in terms of the accumulation of Hg or of other metals known to cause clinical harm.

Sample collection

We collected samples from sites in New Mexico, USA and locations in Belgium, Chile and Peru. Samples were donated by the Universidad Peruana Cayetano Heredia, Lima, Peru. (Permit# 196687-16-2014). The Museo Arqueologico de San Pedro de Atacama, Universidad : Museo Aqueologico Catolica del Norte, Chile (letter dated March 26, 2003), Direction générale opérationnelle de l'aménagement du territoire, du logement, du patrimoine et de l'énergie, Direction extérieure du Brabant wallon , Service de l'archéologie, Nivelles, Belgium. **Table 1** shows the dating and provenance of the samples used in this study (Letter dated February 1, 2017).

The samples were analyzed in the laboratories of the Earth and Planetary Sciences at the University of New Mexico. The New Mexico Health Enhancement and Marathon Clinics (NMHEMC) Research Foundation's IRB committee gave approval for this study (NMHEMC 16- 23).

Sample preparation

Samples were crushed manually using a pestle and mortar. The samples were then pulverized using a SPEX mixer mill with carbide vessel and mixing balls. About 1.000 to 2.000 grams of the sample were weighed and digested using a mixture of 3 ml concentrated nitric acid (HNO3) and 2 ml concentrated hydrochloric acid (HCl). Samples were digested using DigiPrep heating block equipped with temperature controller at 95^0C for about two hours. After digestion was completed, samples were filtered (0.45 micron) and brought to final volume of "25 ml".

ICP-OES Analysis

Digested samples were transferred into 15 ml glass test tubes and were setup on the Inductively Coupled Plasma – Optical Emission Spectroscopy (ICP-OES) (PerkinElmer, Optima 5300DV ICP-OES; and for Hg FIMS) autosampler. The system was optimized using mercury optical alignment and manganese (Mn) view touch alignment. The ICP-OES was then calibrated using a blank and three calibration standards. The calibration standards that were diluted sequentially in order to achieve a linear calibration curve. A set of quality control check samples (Initial Calibration Blank Verification "ICBV", Initial Calibration Verification "ICV", and Continuing Calibration Verification ("CCV") were measured to verify and validate calibration and data quality. Samples were analyzed in triplicate readings; data were reduced, verified, validated, and reported in mg/Kg unit of measurement.

FIMS Mercury Analysis

Digested samples were diluted two times using three percent hydrochloric acid (HCl). Samples were transferred into 15 ml glass test tubes and were setup on the Flow Injection Mercury System (FIMS) autosampler. The system was optimized and calibrated for mercury (Hg) using a blank and three calibration standards that were diluted sequentially in order to achieve a linear calibration curve. A set of quality control check samples (Initial Calibration Blank Verification "ICBV", Initial Calibration Verification "ICV", and Continuing Calibration

Table 1: The ID code numbers of brain samples (16), their provenance and dating are listed below.

Brain ID code	Provenance	Archaeological date	14C date (if applicable)
Ilo	Peru	5th-6th c. AD	/
San Pedro de Atacama	Chile	5th-6th c. AD	/
Four Corner Region	USA	20th c. AD	/
Four Corner Region	USA	20th c. AD	/
Four Corner Region	USA	20th c. AD	/
Secteur 1 fait 058	Nivelles Grand Place (Belgium, Europe)	9th-11th c. AD	/
Secteur 1 fait 118	Nivelles Grand Place (Belgium, Europe)	9th-11th c. AD	/
Secteur 1 fait 133	Nivelles Grand Place (Belgium, Europe)	9th-11th c. AD	/
Secteur 3 fait 009	Nivelles Grand Place (Belgium, Europe)	11th-13th c. AD	1020-1210 AD
Secteur 3 fait 010	Nivelles Grand Place (Belgium, Europe)	9th-11th c. AD	/
Secteur 3 fait 019	Nivelles Grand Place (Belgium, Europe)	8th- 11th c. AD	783-1018 AD
Secteur 3 fait 119	Nivelles Grand Place (Belgium, Europe)	11th- 13th c. AD	1052-1274 AD
Secteur 3 fait 122	Nivelles Grand Place (Belgium, Europe)	11th-12th c. AD	1025-1159 AD
Secteur 3 fait 123	Nivelles Grand Place (Belgium, Europe)	9th-11th c. AD	/
Secteur 3 fait 124	Nivelles Grand Place (Belgium, Europe)	9th-11th c. AD	/
Secteur 3 fait 134	Nivelles Grand Place (Belgium, Europe)	9th-11th c. AD	/

Verification ("CCV") were measured to verify and validate calibration and data quality. Samples were analyzed in triplicate readings; data were reduced, verified, validated, and reported in mg/Kg unit of measurement.

