G4 Iron in the Human Brain: Age-Related Changes and Anatomic Region Specific Differences

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The goal of this presentation is to show the first results of a research work aiming to clarify the role of iron in brain functions, and particularly its implication in neurodegeneration. Since neurodegenerative diseases are strongly age-related and there is a specific region of the central nervous system that seems to be particularly affected in each disease, the main objectives of this research are to study: (1) the changes on iron levels in human brain in relation to age; (2) the regional anatomic differences of iron levels within the brain; and, (3) the differences between individuals with and without evidence of neurodegenerative diseases.

This presentation will impact the forensic science community by giving epidemiology background data concerning iron levels in the healthy human brain. Since no updated and comprehensive data about trace elements in the human brain are available, this study is a relevant scientific contribution for establishing “normal” human brain levels, allowing a comparison with a brain affected by neurodegenerative diseases in an attempt to clarify trace elements’ role in the disease process.

The etiology of neurodegenerative diseases is multifactorial, assuming that it involves a complex interaction between natural aging, environmental factors, and genetic predisposition. The involvement of trace elements, particularly iron, in neuronal damage in distinct areas of the brain has been demonstrated in Alzheimer’s and Parkinson’s disease. However, despite the research work that has been done on the relationship between trace elements and neurodegenerative diseases, the evidence is still fragmentary, and their role remains poorly understood. Most of the current information about the relationship between trace elements and human brain functioning is based on animal studies or relies on determinations in cerebrospinal fluid, blood, and serum. To fulfill this lack, iron levels were quantified directly in human brain tissue in this research. Direct determination of trace elements in samples from patients with neurodegenerative diseases and normal individuals is essential to extend the understanding of the underlying disease mechanisms, to validate animal models, and to develop therapies that can delay or reverse neurodegeneration processes.

Two groups of individuals submitted to autopsy, performed at the North Branch of the National Institute of Legal Medicine and Forensic Sciences of Portugal, in the first quarter of 2012, were studied. Group A consisted of ten individuals in each age sub-group: 50 – 60; 60 – 70; 70 – 80; 80 – 90 and over 90-years-old. Ten healthy accident victims 20 to 30-years-old were included as controls (“baseline”). Group B consisted of individuals submitted to autopsy with previous diagnosis of Alzheimer’s and Parkinson’s disease. After verifying all current legal regulations in Portugal for human tissue collection for scientific research purposes, the following areas were sampled from each individual: (1) frontal cortex; (2) superior (2 – A) and medium (2 – B) temporal; (3) basal ganglia including, caudate nucleus (3 – A), putamen (3 – B) and globus pallidus (3 – C); (4) cingulated gyrus; (5) hippocampus; (6) inferior parietal lobule; (7) visual cortex of the occipital lobe; (8) midbrain including the substantia nigra; (9) pons—locus coeruleus; (10) medulla; and, (11) cerebellum—dentate nucleus. Iron levels were determined by Graphite Furnace Atomic Absorption Spectrometry after the microwave-assisted acid digestion of samples.

Results showed that iron distribution in an adult human brain is not homogeneous: the highest levels are found in basal ganglia and the lowest in pons and medulla. In specific areas, iron deposition seems to be age-related since there is a direct correlation between iron levels and age, namely in putamen, cingulated gyrus, visual cortex of the occipital lobe, midbrain, and cerebellum. However, in caudate nucleus and globus pallidus, iron levels seems to decrease with age. In Alzheimer’s disease, significantly increased iron levels in basal ganglia were found when compared with healthy people of the same age sub-group.

Aging, Iron Accumulation, Neurodegeneration

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