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Selenium and mercury in the human brain tissue

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Introduction

The interaction between mercury (Hg) and selenium (Se) is one of the best-known examples of biological antagonism, yet the underlying mechanism remains unclear [1]. Several studies indicate that the toxic effects of Hg exposure increase when Se status is low. It is widely accepted that the toxicity is inversely proportional to Se:Hg molar ratios in specific tissues (e.g., brain) and increases dramatically for Se:Hg molar ratios < 1 [2].

Considering that the brain is a highly heterogeneous organ, with anatomically and physiologically very different areas, a detailed mapping of trace elements (TE) distribution across the brain tissue, with an in-depth analysis of TE levels in the different brain regions, of normal individuals is a prior work, absolutely necessary for understand the role of essential TE in the brain physiology and to interpret the data obtained from patients suffering from neurodegenerative and other brain diseases.

Objective

To determine the Hg and Se levels in the human brain in 14 different the anatomical regions.

Experimental

Brain samples were collected from individuals submitted to autopsy exam at National Institute of Legal Medicine and Forensic Sciences, North Branch, Portugal, after verifying all current legal regulations regarding human tissue collection for scientific research purposes. It were studied individuals with no neurodegenerative, neurological or psychiatric disorder history in each age group: 50-59 (*n*=10); 60-79 (*n*=10); 70-79 (*n*=10) and 80-89 (*n*=9) and ≥90 years (*n*=3) old.

As suggested by Paine and Lowe [3], fragments (c.a. 1 cm^3) from the following areas were sampled: (1) frontal cortex; (2) superior and middle temporal gyrus; (3) basal ganglia, including the caudate, putamen and globus pallidus; (4) cingulated gyrus; (5) hippocampus; (6) inferior parietal lobule; (7) visual cortex of the occipital lobe; (8) midbrain; (9) pons; (10) medulla; and (11) cerebellum (Figure 1a).

Dried brain samples (100-500 mg) were digested with HNO_3 ≥ 65% and H_2O_2 ≥ 30% through a closed vessel microwave-assisted digestion procedure (Milestone, Italy, MLS-1200 microwave oven) and the solutions were then analyzed by inductively coupled plasma-mass spectrometry (ICP-MS) for Hg and Se quantification using a iCAP-Q (Thermo, UK) instrument. Results were expressed as µg/g in a dry weight basis.

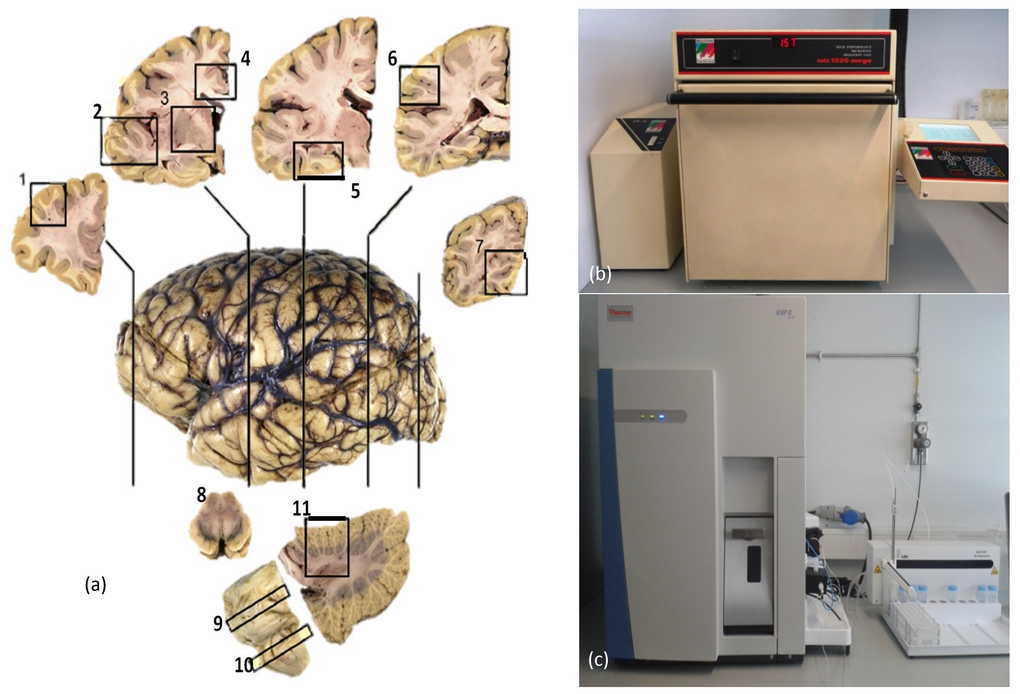

Figure 1 – Brain regions sampled (a), Milestone MLS 1200 microwave oven digestion unit (b) and ICP-MS instrument (c).

Results

Considering the whole data set (n=588; 42 individuals x 14 brain areas), Se and Hg levels were 0.63±0.08 µg/g (range: 0.46–0.98 µg/g) and 0.15±0.09 µg/g (range: 0.05–0.41 µg/g), respectively. The distribution of Hg within brain tissue showed to be homogeneous, but not the Se distribution: highest levels were found in the putamen (a region mainly related to motor functions), and the lowest in the cerebellum (Figure 2). No significant age- or gender-related differences were found for both elements.

