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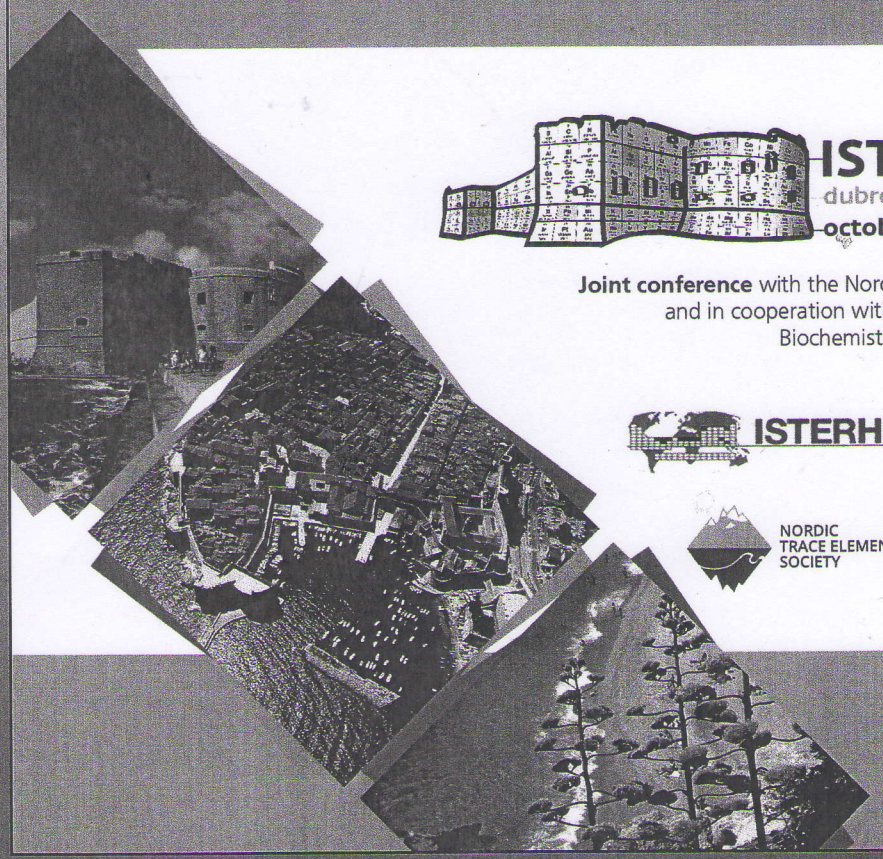
ABSTRACTS XI. ISTERH CONFERENCE
RECENT ADVANCES IN TRACE ELEMENT RESEARCH IN HEALTH AND DISEASE



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Iron in Alzheimer's and Parkinson's diseases

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The major proteins implicated in Alzheimer's disease (AD) and Parkinson's disease (PD) have important functions in metal transport, and particularly are components of an iron regulatory system that fails in aging. The amyloid protein precursor (APP), like ceruloplasmin (CP), facilitates the export of iron from cells by stabilizing cell surface ferroportin, and prevents iron from accumulating in the brain. Tau impacts on iron export by trafficking APP to the cell surface. Elevated CSF ferritin levels predict conversion of MCI to AD, and the major genetic risk factor for AD, Apolipoprotein E, has a striking relationship with CSF ferritin that implies a causal role for iron in AD. Knockout mice for both ceruloplasmin and APP develop iron-mediated PD pathology, remedied by iron chelators. A recent phase 2 trial of deferiprone in PD lowered nigral iron and improved clinical readouts. The involvement of all major proteins implicated in AD in metal trafficking raises the possibility that this major neurodegenerative disorder is caused by a collapse of metal homeostasis, and supports the adjustment of metal regulation as a pharmacological target.

