

Abstract Preview - Step 3/4

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Topic: Neuropathology and pathogenesis

Keyw ords: endothelial factors, brain perfusion, intracranial circulation

Title: Imaging of brain perfusion in multiple sclerosis and neurodegenerative disorders: association with endothelial factors. An interim analysis.

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Text: **Background:** Among the factors contributing to brain damage in Multiple Sclerosis (MS), scientific evidences indicate ischemic changes, venous outflow abnormalities and accumulation of pro-inflammatory and neurotoxic substances.

Objectives: This project aims at acquiring new knowledge about the association of determinants of brain perfusion in patients with MS and neurodegenerative diseases such as Amyotrophic Lateral Sclerosis (ALS), combining Magnetic Resonance (MR) and Ultrasound (US) imaging of the brain and intracranial and extracranial circulation, and endothelial factors.

Methods: 300 MS patients, 50 ALS patients, and 300 healthy subjects (HS) will be recruited over 3 years. To assess the vascular genetic susceptibility, serum levels of homocystein and endothelial factors will be assayed, as well as the association between the C677T polymorphism of methylen-tetrahydrofolate reductase (MTHFR), informative SNPs in VEGF-A, Endothelin 1 and HIF1A genes and micro and macro vascular abnormalities in MS and ALS. With MR, we will assess the arterial inflow and mean transit time using brain Perfusion Weighted Imaging (PWI), the state of the deep intracranial veins using Susceptibility Weighted Imaging (SWI), and measure iron deposits in the basal ganglia using dedicated software. Extracranial and transcranial color-Doppler US with time intensity curve analysis was used to quantitatively evaluate cerebral inflow and outflow parameters and cerebral perfusion.

Results: In the first year we recruited 228 MS patients, 33 ALS patients and 67 HS. Homocystein levels (HL) were assessed in 132 patients, VEGF-A in 50 patients and in 25 HS. Median HL were similar in MS and ALS patients (13.2 vs 16.0, $\mu\text{mol/L}$, $p=0.2$). Higher-than-normal HL were found in 32.2% of MS (CI 24-41%) and 66.7 % of ALS patients (CI 30-92%), but not significantly different in the two groups ($p=0.08$). Instead, median HL were significantly higher in males with MS compared to females (17.3 vs 13.9 $\mu\text{mol/L}$, $p<0.001$). VEGF-A values tended to be higher in MS patients vs HS (251.7 vs 145.7 U/mL, $p=0.4$). 101 patients (78 RR, 2 PP, 11 SP and 10 ALS) underwent contrast-enhanced brain MR, and 68 patients (54 RR, 1 PP, 10 SP and 3 ALS) underwent US evaluation.

Conclusions: Combining different imaging modalities and laboratory analysis may provide new insights into the vascular aspects of MS pathogenesis. These preliminary results favor an altered vascular profile in MS and ALS patients. Definitive results will be available at project termination in 2016.

Study Support: Research and University Ministry

Unlabeled/Unapproved Drugs: No

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