Selenium levels tended to a slight increase with Hg levels (Figure 3).

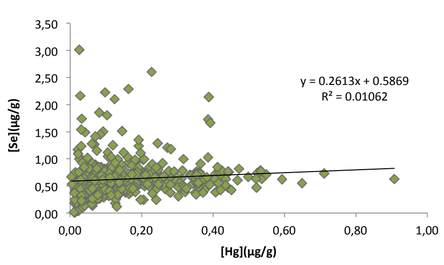

Figure 3 – Relationship between Se and Hg levels.

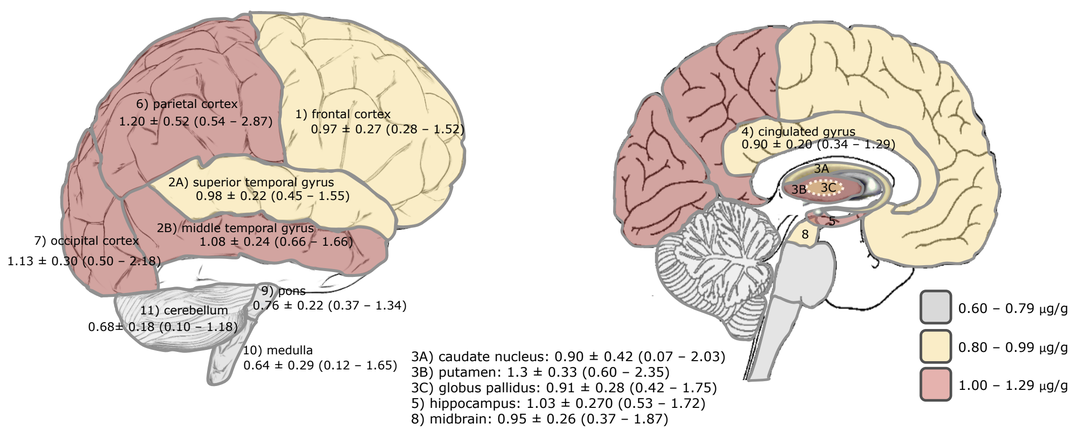

Figure 2 – Results (µg/g dry weight basis), expressed as mean±SD (range), for Se in the 14 brain areas studied.

Se:Hg molar ratios < 1 were not found in any brain region; values ranged from 11.6±9.1 in the midbrain to 30.0±23.0 in the caudate nucleus. Se:Hg molar ratio was not correlated with age (Figure 4).

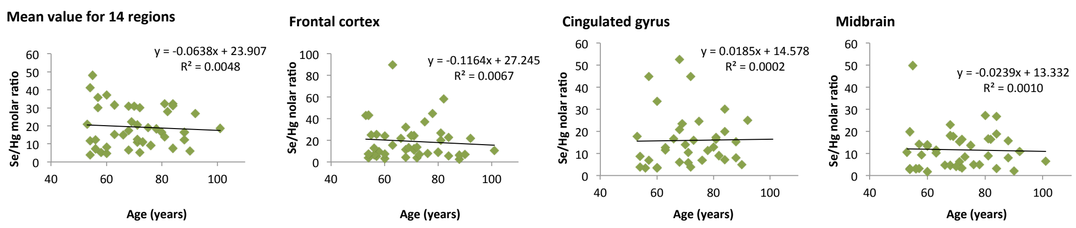

Figure 4 – Relationship between Se/Hg molar ratio and age (years). Mean Se/Hg molar ratio (a) for each individual (all the 14 brain regions) and Se/Hg molar ratio in the frontal cortex (b), cingulated gyrus (c), and midbrain (d).

Conclusion

Although Se levels remain quite unchanged with age, the "normal" (physiologic) levels of Se significantly varies among different brain regions. The distribution of Hg within brain tissue showed to be homogeneous but not the Se:Hg molar ratio, suggesting that some brain regions may be more susceptible to Hg toxicity. Se:Hg molar ratio was not correlated with age, which suggest that individuals experience the same protective advantages of Se against Hg toxicity irrespective of their age.

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References: **[1]** Khan, M., Feiyue, Y. Mercury-selenium compounds and their toxicological significance: Toward a molecular understanding of the mercury-selenium antagonism. *Environmental Toxicology and Chemistry* 2009, 8, 1567-77. **[2]** Brockman, J. D., Raymond, L. J., Ralston, C. R., Robertson, J. D., Bodkin, N., Sharp, N., Ralston, N. V. The Nail as a Noninvasive Indicator of Methylmercury Exposures and Mercury/Selenium Molar Ratios in Brain, Kidney, and Livers of Long-Evans Rats, *Biological Trace Elements Research* 2011, 144, 812-20. **[3]** Paine S, Lowe J. Approach to the post-mortem investigation of neurodegenerative diseases from diagnosis to research. *Diagnostic Histopathology* 2011 17(5), 211-216.