Macro and microelements and Alzheimer's disease protein biomarkers in cerebrospinal fluid

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The homeostasis of macro and microelements is altered in the brain of patients suffering from Alzheimer's disease (AD). In this study we analysed 24 macro and microelements in cerebrospinal fluid (CSF) and correlated its concentration with AD protein biomarkers ($A\beta_{1-42}$, t-tau, p-tau_{181}, p-tau_{199}, p-tau_{231} and VILIP-1) in CSF of 63 patients with AD, 31 with mild cognitive impairment (MCI), and 11 healthy controls (HC). A significantly negative correlation was found between $A\beta_{1-42}$ and Co, while significantly positive correlations were obtained between t-tau and Li, As, Se, Sr; p-tau_{181} and B, Na, Mg, S, K, Ca, Cr, Fe, Co, Mn, Ni, Cu, Zn, As, Se, Mo, Tl, Hg; p-tau_{199} and B, Na, Mg, S, K, Ca, Cr, Fe, Co, Mn, Cu, As, Se, Sr, Mo, Cd, Ba, Tl, Hg; p-tau_{231} and Li, B, Na, Mg, S, K, Cr, Fe, Co, Mn, Ni, Cu, Zn, Se, Sr, Mo, Tl, Hg; VILIP-1 and Li, B, Na, Mg, S, K, Ca, Cr, Fe, Co, Mn, Ni, Cu, Zn, As, Se, Sr, Mo, Cd, Ba, Tl, Hg. Although possible explanation of altered levels of elements in AD brain will await identification of their environmental sources or detection of their release from brain tissue due to cell death, these results suggest CSF element analysis potential as marker of AD neurodegenerative process. *Funded by: CSF project IP-2014-09-9730.*

Macro and microelements as biomarkers of mild cognitive impairment

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About 10% of patients with mild cognitive impairment (MCI) convert to Alzheimer's disease (AD) each year. As homeostasis of elements is disturbed in the AD brain, measurement of their levels in cerebrospinal fluid (CSF) has a diagnostic potential in identification of MCI patients who will progress to AD. We studied the difference in macro and microelement levels in groups of MCI patients with and without pathological levels of AD protein biomarkers ($A\beta_{1-42}$, t-tau, p-tau_{181}, p-tau_{199}, p-tau_{231}, VILIP-1). Levels of S, Co, Mo, and Tl were significantly increased in the MCI group with pathological $A\beta_{1-42}$ levels, while levels of K, Cr, Fe, Cu, As, Se, and Hg were significantly increased in the MCI group with pathological p-tau_{181} levels. Significant increase in Ca and As was found in the MCI group with pathological p-tau_{199} levels, while the MCI group with pathological p-tau_{231} levels had increased Li, B, Na, Mg, S, K, Ca, Cr, Fe, Co, Mn, Ni, Cu, Zn, As, Se, Sr, Mo, Cd, Ba, Tl, and Hg. The MCI group with pathological VILIP-1 levels had significantly higher Na, Mg, S, K, Ca, Cr, Fe, Mn, Cu, As, Se, Sr, Ba, and Hg. Despite small cohort of MCI patients (n=31), result indicate potential of elements concentration as a diagnostic marker of disease progression. *Funded by: CSF project IP-2014-09-9730 .*

The influence of lead (Pb) on macrophage cellular membrane modification

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Lead (Pb) is common heavy metal, it can get into the body by various routes, pollution and the air so as water and soil is dangerous. The increasing numbers of people struggling with cardiovascular diseases, research on factors contributing to the development of these diseases, deserve special attention. This study aims to verify whether the Pb can result in a modification of the macrophage cell membrane by affecting the content of the various fatty acids (FA). The study was performed on human leukemic cell line. Profile of 16 FA was analyzed by gas chromatography. The correlation between the membrane FA content and the Pb was observed. Arachidonic acid (20:4n6) showed the greatest increase *vs* control and the concentration of gamma-linolenic (18:3n6) decreased significantly. The study shows that Pb affects on the lipid`s profile of cell membranes of macrophages thus can induce changes in its properties. The results may indicate about atherogenic character of Pb.