Results

(Figures 1-5)

Discussion

It is generally accepted that we have reached the Anthropocene that is the geological period in which human activities are changing the geology of the world we live in **[6].** However, the start of this period continues to be debated, for example, some opine that the advent of humans on earth millions of years ago marks its beginning, others think that the industrial revolution marks its onset and yet others propose that the detonation of the first atomic bomb should mark the onset of the Anthropocene **[7]**.

Clearly the changes wrought in the geology and consequently the amount of neurotoxin accumulation in the human brain because of geochemical enrichment is heavily impacted by regional variations **[4]**. Our results support this conclusion

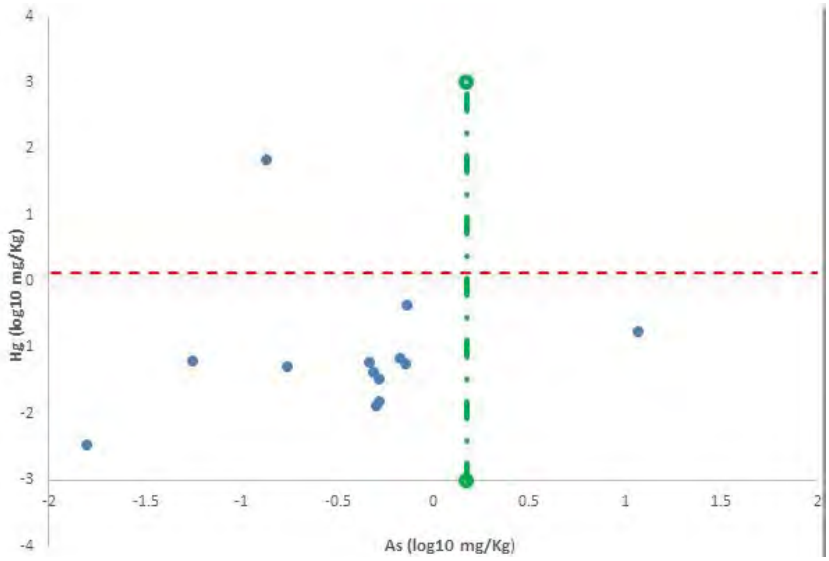

Figure 1: Hg $\log_{10}$ concentration versus As $\log_{10}$ concentration in brain and nerve tissues (blue solid circles). Dashed lines denote Hg tipping point (red) and As tipping point (green). Four Corner Region-USA is far beyond Hg tipping point and Chile is beyond the As tipping point.

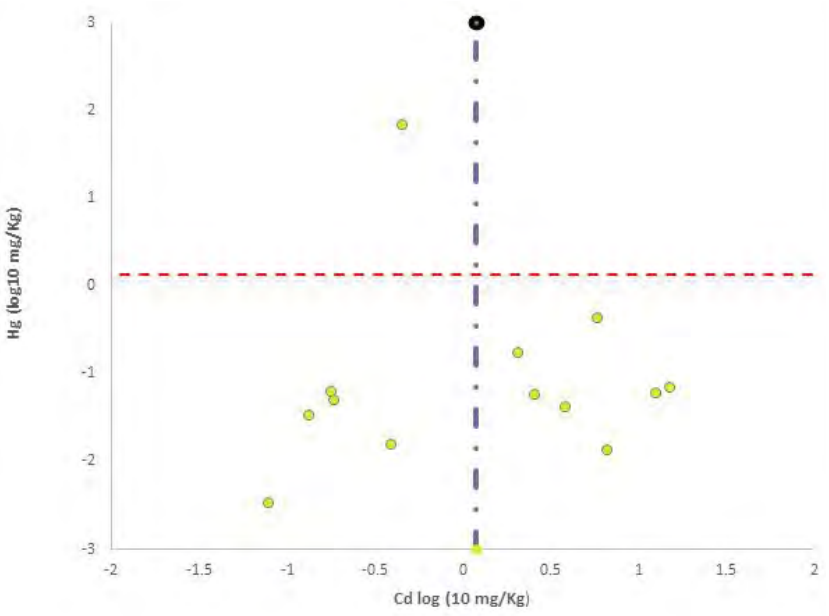

Figure 2: Hg $\log_{10}$ concentration versus Cd $\log_{10}$ concentration in brain and nerve tissues (yellow solid circles). Dashed lines denote Hg tipping point (red) and Cd tipping point (purple). Ancient brains from Nivelles (Belgium), Peru, and Chile are beyond the Cd tipping point.

