



3rd
INTERNATIONAL
CONGRESS ON
ENVIRONMENTAL
HEALTH 2014

PORTO, 24th to 26th SEPTEMBER 2014

**PROCEEDINGS
BOOK**

EMERGING RISKS AND CHALLENGES ON ENVIRONMENT,
HEALTH AND SAFETY

Allied Health Sciences School of Polytechnic Institute of Porto,
Portugal

Title:

3th International Congress of Environmental Health: Proceedings Book
3^o Congresso Internacional de Saúde Ambiental: Livro de Resumos

Edition:

1st Edition / Book in 1 Volume, 520 pages

Authors / Editors:

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Santos, Joana; Carvalhais, Carlos; Rebelo, Andreia; Freitas, Marisa; Xavier, Ana

Publisher:

(ESTSP-IPP)

Scientific Area of Environmental Health of Allied Health Sciences School of Polytechnic Institute of Porto
Área Científica da Escola Superior de Tecnologia da Saúde do Instituto Politécnico do Porto

Design / Layout:

4CS

Local / Date:

Porto / November 2014

ISBN:

978-989-20-5086-7

Legal Deposit:

384046/14

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Anatomic region differences and age-related changes on Na⁺ and K⁺ levels in human brain

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INTRODUCTION:

Neurodegenerative diseases (ND) have been the subject of intensive research in last years in an attempt to understand the mechanisms underlying the neurodegeneration process. The etiology of these diseases is multifactorial, involving a complex interaction between the aging, genetic predisposition and environmental factors. In particular, the role of metals as risk factors for neurodegenerative disorders is currently being studied. As regards to this topic, the knowledge of metal distribution in the brain is of major importance [2]. Evidence suggests that Alzheimer's disease (AD) is associated with impaired depressed Na⁺/K⁺ ATPase levels in AD brain that might lead to a cellular ion imbalance [1]. Recent studies show that a pronounced variability exists in the distribution of several elements (Ca, Fe, Mg) in brain tissues according to brain area and the age of individuals [3,4].

OBJECTIVES:

The goals of this work were to study: (1) the regional anatomic differences of Na⁺ and K⁺ levels within the brain; (2) the changes on Na⁺ and K⁺ levels in relation to age; and 3) the differences in Na⁺ and K⁺ levels between individuals with and without evidence of ND.

MATERIALS AND METHODS:

From each neurologically and psychiatrically healthy individual submitted to autopsy (n=44) the following 14 areas were sampled: (1) frontal cortex; (2A) superior and (2B) middle temporal; (3A) caudate nucleus, (3B) putamen, (3C) globuspallidus; (4) cingulated gyrus; (5) hippocampus; (6) inferior parietal lobule; (7) occipital lobe; (8) midbrain; (9) pons; (10) medulla; and (11) cerebellum. Samples from individuals with previous diagnosis of Alzheimer's (n=2) and Parkinson's disease (n=1) were also collected. After microwave-assisted acid digestion of the samples Na⁺ and K⁺ levels were determined by atomic absorption spectrometry (AAS).

RESULTS AND DISCUSSION:

Considering the mean value for the 14 areas studied, K (12.5 ± 1.3 mg/g) was present at higher levels than Na⁺ (7.6 ± 1.3 mg/g). The distribution of Na⁺ and K⁺ within the brain tissue showed to be not homogeneous. Highest levels of K⁺ were found in the middle temporal gyri (15.9 ± 3.5 mg/g) and putamen (15.5 ± 2.4 mg/g), whereas highest levels of Na⁺ were found in the frontal cortex (11.5 ± 2.4 mg/g). Medulla and cerebellum were the regions with the lowest levels of K⁺ and Na⁺, respectively. In specific brain areas, Na⁺ and K⁺ levels were age-related. Positive correlation between Na⁺ levels and age was found in several brain areas (e.g., middle temporal gyrus, caudate, cingulated gyrus, hippocampus, inferior parietal lobule). For K⁺, a negative correlation with age was observed in the frontal cortex. When compared with age-matched controls, Na⁺ levels from individuals affected by Alzheimer's disease were found significantly increased in some brain regions. In both Alzheimer's disease patients, increased Na⁺ levels were found in the superior temporal gyri (20.8% and 12.8%) and globuspallidus (52.5% and 56.8%, respectively). For K⁺, no significant differences

were observed. In the Parkinson's disease patient, Na⁺ levels were decreased in most of the brain areas except frontal cortex, hippocampus and cerebellum. The K⁺ content was increased in 9 of the brain regions and decreased in the remaining 5 regions.

CONCLUSION:

In conclusion, K⁺ is present at higher levels than Na⁺. The elements levels at the different brain regions vary significantly, although the K⁺ and Na⁺ levels are not correlated with each other in the same brain regions. Therefore, the K⁺/Na⁺ ratio also varies significantly from region to region. Generally, Na⁺ increase seems to be age-related, however this tendency was not constant in the different brain regions. Patients with ND presented altered Na⁺ and K⁺ levels in some brain regions but results are inconclusive. This study provides a comprehensive picture of Na⁺ and K⁺ distribution within the brain tissue. This data may be a relevant contribution for defining "normal" human brain levels of Na⁺ and K⁺, allowing future interpretation of the levels found in ND, in an attempt to clarify their role in the disease process.

ACKNOWLEDGMENTS:

The authors are grateful to Universidade do Porto for financially support the project "Trace elements in human brain: age-related changes and anatomic region specific differences".

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