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Title:

Decreased glucose-derivate uptake in primary somatosensorial cortex in the brain of female AIP mice.

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Abstract:

Brain magnetic resonance imaging studies performed in some patients with acute intermittent porphyria (AIP) showed reversible white-matter lesions, compatible with the hypothesis of vasospasm due to a diminution in the nitric oxide production in the brain. In this study we try to identify low perfusion areas in the brain of AIP mice.

The cerebral blood flow (CBF) values were measured by functional magnetic resonance imaging (fMRI) in wild type and AIP female mice before and during an acute attack induced by phenobarbital. In order to verify relationship between CBF and glucose metabolism, specific regional brain fluoro-2-deoxy-D-glucose (^{18}F-FDG) uptake was evaluated by autoradiography. All autoradiographic slices form each animal were digitalized and aligned to create an autoradiographic three-dimensional (3D) volume stack from each brain (PMOD software). Those 3D volumes were spatially normalized to a standard space in order to perform a voxel-based analysis using Statistical Parametric Mapping (SPM), resulting in statistical image that anatomically localize significant information. Finally, classical histological analysis was performed in another cohort of animals before and after phenobarbital administration.

No histological differences were present between AIP and wild type mice groups with respect to mass and number of neural cell or to neural fibers structures. No structural changes were observed in the brain after repeated acute attacks induced by phenobarbital. MRI analysis showed major depression of cerebral blood flow in female AIP mice when compared with wild type animals (0.65 ±0.23 AU vs 1.5 ± 1.2 AU respectively, p=0.01). The phenobarbital administration reduced brain perfusion in wild type animals (to 1.04 AU, p=0.02) but did not modify blood flow in AIP mice. By regions, the cortex from females AIP mice showed attenuated perfusion when compared to control wild type (0.73±0.2 AU vs1.7± 0.12 AU respectively, p=0.02). No blood flow differences were observed after phenobarbital administration.3D autoradiography following SPM analysis confirm low ^{18}F-FDG uptake in the brain of AIP mice when compared to wild type mice. Significant differences (p =0.01) were localized in primary somatosensorial cortex (Figure).

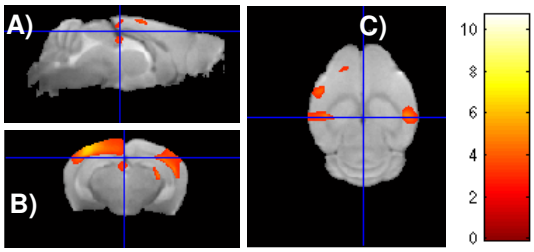

Figure: Statistical t map of SPM analysis showing hypometabolism in AIP mice primary somatosensorial cortex overlaid on a canonical MRI. A) Sagital B) coronal C) axial images.

In conclusion, primary somatosensorial cortex was identified as a region with attenuated perfusion and glucose hypometabolism in the brain of female AIP mice. Measurements of perfusion and/or glucose metabolism in the substructures of the brain cortex could provide a new tool for the future investigation of related central nervous system abnormalities observed in patients with AIP.