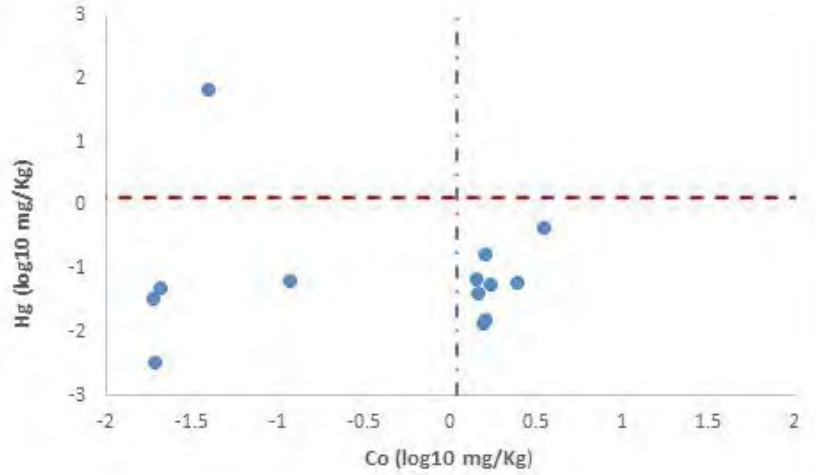

Figure 3: Hg $\log_{10}$ concentration versus Co $\log_{10}$ concentration in brain and nerve tissues (blue solid circles). Dashed lines denote Hg tipping point (red) and Co tipping point (purple). Ancient brains from Nivelles (Belgium), Peru and Chile are beyond the Co tipping point.

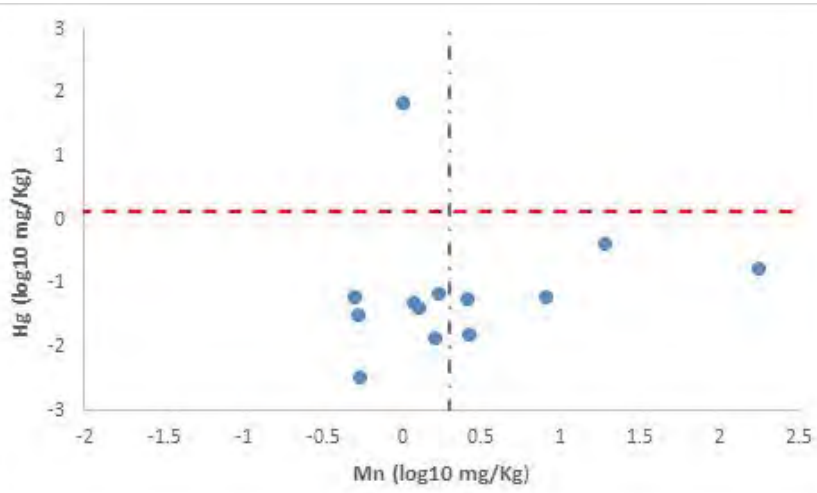

Figure 4: Hg $\log_{10}$ concentration versus Mn $\log_{10}$ concentration in brain and nerve tissues (blue solid circles). Dashed lines denote Hg tipping point (red) and Mn tipping point (purple).Ancient brains from Nivelles (Belgium), Peru and Chile are beyond the Mn tipping point.

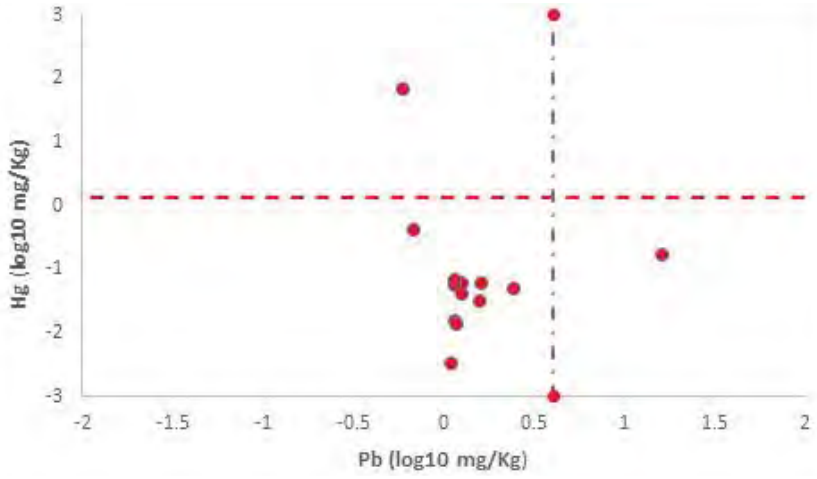

Figure 5: Hg $\log_{10}$ concentration versus Pb $\log_{10}$ concentration in brain and nerve tissues (red solid circles). Dashed lines denote Hg tipping point (red) and Pb tipping point (purple). Ancient brain from Chile is beyond the Pb tipping point.

because the type of toxin found in the brains by our analyses varies widely with the provenance of the specimens examined.

The neurotoxin content of the human brain may also eventually impact the prevalence of neurodegenerative diseases **[7]**. Thus the prevalence of Parkinson's disease is influenced by the use of pesticides **[8]** and Alzheimer's disease by neurodevelopmental changes wrought by regional variations in anthropogenic effects (heavy metal content of the soil) **[9]**.

Tipping points are oscillating systems which are a feature of biological systems **[10]**. In human biology a tipping point is defined by a transition point in which the system ceases to oscillate. This point leads to irreversible collapse of metabolism **[11]** and death. Because of pollution of the environment by mercury in the Four Corner region of the USA and clinical evidence we choose to compare the tipping points of all other toxins analyzed in this study to the mercury tipping point found in the Four Corner Region, USA.

The effects of heavy metals on tipping points have previously been described during the Renaissance **[12]**. However, our study is the first to examine the influence of heavy metals content in nervous tissues on tipping points occurring in many regions of the world.

In **Figure 1** we showed the tipping points of metals from nervous tissues of patients with a genetically determined childhood neuropathy **[2]** occurring in the Four Corner Region of the South-Western USA. This clearly indicates that these patients had exceeded the critical transition for mercury and arsenic, their metabolism stopped and they died. This conclusion is supported by their clinical histories. These patients had an average lifespan of only 10 years **[13]**.

In **Figure 2.** we illustrate the tipping points for mercury and cadmium. Unlike in **Figure 1** the critical transitions in brains from Nivelles (Belgium), Peru, and Chile are beyond the Cd tipping point. Cadmium has no physiological functions and its presence in the human body is regulated by absorption and excretion patterns largely dependent on dietary and environmental factors. **[14]**

Figure 3 shows the tipping points for cobalt. Ancient brains from Nivelles (Belgium), Peru and Chile are beyond the Co tipping point **[15].** Modern orthopedic surgical procedures are examples of cobalt toxicity which are becoming increasingly frequent in the Anthropocene.

Figure 4 illustrates the tipping point for manganese. The tipping point for this metal is exceeded in ancient brains from Nivelles (Belgium), Peru and Chile.

In **Figure 5** gives the tipping point for lead. An ancient (~1500 years) brain from Chile was beyond the Pb tipping point. Lead is a naturally occurring poison in the earth's crust and its levels are increasing in the Anthropocene. Lead has no clinical functions and it is especially harmful to children's nervous tissues **[16]** but it can affect every organ in the body thus lead tipping points may predict the prevalence of hypertension in adults and developmental abnormalities in children.

Although the clinical effects of tipping points are, as yet, not predictable by statistical modeling alone, nevertheless our analyses of human nervous tissues suggests that the Anthropocene will affect the toxic metal content with discernible biological effects.

Conclusions

We find that neurotoxins are present in human nervous tissues and have consequences for human health and well being in the Anthropocene. In Belgium, North and South America the levels of these neurotoxins show that tipping points: have been reached though these vary by region. Thus when modeled statistically, tipping points may reach critical levels in the Anthropocene and predict clinical effects.

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Competing interests statement

The authors declare no competing interests

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